THE WORLD AFTER THE PANDEMIC

TÜRKİYE SCHOLARSHIPS BURSLARI

YTB

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SCIENCE & TECHNOLOGY

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YTB YAYINLARI

THE WORLD AFTER THE PANDEMIC
"SCIENCE & TECHNOLOGY"

YTB PUBLISHING: 12

ISBN 978-975-17-4879-9
ANKARA, JULY 2021

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DESIGN & LAYOUT
RIHTIM AJANS (www.rihtimajans.com.tr)

PRINTING & BINDING
MİM İÇ VE DIŞ MEKAN BASKI SİSTEMLERİ REKLAM MATBAACILIK LTD. ŞTİ.
Zübeyde Hanım Mah. Sebzebahçeleri Cad. 103/8 İskitler-Altındağ/ANKARA
(Sertifika no: 48752)

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Presentation

Abdullah EREN
President of YTB

Türkiye Scholarships, which is one of the most popular projects of our country in recent years and prone to producing long-term results, encourage scholarship students to produce academic works while they are still at university stage. These works, which are regarded as one of the success criteria of Türkiye Scholarships program, also contribute to the world academy.

Academic studies, which we accept as one of the main purposes of international student mobility and which are signed by our students, can inform us and our higher education firsthand about other countries or their perspectives on situations. Moreover, in an environment where many different views come together, it is possible to get closer to the right one.

In this context, Türkiye Scholarships rewarded and brought together valuable articles about "International Students's Work Competition", "The World After Pandemic" and "10th Year of YTB (Presidency for Turks Abroad and Related Communities)". It is flattering in itself to witness students' reasoning in the fields of social, science and health sciences, in matters which are significant both for us and for the whole world. Prepared to spread their ideas, this book will also be one of the points in their careers.

I would like to thank those who contributed to the preparation of this study, especially the Istanbul Academy of Sciences Foundation and the evaluation boards, which showed that education is not a unilateral issue and that we have much to learn from our students.

Takdim

Abdullah EREN
YTB Başkanı

Ülkemizin son yıllarda gözde ve uzun vadeli sonuçlar doğurmaya yatkın projelerinden biri olan Türkiye Bursları, bursiyerlerini henüz üniversite aşamasındayken akademik eserler üretmeye teşvik etmektedir. Türkiye Bursları programının başarı ölçütlerinden biri olarak görülen bu eserler, dünya akademisine de katkı sunmaktadır.

Uluslararası öğrenci hareketliliğinin temel amaçlarından kabul ettiğimiz ve öğrencilerimizin imzası bulunan akademik çalışmalar, bizleri ve yükseköğretimimizi, başka ülkeler veya onların olaylara bakış açıları hakkında ilk elden bilgilendirebilmektedirler. Dahası, pek çok farklı görüşün bir araya gelmesiyle oluşan bir ortamda, doğru olana daha fazla yaklaşabilmek de mümkün olmaktadır.

Bu çerçevede düzenlenen "Uluslararası Öğrenciler Eser Yarışması", "Pandemi Sonrası Dünya" ve "YTB'nin 10. Yılı" hakkındaki değerli makaleleri ödüllendirmiş ve bir araya getirmiştir. Hem bizler hem de tüm dünya için önem arz eden konularda, desteklediğimiz öğrencilerin sosyal, fen ve sağlık bilimleri alanında akıl yürütmelerine şahit olmak bile başlı başına gurur vericidir. Onların fikirlerini yaygınlaştırmak için hazırlanan bu kitap, kariyerlerindeki duraklardan da biri olacaktır.

Eğitimin tek taraflı bir mesele olmadığını, öğrencilerimizden de öğreneceğimiz çok şeyin olduğunu gösteren bu çalışmanın hazırlanmasında emeği geçenlere, özellikle makalelerin değerlendirilmesinde yardımcı olan İstanbul Bilimler Akademisi Vakfı'na ve değerlendirme kurullarına teşekkür ederim.

CONTENTS


Life Sciences and Medicine

The World After Pandemic:

A Comprehensive Overview on COVID-19 Pandemic

Ayomidé Joseph Zannou*

Abstract

The onset of 2020 has been marked by arguably the most significant event since the turn of the millennium which gave a rise to a new pandemic disease that shook the very core of the planet. The novel COVID-19 caused worldwide havoc dismantling every aspect of political, economic, and social order. After spreading from China seafood wholesale market, the pandemic has now expanded its reach to every country of the world, negatively affecting human health, social life, psychology, economy, education, tourism, and agriculture sectors. Millions of people across the world have been infected with the deadly virus

Özet

2020'nin başlangıcı, milenyumun başlangıcından bu yana, dünyayı sarsan yeni bir salgın hastalığa yol açan en önemli olaya sahne olmuştur. COVID-19, ekonomik ve sosyal düzeni her açıdan etkileyen dünya çapında bir tahribata neden olmuştur. Salgın, Çin'in Huanan deniz ürünleri toptan satış pazarından yayıldıktan sonra bütün ülkelere ulaşarak insan sağlığını, sosyal yaşamı, psikolojiyi, ekonomiyi, eğitimi, turizmi ve tarımı olumsuz yönde etkilemiştir. Pandemiden sonraki yaşam, insan yaşamının her açıdan ani bir biçimde önemli ölçüde değişmesi ile öne çıkmaktadır. Karantina önlemlerinin ve seyahat kı-

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many of which lost their lives in the process, and the figure has kept rising every single day. Life after the pandemic was significantly marked by abrupt changes in every aspect of human endeavor. Implementation of quarantine measures and travel restrictions have been aiming at slowing down the spread of the virus but the advent of COVID-19 has already given mankind an important life lesson. This article provides a comprehensive overview of the world after the pandemic. Various impacts of COVID-19 and future trends are briefly discussed, and possible strategies are proposed to sustainably manage such catastrophic events that pose a serious threat to human society.

Keywords: *COVID-19, Global Economy, Education, Food Security, Solutions*

sıtlamalarının uygulanması virüsün yayılmasını yavaşlatmayı amaçlıyor, ancak COVID-19'un ortaya çıkışı insanlığa çok önemli bir yaşam dersi vermiştir. Bu makale, pandemiden sonraki dünyaya kapsamlı bir genel bakış sağlamaktadır. Bu makalede, COVID-19'un çeşitli etkileri ve gelecekteki trendler kısaca tartışılmış ve toplum üzerinde ciddi tehdit oluşturan bu tür felaket olaylarını sürdürülebilir bir şekilde yönetmek için olası stratejiler önerilmiştir.

Anahtar Kelimeler: *COVID-19, Küresel Ekonomi, Eğitim, Gıda Güvenliği, Çözümler. Eğitim, Gıda Güvenliği çözümler*

*

I. Introduction

On 31 December 2019, when hours remained for the world to embrace the new year, 2020, World Health Organization (WHO) China country office has received some discomforting report from Chinese authorities. It was about a detected case of pneumonia-like disease of unknown origin. Little did the rest of the world know that an extremely aggressive pandemic was lurking around to launch its eventual conquering of the world. They virtually had no idea that an invisible powerful force was about to hit mankind like never happened before just at the dawn of a brand new year. Within a few days into 2020, cases began to emerge as two-digit numbers and continued to pile up afterward at unprecedented speed. The spread of the new disease outbreak was so fast that it was not even a couple of weeks into the new year when the first case outside China was detected in Thailand. Indeed, this was the beginning of arguably the most significant event since the turn of the millennium that literally shook the very core of the planet. It was at this moment that the mainstream media and individual dialogues began to shift their focal point towards the novel outbreak as it progressively caused a serious concern on public health. As part of an effort to build acquaintance with the new "mystery" disease, Chinese health authorities launched heavy surveillance, follow-up operations, and epidemiological investigations. Consequently, highly suggestive evidence began to emerge identifying its origin as the Wuhan seafood wholesale market which was closed on the first day of the new year.

A breakthrough on identifying the causal agent of the new disease outbreak was accomplished on 12 January 2020. Chinese scientists identified the agent as 2019-nCoV (latter named as COVID-19 by WHO), and released its genetic sequence to the world. It was evident that this virus was distinct from previously known adenovirus, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV), avian influenza, and other common respiratory viruses. Now having crucial information at their disposal, countries around the world scrambled to develop specific diagnostic PCR (Polymerase Chain Reaction) tests for the purpose of detecting the disease infection. Surprisingly, it was not until 11 March 2020 that the novel COVID-19 attained a global pandemic status that was well into more than two months since the first cases were reported. The declaration statement by WHO noted that a previous couple of weeks saw a dramatic increase in the number of cases outside China by 13-fold, and the number of countries with cases increased three-fold which stirred concern over the alarming rate of spread of the disease. Subsequently, countries across the globe were prompted to take seriously restrictive measures to contain the novel virus—a move that has never been seen before in recent memory. This article provides a comprehensive overview of the world after the pandemic.

II. The Spread

COVID-19 is a respiratory disease, and it is highly potent that any close contact with an infected person could easily mean contracting the virus. As of October 2nd, 2020, roughly nine months after the first cases were reported in China, the novel COVID-19 had already infected more than 34 million people all over the world[1]. Out of this figure, over one million people lost their lives while approximately 23 million people were lucky enough to survive and recover from the novel virus[2]. The pandemic has reached almost 215 countries and territories worldwide, and the number of cases was still rising at the period of writing this article. The USA, Brazil, and India alone made up over 50% of the total cases recorded globally since the first outbreak. These countries also recorded the highest death cases among other nations. Meanwhile in Turkey, the presence of COVID-19 was first detected on 11 March 2020, and within six months, approximately 311,000 cases were recorded in the country, and while almost 273,000 people were recovered, approximately 7500 people have lost their lives to the deadly virus[3]. Moreover, global daily new cases have peaked around 300,000 out of which approximately 5000 deaths were being recorded on a daily basis[4]. Despite the earlier hopes that the pandemic would slow down during the hot summer season, there has been a drastic increase in the worldwide spread of the virus even in places where the average daily temperature was higher than the average.

1 World Bank, "The Global Economic Outlook During the COVID-19 Pandemic: A Changed World."

2 World Bank.

3 World Bank.

4 World Bank.

III. Impact of COVID-19 on Social Life

Human beings are social animals, and mutual interactions among themselves have always been at the very core of their survival. When this mutual interaction is affected by an unexpected event or phenomenon, humans are called upon or forced to modify and change their social life. This change in social life is only in the interest of humans even if there are those against it. Since COVID-19 broke out in China and spread to Turkey and other countries, different measures have been taken by governments to contain the virus. Countries around the world have been enforcing strict quarantine measures to control the spread of this deadly virus through locking down their citizens and the closure of public places. People were obliged to keep social distancing between themselves and their peers for their own sake. Due to these measures, people were unable to enjoy normal human social activities such as the celebration of religious, cultural, marriage, and festive events. Moreover, the closure of public places meant people could not gather in movie theatres, cafes, restaurants, hotels, etc. These phenomena have literally dismantled the social order that humans used to maintain for a prolonged period. The restrictions created a kind of mistrust between the people and even within family members because when someone coughs, sneezes, or has a fever, they are automatically suspected to be contracting the virus. Social greetings between fellow humans, which were normally done either by kissing or handshaking, have just been kept to the minimum or only to verbal communications at a safe distance. For instance, in Turkey, where men have a very special way of greeting each other through gently colliding their heads, this act of fraternity has been abandoned to avoid human-to-human transmission of the coronavirus.

IV. Impact of COVID-19 on Human Psychology

The COVID-19 pandemic is an epidemiological and psychological crisis. Various measures taken to reduce the spread of the virus such as social distancing, lockdowns, and self-isolation may have some adverse effects on the mental health of the society. People were reportedly being affected with persistent anxiousness that emanated from uncontrolled worry or stressful fear about their health, and overwhelming thoughts of the uncertainty of things about to happen. Studies conducted on these issues indicated that the considerable number of people have been struggling with restlessness and irritability followed by difficulty concentrating, sleep problems, and generally feeling on edge[5-6-7]. In addition, an extensive study from China reported that approximately 35% of the people were psychologically affected by the pandemic[8]. In Turkey[9], observed and summarized the psychological impacts of COVID-19 as depression, health anxiety, financial worry, perceived social support, and loneliness. Moreover in Turkey, physical and mental fatigue–described as feeling tired quickly–feeling mentally and physically exhausted, experiencing lack of energy, inability to start and perform everyday activities,

5 Wang et al. 2020

6 Li et al. 2020

7 Xiao et al. 202

8 Qiu et al., "A Nationwide Survey of Psychological Distress among Chinese People in the COVID-19 Epidemic : Implications and Policy Recommendations."

9 Tull et al. (2020)

lack of desire to do things, difficulty thinking clearly, and to concentrating on a particular task were observed in 64% of the subjects[10]. The underlining impact of COVID-19 on human psychology has reportedly led some people to commit suicide[11]. These people were obviously overwhelmed by the distressful and uncomfortable thoughts or fear of the pandemic. These psychological issues were rather severe on people with pre-existing psychiatric disorders[12].

Additionally, frequent exposure to the news media about worldwide events related to the outbreak such as daily fatalities or infection rates of the pandemic followed by fear of COVID-19 increased depression, anxiety, and stress resulting in a decrease in life satisfaction (Fig 1).

V. Impact of COVID-19 on Tourism Sector

The tourism sector has been a major global industry with an estimated annual average growth rate of 4-5%. It also makes up 8% of the global GDP and 10% of employment[13]. However, it is also very vulnerable to crises of different origins such as natural disasters, epidemics, economic crises, political crises, and terrorism. One of the most notable strategic measures implemented by governments to reduce the number of cases due to COVID-19, and thereby contain the spread of the virus within a country or from one country to another is lockdown accompanied by the slogan "Stay-at-home to save lives". Consequently, museums and touristic sites were closed to discourage public gatherings. Hence, hotels, airlines, and restaurant businesses were emptied and handicapped by the worldwide travel restrictions imposed by governments to contain the

10 Morgul et al., "COVID-19 Pandemic and Psychological Fatigue in Turkey."

11 Thakur and Jain, "COVID 2019-Suicides: A Global Psychological Pandemic."

12 Thakur and Jain.

13 WTO, "International Tourism Highlights."

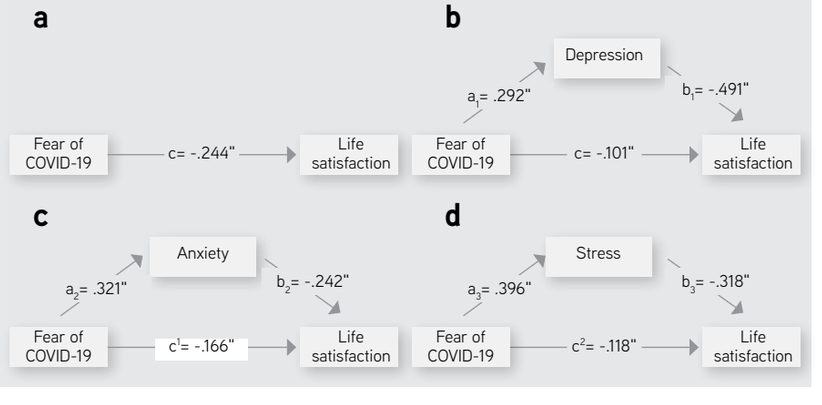

Figure 1. Mediated outcomes on life satisfaction (panels b, c, and d) showing indirect effects of fear of COVID-19 through psychological distress in Turkey**.

**Satici et al., "Adaptation of the Fear of COVID-19 Scale: Its Association with Psychological Distress and Life Satisfaction in Turkey."

pandemic. Thus, the global tourism industry was adversely hit and has been collapsing down like never before. World Travel and Tourism Council (WTTC) and the World Tourism Organization (WTO) reported that the virus was expected to decrease the revenue of the global tourism industry by 34-80% by the end of 2020. This loss is estimated to be at least $1.2 trillion[14].

Particularly in Turkey, following the cancellation of all commercial passenger flights to/from Turkey on March 28, 2020, human mobility was virtually halted which subsequently had a drastic effect on the tourism industry. Indeed, tourism is one of the most important sectors for the Turkish economy. The number of foreign visitors in Turkey in January and February 2020–i.e. before the COVID-19 outbreak was roughly similar to the same period in the previous year (Fig 2). However, after the first detection of COVID-19 followed by quarantine measures, foreign arrivals reduced by half in March compared to last year to subsequently plunge, and become virtually zero in April and May 2020. The months of June and July have also seen the disastrous consequences of COVID-19 on the tourism sector (Fig 2).

VI. Impact of COVID-19 on Education

The novel COVID-19 has also extended its devastating reach to the education sector. The desperate worldwide effort to curb the spread of the virus persuaded 193 countries to implement nationwide school closures which affected approximately 1.6 billion learners (Fig 3A)[15]. Due to this measure, people faced various social and economic issues such as student debt, food insecurity, homelessness, as well as access to health care, housing, internet, and disability services. Unprivileged children and their families were affected to a greater extent resulting in interruption of the learning process, compromised nutrition, childcare problems, and consequent economic cost to families who could not work.

14 UNCTAD, "Coronavirus Will Cost Global Tourism at Least $1.2 Trillion. Available in: Https://Unctad.Org/En/Pages/Newsdetails.Aspx?OriginalVersionID=2416."

15 UNESCO, "COVID-19 Educational Disruption and Response."

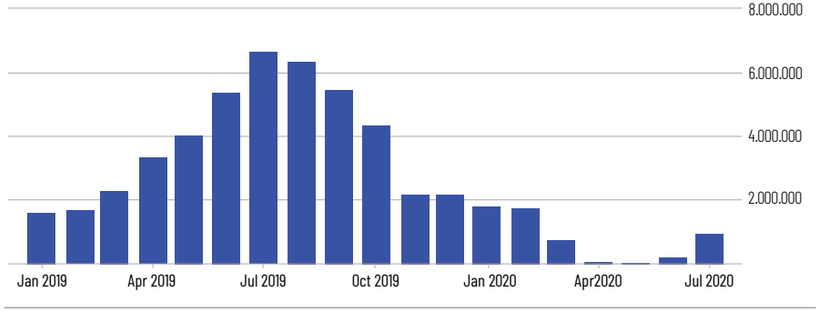

Figure 2. Impact of COVID-19 on tourist arrivals in Turkey***

*** "Https://Tradingeconomics.Com/Turkey/Tourist-Arrivals."

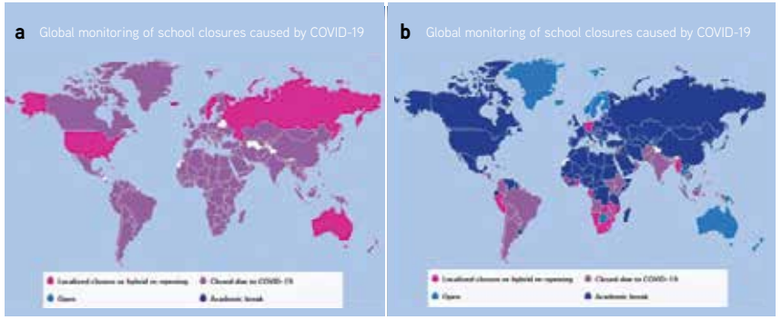

Figure 3. Impact of the COVID-19 pandemic on education as of (a) 31 March 2020 (b) 30 August 2020 ****

**** ps://En.Unesco.Org/Covid19/Educationresponse."

As a result of school closures, many schools sought alternative educational platforms for distance learning programs and open educational applications. Teachers and instructors prepared online content and offered online classes through the internet connection. However, this method of education delivery came with its own limitation that its success relied on the availability of infrastructure and familiarity with the tools. As of 30 August 2020, 705 million students had been affected, 34 countries were implementing nationwide closures impacting about 40.3% of the world's student population (Fig 3b).

In Turkey, school and higher educational institutions were effectively closed beginning from 16 March which directly affected 24 million active students[16];[17]. Based on assessment of other countries' experience, education has been resumed on 23 March via platform-EBA (Educational Informatics Network) and national television channel-TRT (Turkish Radio and Television Corporation) where the government collaborated with the leading GSM operators in Turkey to support the students' access to the EBA online portal right from their homes. In order to facilitate this, students were provided with an 8 GB of internet package free of charge which could be used to access internet service for attending online courses and other educational activities at the EBA portal[18].

VII. Impact of COVID-19 on Global Economy

The pandemic caused the largest global recession in history, and 2021 is projected to be the worst recessions on record since 1931 (Fig 4). Moreover, every region is subject to substantial growth downgrades[19]. East Asia and the Pacific will grow by a scant 0.5%. South Asia will contract by 2.7%, Sub-Saharan Africa by 2.8%, Middle East and North Africa by 4.2%, Europe and Central Asia by 4.7%, and Latin America by 7.2%[20]. These downturns are expected to reverse years of progress toward development goals and tip tens of millions of people back into extreme poverty. In June, the OECD cut its forecast

16 Özer 2020

17 UNESCO 2020

18 Özer, "Türkiye'de COVID-19 Salgını Sürecinde Milli Eğitim Bakanlığı Tarafından Atılan Politika Adımları."

19 Açikgöz and Günay, "The Early Impact of the COVID-19 Pandemic on the Global and Turkish Economy."

20 Fernandes, "Economic Effects of Coronavirus Outbreak (COVID-19) on the World Economy."

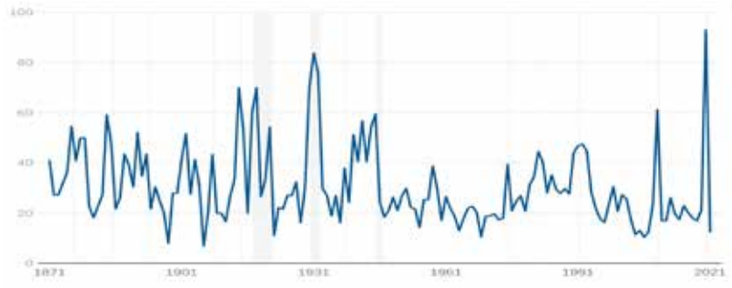

Figure 4. Share of economies in recession, 1871-2021*****

***** World Bank, "The Global Economic Outlook During the COVID-19 Pandemic: A Changed World."

for global economic growth in 2020 to -6.0%, unemployment climbs to 9.2% from 5.4% in 2019. They also projected a double hit scenario where the economic output will plummet to 7.6% before climbing back to 2.8% in 2021. The World Bank projected the global GDP growth to decline to -5.2% under which scenario 89-117 million people are pushed to extreme poverty in 2020. Finally, June's update of IMF showed a decline in global GDP growth to -4.9% implying a cumulative output loss of $12.4 trillion. Accordingly, global economic growth is projected to fall to 2.4% in 2020, compared to 2.9% in 2019, but it could fall as low as 1.5% due to the drop in overall global economic activities.

Turkish economy is expected a tourism boom and global demand shift in some sectors such as textiles, furniture, iron and steel, and food. Therefore, the expectation for Turkish economy growth to 2.7% from 0.9% to 2.7% in 2019-2020 was predicted[21]. However, these predictions will not come true at least in the short term since the COVID-19 pandemic has spread throughout the country, and now Turkey estimates the potential economic costs of this crisis. In March 2020, exports decreased by 17.81% and imports increased by 3.13 % compared with March 2019 due to the pandemic. Moreover, the Turkish current account deficit recorded $1,804 million indicating an increase of $1,528 million compared to January of the previous year. In addition, Turkey has around 50 million visitors and $34.5 billion of tourism income in 2019 but this sector was damaged by travel restrictions causing historical economic turmoil[22]. Additionally, uncertainty will bring more risks for investors[23], and it showed that the Turkish economy is under the pressure of financial risk[24].

VIII. Impact of COVID-19 on Agriculture

The agriculture sector has also been hit by the COVID-19 disruption although it was not as bad as other sectors. International efforts to control the virus by limiting human

21 Açikgöz and Günay, "The Early Impact of the COVID-19 Pandemic on the Global and Turkish Economy."

22 Dushime and Hashemipour, "The Psychological Effect of the COVID-19 Pandemic in Turkey and the World at the Context of Political Psychology."

23 World Government Bonds, "Turkey 5 Years CDS-Historical Data [Online]."

24 Açikgöz and Günay, "The Early Impact of the COVID-19 Pandemic on the Global and Turkish Economy."

movement is inevitably causing economic shocks and social costs that affect the functioning of agricultural and food systems worldwide. The COVID-2019 affects agriculture in two significant aspects: supply and demand for food which are related directly to labour and food security[25],[26].

The demand for food has decreased due to uncertainty and the reduction of people's spending capacity, although this decrease is still slight; the situation could worsen if the pandemic continues for a long time, due to reduced income and job losses[27]. Also, the announcements of social isolation and movement restrictions affect the food supply chain and disconnect the network between the agricultural system (the farm with the consumer's table) and processes such as manufacturing, packaging, distribution, and storage system (Fig 5). Moreover, food distribution channels of almost all countries across the income spectrum have been highly disrupted, with strong negative consequences for the most vulnerable[28]. stated five points that created widespread media coverage of sudden decreases in food security: (i) loss of income from workers who are fully or partially furloughed affecting their ability to purchase food; (ii) stay-at-home orders and restricted physical access to food markets and/or indigenous food gathering activities; (iii) closure or diminished capacity of institutions that support food social safety nets, such as food banks and school feeding programs; (iv) market disruptions; (v) wastage of fresh vegetables, fruits and milk due to the inability by farmers or entrepreneurs to transport them from point of production to local markets or supermarkets in nearby towns or cities.

25 (FAO 2020

26 Siche 2020)

27 FAO, "Food and Agriculture Organization. FAO Director-General Urges G20 to Ensure That Food Value Chains Are Not Disrupted during COVID-19 Pandemic. Available in: Http://Www.Fao.Org/News/Story/En/Item/1268254/Ico De/."

28 Stephens et al. 2020

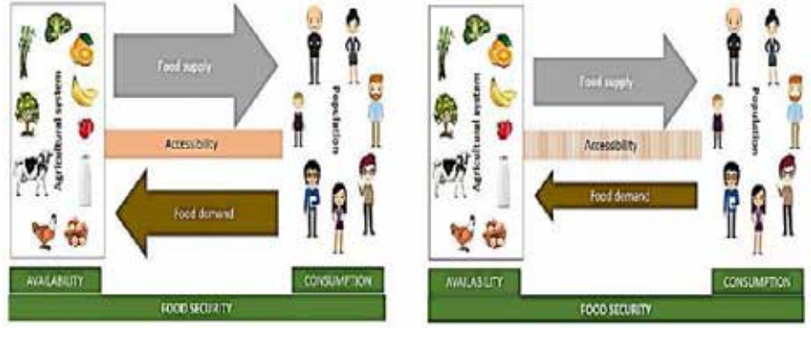

Figure 5. Food security system (A) without COVID-19 and (B) with COVID-19******

****** Siche, "What Is the Impact of COVID-19 Disease on Agriculture?"

Additionally, sectors like horticulture, livestock production systems, and processing but also for planting and harvesting of crops that are relatively labour-intensive have been particularly affected severely by lack of labour[29];[30]. Moreover, restrictions on movement may prevent farmers from accessing markets and result in food waste. In many countries, farmers are now unable to sell their produce in local markets or to local schools, restaurants, bars, hotels, and other leisure establishments, which have been temporarily closed[31].

As Turkey implements measures to combat COVID-19, the food and agricultural sector has faced challenges as well. Export restrictions from Black Sea regional trading partners, weekend lockdowns (including the closing of all grocery stores), and fluctuating produce prices have all been topics of discussion among government officials, the media, and the private sector. Due to the COVID-19, retail prices had increased for 77 products, while decreasing for 33 products and experiencing no change for the remaining 132 products[32].

IX. The Future

The future seems to be unpredictable. With the rising issue of environmental and global climate changes, epidemic diseases have been observed more frequently in recent years, especially as a result of the destruction of natural habitats and ecological areas. Putting aside the question of whether they were the results of human activity or natural disasters, human experience in the past has seen a string of epidemics that came to pass wiping out millions of lives in their wake. Not to mention those that occurred in the distant past–eg, the black death, plague of Justinian and Antonine plague–, roughly 100 million human lives were lost due to cholera and various types of flu pandemics only in the past 170 or so years.

Although the future holds dubiety in every front of human endeavour, one thing can be projected for certain: pandemic diseases will be at the core of the future agenda. The quote "the future lies from the past" has some merit for some reason. At this age of technology and human advancement on every front, why did we remain fragile when it comes to pandemic diseases? Did we really take lessons from our past? The present global scenario boldly says "NO". But if we don't, the concurrent COVID-19 experience, in particular, has forcibly been teaching us an appalling fact which we have not been able to tell for years that pandemic diseases may pose a serious threat to our very existence as a society. In a world of packed cities, growing population, constant travel, and an ever-warming planet, the danger and consequences of a massive disease outbreak could be more perilous than ever.

29 Stephens et al. 2020

30 International Labour Organizarion 2020

31 International Labour Organizarion.

32 he, "What Is the Impact of COVID-19 Disease on Agriculture?"

The fight against the latest pandemic, COVID-19, has already begun with the prevention, avoidance, and containment measures but as part of finding a long-term and sustainable solution, the race for the development of an effective vaccine has been going on since the advent of the deadly outbreak. Various pre-clinical, phase-I, phase-II, phase-III and combined phase trials have been conducted by a number of private and government companies around the globe of which some promising results were found to give a glimpse of hope to humanity to win the desperate battle against the COVID-19 pandemic. Nevertheless, should vaccines be taken for granted in the future? Even with the first effective mass-released vaccines are insight and let us say, for the sake of argument, that we managed to control the COVID-19 outbreak globally, but how can we cope with yet another unforeseen deadly pandemic of unknown origin in the future? Are we really ready for similar catastrophic events that pose a serious threat to public health? These underlining questions may remain unanswered until we come up with some long-lasting approaches that will sustainably address these issues.

X. The Solution

Humans have been hit by various deadly disease outbreaks throughout history only to lose millions of lives in the process. Are these worrisome events a natural selection process periodically happening to check the human population? or man is simply paying the price for his own treatment of mother nature? So, what exactly is going wrong? Our ever-existing intimate relationship with mother nature might help us get a clue in this regard. Human connection with microbes has always been strong throughout the ages. Paying attention to the patterns of concurrent and past epidemics, it could be asserted that human activities such as the devastation of nature could trigger aberrations in the natural balance of the ecosystem and biodiversity. It is evident that the impact of humanity on nature and the food chain, especially in the past few hundred years, has negatively affected sustainable life. Hence, understanding the impact and extent of human activities on the surrounding natural world, and their direct relationship with disease outbreaks is a vital step in our quest to manage pandemics on a sustainable basis.

With the pandemic looming around every corner, health experts are strongly emphasizing that a healthy, regular, and balanced diet is an effective and very important mechanism in dealing with the virus and many other health disorders[33]. In order to strengthen the immune system of human beings and to protect themselves against harmful microbes and other diseases associated with lack of adequate nutrition, they must consume the minimum diet requirement and have enough income to provide these micronutrients[34]. Food security does not only assume that enough food is available, but also the quality, and the nutrient contents of the foods (protein, carbohydrates, vitamins, certain minerals, and antioxidants) are also important components that need to be assured[35];[36]. Moreover, the deficiency of nutrients due to the poor diet could lead to

33 Jayawardena et al., "Enhancing Immunity in Viral Infections, with Special Emphasis on COVID-19: A Review."

34 Jayawardena et al.

35 Wintergerst et al. 2007

36 FAO et al. 2020

what is known as 'hidden hunger' leading to the most serious health and related social problems[37]. For the purpose of prevention of widespread micronutrient deficiencies, enhancing the level and content of essential nutrients of edible crops within the context of bio-fortification strategy is a possible option that could be attained through classical plant breeding (genetic) or fertilization (agronomic) applications[38].

From a holistic point of view, the Ministry of Health, Ministry of Agriculture, and scientific institutions are expected to collaborate in order to ensure food security and quality. Taking the following measures for more sustainable living is important for any underdeveloped (Turkey in particular) and developing country's future food security:

- Sustainable planning of production and manufacturing should be made in line with the population and consumption data of the country. Public production patterns should be created and support purchases should be made.

- Agriculture depends on utilizing natural resources, and the way it is done relies on the ecological conditions of nature. Therefore, agricultural production should be managed based on maintaining the ecological balance of nature.

- Biodiversity should be protected, especially endemic plant and animal species.

- Investments should be made in seed breeding and technologies, and local seeds should be reproduced and protected in a sustainable manner. A local gene bank should also be established in order to preserve and conserve endangered species.

- The energy required for agriculture should be provided with renewable energy sources and investments should be made from natural resources to energy production technologies in order to avoid foreign dependency.

- As public health depends directly on agriculture and food security, the Agriculture and Health problem should be organized and supported by the public.

Acknowledgments

The author would like to express his gratitude to Dr. Mohammed Ahmed for his constructive suggestions and technical support in reviewing this article.

37 Ritchie and Roser, "Micronutrient Deficiency. Published Online at OurWorldInData.Org. Retrieved from Https://Ourworldindata.Org/Micronutrient-Deficiency."

38 Cominelli, Pilu, and Sparvoli, "Phytic Acid and Mineral Biofortification Strategies: From Plant Science to Breeding and Biotechnological Approaches."

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Impact of COVID-19 on Human Bacterial Flora: Possibility of Flora Dysbiosis

Nahdhoit Ahamada Rachid*

Abstract

The new coronavirus disease caused by SARS-Cov-2 firstly observed in China has become a pandemic since January 2020. It caused approximately 917.417 deaths in the world by 13 September 2020. Confinement, quarantine, social distancing, wearing masks, regular hand washing, and disinfection are the measures taking against the COVID-19 infection. In addition to that, antibiotics, antivirals, and other chemicals are administered to the infected individuals while studies and works are still proceeding to find a vaccine against this virus. However, taken preventive as well as treatment measures are thought to

Özet

İlk olarak Çin'de görülen SARS-Cov-2'nin neden olduğu yeni koronavirüs hastalığı, Ocak 2020'den itibaren bir pandemi haline geldi. 13 Eylül 2020'ye kadar dünyada yaklaşık 917417 ölüme neden olmuştur. Karantina, maske takmak, sosyal mesafeyi korumak, sürekli elleri yıkamak ve dezenfekte etmek, COVID-19 enfeksiyonuna karşı alınan önlemlerdendir. Ayrıca, bu virüse karşı bir aşı bulmak için çalışmalar devam ederken, enfekte olan kişilere antibiyotikler, antiviraller ve diğer kimyasallar uygulanmaktadır. Bununla birlikte, önleyici yöntemlerin ve tedavilerin, insanlarda ikincil bakteri ve mantar enfeksiyonu-

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cause microbial dysbiosis in human that can cause secondary bacterial and fungal infection as well as other immune problems. This review stands to analyze the possibility of bacterial dysbiosis in humans during/ after the COVID-19 period. This can contribute also, to improve the preventive measures, treatments of infected cases, and lifestyle adoption after the COVID-19 infection period.

Keywords: *COVID-19, Microbial Dysbiosis, Bacterial Flora, Infection*

nun yanı sıra diğer bağışıklık sorunlarına neden olabilecek mikrobiyal disbiyoza neden olduğu düşünülmektedir. Bu yazı, COVID-19 dönemi sırasında / sonrasında insanda bakteriyel disbiyoz olasılığını analiz etmeyi amaçlamaktadır. Bu yayın önleyici tedbirlerin ve enfekte kişilere uygulanan tedavi şekillerinin geliştirilmesi, ayrıca COVID-19 salgın sürecinden sonra yeni yaşam tarzının benimsenmesine katkıda bulunabilir.

Anahtar kelimeler: *COVID-19, Mikrobiyal Disbiyoza, Bakteri Florası, Infeksiyon*

*

I. Introduction

In December 2019, China has announced the first cases of epidemic CORONAVIRUS DISEASE 2019 (COVID-19) in their territory.[1] This epidemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which is a member of the virus family called Coronavirus, was spread to the rest of the globe and declared one month later by the World Health Organization (WHO) as a pandemic.[2],[3] On 13 September 2020, the WHO reported a total of 28 637 952 cumulative cases, 917 417 cumulative deaths with the most infected cases (51%) and death (55%) has been registered in the American continent.[4] In this same report, data show that the United States of American registered the most infected cases (6 386 832) and deaths (191 809) in the world.[5]

1 Chaolin Huang et al., "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China." The Lancet 395, no. 10223, 2020. pp. 497-506.

2 Ibid. pp. 497.

3 Hanieh-Sadat Ejtahed et al., "The most important challenges ahead of microbiome pattern in the post era of the COVID-19 pandemic". Journal of Diabetes & Metabolic Disorders, 2020. pp. 1-3.

4 "Coronavirus disease (COVID-19) Weekly Epidemiological Update," World Health Organization. Last modification September 14, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200914-weekly-epi-update-5.pdf?sfvrsn=cf929d04_2/

5 Ibid.

The genotypic study of the virus revealed a similarity of 96.2% with the SARS-like bat coronavirus.[6] Other study shows a similarity of 99% between the strain of SARS-CoV-2 which infect human and that isolated from pangolins.[7] Unfortunately, the main host of the COVID-19 is still unknown. It is reported that this novel strain of coronavirus has an affinity to infect humans than the previous strains such as MERS and SARS-CoV. That is can be due to the strain structure which shows a higher affinity to bind to the angiotensin-converting enzyme 2 (ACE2) used as receptors.[8]

Even if it causes pneumonia, a good number of the human body have been detected to be infected by this novel virus. The PCR test of samples taken from the faecal materials of patients, eyes and, brains of patients have shown positive results with the COVID-19 test kits.[9] The transmission of this novel coronavirus strain has been thought to be by close contact (human to human or human with other mammals), aerosol droplets through the nose, eyes, and mouth.[10],[11],[12], The incubation period is also estimated to be longer than the precedently known coronavirus strains such as SARS-CoV and MERS-CoV.[13] The affinity of this virus to infect the body and the longest incubation period (most of the cases remain asymptomatic during this period) could be the causes of the faster spreading of the disease.

Symptoms of this new pandemic can differ from a patient to another. Some COVID-19 patients do not develop severe or critical disease and only coronavirus-like infection symptoms appear.[14] They consist of high temperature (mild fever), headache, dry cough, and fatigue; diarrhoea, nasal congestion, vomiting, and nausea are rare.[15],[16],[17] Patients with these symptoms can rapidly develop severe or critical diseases with

6 Peng Zhou et al., "A pneumonia outbreak associated with a new coronavirus of probable bat origin." Nature 579, no. 7798, 2020. pp. 270-273.

7 Lisheng Wang et al., "Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence." International Society of Chemotherapy 55, no. 6, 2020. 105948.

8 Ibid.

9 Ibid.

10 Hanieh-Sadat Ejtahed et al., The most important challenges ahead of microbiome pattern in the post era of the COVID-19 pandemic, pp. 1-3.

11 Lisheng Wang et al., "Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence," 105948.

12 Catrin Sohrabi et al., "World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19)." International Journal of Surgery 76, 2020. pp. 71-76.

13 Sayed Adeel Hassan et al., "Coronavirus (COVID-19): A Review of Clinical Features, Diagnosis, and Treatment." Cureus 12, no. 3, 2020.

14 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19." Gut, 2020.

15 Hanieh-Sadat Ejtahed et al., "The most important challenges ahead of microbiome pattern in the post era of the COVID-19 pandemic" pp. 1-3.

16 Lisheng Wang et al., "Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence"105948.

17 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19."

clinical presentations like dyspnoea, acute respiratory distress syndrome (ARDS), and secondary infections such as gastrointestinal tract (GIT) infection and heart injury.[18],[19]

For the prevention, until now different vaccines are yet to be achieved. Currently, prevention is done by measures like the use of disinfectants and antiseptic products such as detergents, hydro alcoholic gels to wash hands and household items frequently to limit the rapid transmission of the virus. In addition, wearing masks has become imperatively necessary, whereby some countries Turkey making it compulsory. Other measures such as confinement and quarantine adopted in the majority of countries have shown a great effect on the reduction of infected cases. For the treatment of infected cases, any specific treatment has not been defined. Antibiotics, vitamins, probiotics, antivirals, and convalescent plasma are administered to the patients depending on the level of their infection.[20],[21],[22]A mix of antiviral, antibiotics, and antimalaria like the Hydroxychloroquine and azithromycin used in France,[23] Hydroxychloroquine sulfate (Plaquenil/generic) used in Turkey[24] have shown good effects for the recovery of the majority of cases.

Human microbiota refers to the microbial community including bacteria, fungi, viruses, and protozoa in the human body.[25] The human normal bacterial flora (HNBF) are those living in the human body with a commensal relationship with the host. HNBF participates in the immune modulation of the host. However, Multiple factors like age, lifestyle, environment, and mode of nutrition cause the dysbiosis of this bacterial community in the host body.[26],[27] Studies show a reduced number of the human microbiota in infant and older subjects while a fort augmentation of this number and diversity in the adult persons.[28] In addition, fort dose of antibiotics could reduce the amount of the HNBF.[29]

18 Lisheng Wang et al., "Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence,"105948.

19 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19."

20 Suxin Wan et al., "Clinical features and treatment of COVID-19 patients in northeast Chongqing." Journal of Medical Virology 92, 2020. pp. 797-806.

21 Matthieu Million et al., "Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France." Travel Medicine and Infectious Disease 35, 2020.

22 Hülya Sungurtekin et al., "Prognosis of COVID-19 Patients Requiring Intensive Care Unit Care." Signa Vitae 16, no. 1, 2020. pp. 147-151.

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25 Saroj Khatiwada, and Astha Subedi, "Lung microbiome and coronavirus disease 2019 (COVID-19): Possible link and implications" Human Microbiome Journal 17 (2020): 100073. Doi: 10.1016/j.humic.2020.100073.

26 Jack A Gilbert et al., "Current understanding of the human microbiome." Nature medicine 24, no. 4, 2018. pp. 392-400.

27 D Mariat et al., "The Firmicutes/Bacteroidetes ratio of the human microbiota changes with age." BMC Microbiology 9, no. 1, 2009. pp. 123.

28 Ibid.

29 Jack A Gilbert et al., "Current understanding of the human microbiome," pp. 392-400.

Detergents and sanitizers contain some products which are thought to be absorbed from the skin and lead to elimination of internal as well as external HNBF.[30]

Preventive and treatment measures like regularly hand disinfection, using antibiotics during this new pandemic can disturb the human and environmental microbiota. Our analyses of the impacts of the pandemic on human health will therefore focus on the human bacterial flora. In this study, the human bacterial commensal and its important role will be discussed and analysed in detail. Finally, the susceptible impacts of the new pandemic towards the human commensal bacterial biodiversity will be elaborated.

II. Bacterial Flora Related to Human Health

Microbial cells which colonize the human body are estimated to be more than the human somatic cells. Until now, the exact number of the total microbial cells in our body has not yet been defined. However, the number and diversity of bacterial flora are estimated to be more than the other microbial flora including viruses and fungi.

The HNBF is necessary for primary corporal functions like human nutrition and immunology. Bacterial species like Streptococcus cristatus inhibit the formation of biofilm in the human mouth forming by p. gingivalis which is a periodontal pathogen.[31] In other human environment like the genitourinary tract especially in the vagina, the lactobacillus genus which was earlier named Döderlein's bacilli was isolated and found to have the ability to inhibit the growth of pathogens.[32] Among the healthy microbiota in humans, we can enumerate the gram-negative non-spore-forming bacterium Bacteriodes fragilis. This bacterium which predominates in the human colon has the capability to synthesise different polysaccharides.[33] One of these synthesized polysaccharides is the most predominantly expressed sugar, the polysaccharide A (PSA), which has an important immunomodulatory capacity since it has the ability to induce the secretion of anti-inflammatory interleukin (IL)-10 acting against inflammatory disease and viral encephalitis.[34]

Gastro-intestinal tract (GI) bacterial flora

The human GI tract constitutes one of the complex and dynamic ecosystems of the human body. It is an interface between host cells, environmental factors like food particles

30 Chandanapalli Sai Himabindu et al., "Hand sanitizers: is over usage harmful?" World Journal of Current Medical and Pharmaceutical Research, 2020. pp. 296-300.

31 Angela H. Nobbs et al., MICROBIOTA OF THE MOUTH: A BLESSING OR A CURSE?", in The human microbiota: how microbial communities affect health and disease, ed. David N. Fredricks 2013, pp. 135-165.

32 Laura K. Sycuro and David N. Fredricks, "MICROBIOTA OF THE GENITOURINARY TRACT.", in The human microbiota: how microbial communities affect health and disease, ed. David N. Fredricks (New Jersey, Wiley-Blackwell, 2013), New Jersey, Wiley-Blackwell, pp. 167- 211.

33 Chen Wang et al., "Roles of intestinal bacteroides in human health and diseases." Critical Reviews in Food Science and Nutrition, 2020. pp. 1-19.

34 Ibid. Pp. 1-9.

and, a variety of resident microorganisms and their secreted products.[35],[36] The composition of the GI tract microbial community has been previously studied by culture-dependent methods which unfortunately was not able to detect the whole genome of the proper GI tract microbiota.[37],[38] With culture-independent methods, approximatively 1000 bacterial species has been estimated and it is revealed that the bacterial cells which inhabit this human part can be estimated to exceed 1014 bacterial cells which are approximately 10 times more than the host cells.[39],[40]

In general, the human body started to be colonized by microorganisms from birth; since during the baby deliverance, the vaginal bacteria contaminate the baby.[41],[42] After that, breastfeeding, illness, and treatments develop the number and diversity of human microbiota.[43],[44] The results of culture-independent studies show that the most dominant human GI tract bacterial group consists of Clostridium rRNA subcluster XIVa and Clostridium rRNA subcluster IV groups which are belonging the Firmicutes division, and the Cytophaga-Flavobacterium-Bacteroides (CFB) group.[45],[46] Members of Clostridium, Eubacterium, Anaerqfilum genera are detected in this human body internal part.[47] Indeed, the number and diversity of the bacterial community of this environment depend on several factors like the food, the environment where the host is and the age.[48], [49],[50] Thursby and Juge (2017) reported that members of Bacteroidetes and Clostridium cluster IV are abundant in individuals over 65 years, while in the younger ones the Clostridium cluster XIV remain the most observed group.[51]

As a part of the human GI tract ecosystem, the bacterial flora of this environment has an impact on the host's health. They are effective in the protection of the host against

35 Janet M. Manson et al., "The Commensal Microbiology of the Gastrointestinal Tract", in GI Microbiota and Regulation of the Immune System, ed. Gary B. Huffnagle and Mairi C. Noverr (New York, Ny Springer New York, 2008), pp. 15-28.

36 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota." Biochemical Journal 474, no. 11 (2017): pp. 1823-1836.

37 Janet M. Manson et al., "The Commensal Microbiology of the Gastrointestinal Tract," pp. 15-28.

38 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

39 Janet M. Manson et al.," pp. 15-28.

40 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

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42 Jeremy E Koenig et al., "Succession of microbial consortia in the developing infant gut microbiome." PNAS 108, (2011): pp. 4578-4585.

43 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

44 Jeremy E Koenig et al., "Succession of microbial consortia in the developing infant gut microbiome," pp. 4578-4585.

45 Janet M. Manson et al., "The Commensal Microbiology of the Gastrointestinal Tract," pp. 15-28.

46 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

47 Janet M. Manson et al., "The Commensal Microbiology of the Gastrointestinal Tract" pp. 15-28.

48 Ibid.

49 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

50 Jeremy E Koenig et al., "Succession of microbial consortia in the developing infant gut microbiome," pp. 4578-4585.

51 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp.1823-1836.

pathogens and providing nutrients to the host cells.[52] In the human GI tract, the colonic bacteria have the ability to express enzymes that are necessary for the fermentation of complex carbohydrates for generating essential metabolites like Short Chain Fatty Acids (SCFAs).[53] In this human tract, bacteria belonging to Firmicutes, Bacteroidetes, and Actinobacteria are the most producers of the predominant SCFAs such as propionate, butyrate, and acetate.[54],[55] For example, Roseburia intestinalis, Eubacterium rectal are known to produce butyrate which contributes significantly to intestinal health as this metabolite is the preferred source of energy for the colon cells.[56] In addition, this SCFA has a protective role against colorectal cancer.[57] In the case of propionate produced by bacteria like Phascolarctobacterium succinatutens, Veillonella spp. and, Megasphaera elsdenii it is known to contribute to gluconeogenesis in the liver and reduction in cholesterol.[58]

In addition, the GI microbiota has a crucial role in the synthesis of essential vitamins which can not be produced by the host (human or animal). Lactic acid bacteria, Bifidobacteria, and other colonic bacteria are considered as key organisms in the synthesis of vitamins like vitamin B12, folate, vitamin K, riboflavin nicotinic acid.[59],[60] Alteration of some vitamins like niacin are associated with the development of diseases like type 2 diabetes and obesity.[61],[62] On the other hand, the oral administration of probiotics (live microbial food ingredients that have beneficial effects on human health[63]) has a great effect on the protection of the host against infections and induces a minimization of Salmonella enterica contamination risk.[64]

Bacterial flora in the respiratory tract (RT)

The human respiratory tract is subdivided into the upper and lower respiratory tract. The upper respiratory tract (URT) is extending from the nasal cavity to the esophagus, while the lower respiratory tract (LRT) is composed of tracheae, primary bronchitis,

52 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp.1823-1836.

53 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

54 Janet M. Manson et al., "The Commensal Microbiology of the Gastrointestinal Tract," pp. 15-28.

55 Elizabeth Thursby and Nathalie Juge, "Introduction to the human gut microbiota," pp. 1823-1836.

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58 Petra Louis and Harry J. Flint, "Formation of propionate and butyrate by the human colonic microbiota," pp. 29-41.

59 Janet M. Manson et al., "The Commensal Microbiology of the Gastrointestinal Tract pp. 15-28.

60 Jeremy E Koenig et al., "Succession of microbial consortia in the developing infant gut microbiome," pp. 4578-4585.

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63 S. Salminen et al., "Probiotics: how should they be defined?" Trends in Food Science & Technology 10, no.3 (1999): pp. 107-110.

64 Aravind Sundardaraman et al., "Role of probiotics to combat viral infections with emphasis on COVID-19." Applied Microbiology and Biotechnology 104, no. 19, 2020. pp. 8089-8104.

and lungs. With the culture methods for bacterial identification, the lung of a healthy human was thought to be sterile.[65] Recently with the new molecular methods such as New Generation Sequencing (NGS), normal bacterial flora is detected in this part of the human body.[66] A quantitative study of the microbial community in healthy humans results in a lower number of bacteria in the LRT comparing to the URT.[67] In addition, comparing to the gastrointestinal tract, the lungs hold less bacterial biomass.[68] Studies run in healthy adult humans show the presence of mainly anaerobic bacteria such as the genus Prevotella in the LRT.[69,70] Charlson et al., show that the bacteria belonging to phyla Bacteroides, Prevotella, Firmicutes, proteobacteria, and genera Veillnella, Fusobacterium, Streptococcus, Pseudomonas are more frequently found, while genera like Haemophilus are less common in the LRT.[71] In other studies, increasing the bacterial load has been observed over the first two weeks of life and lung bacterial community shift has been demonstrated: Gamma-proteobacteria and Firmicutes are shifted towards Bacteroidetes.[72] For maintaining respiratory tract immunity, probiotics such as Lb. plantarum GG has been found to colonize this organ even they are mainly colonizing in the gut.[73]

As it is more evident that the presence of some human bacterial flora reinforces the human immune system, microbial dysbiosis (alteration of the quantity or quality of the microbiome) also contributes to the development of chronic inflammatory lung disease like asthma. Studies of the respiratory tract microbiota stand to understand the role of the healthy bacterial flora of this tract in the immune system. However, the direct role of this flora is not determined but an increase and decrease of the bacterial group in unhealthy and healthy individuals have been observed. It is reported that in asthma patients, an increase of Proteobacteria phylum is observed while a decrease of the genus Prevotella is noted.[74,75] A cross-relation has been observed between the LRT and the

65 Kazuhiro Yetera et al., "The microbiome in the lower respiratory tract." Respiratory Investigation 56, no. 6, 2018. pp. 432-439.

66 Kazuhiro Yetera et al., "The microbiome in the lower respiratory tract," pp. 432-439.

67 Emily S. Charlson et al., "Topographical Continuity of Bacterial Populations in the Healthy Human Respiratory Tract." American Journal of Respiratory and Critical Care Medicine 184, no. 2, 2011. pp. 958-963.

68 Aravind Sundararaman et al., "Role of probiotics to combat viral infections with emphasis on COVID-19," pp. 8089-8104

69 Kazuhiro Yetera et al., "The microbiome in the lower respiratory tract," pp. 432-439.

70 Markus Hilty et al., "Disordered Microbial Communities in Asthmatic Airways." PLoS ONE 5, no. 1, 2010. pp. 1-9.

71 Emily S. Charlson et al., "Topographical Continuity of Bacterial Populations in the Healthy Human Respiratory Tract," pp. 958-963.

72 Aravind Sundararaman et al., "Role of probiotics to combat viral infections with emphasis on COVID-19." pp. 8089-8104.

73 Laura Tapiovaara et al., "Probiotics and the Upper Respiratory Tract - A Review." Pediatric Infectious Diseases 1, no.3, 2016. pp. 9

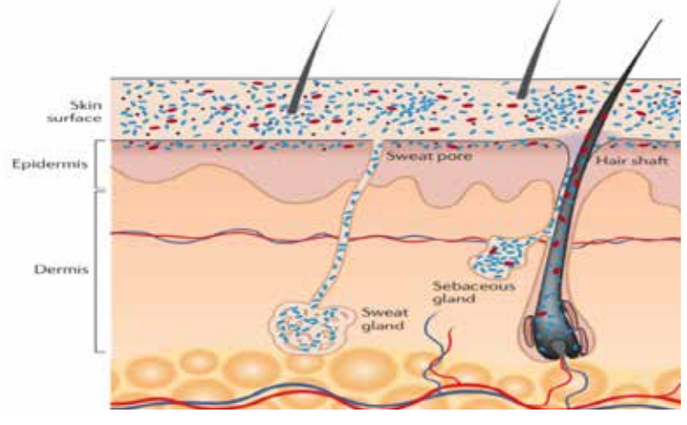
74 Markus Hilty et al., "Disordered Microbial Communities in Asthmatic Airways," pp. 1-9.

75 Robert P. Dckson et al., "The Microbiome and the Respiratory Tract." Annual Review of Physiology 78, no. 1, 2016. pp. 481-504.

GI tract microbiota.[76,77] GI tract microbiome dysbiosis is usually associated with lung disease. Since treatment of animals targeting the modification of the GI tract microbiome show a significant alteration of the host's CD4 T cells expressed in response to the allergic airway problems.[78]

Skin commensal bacteria

The structure of healthy skin promotes an integral barrier of pathogen microorganisms or toxic substances. The skin in general is composed of the skin surface, epidermis and, dermis. Inside this skin structure, we can observe the sweat and sebaceous glands and the skin appendages (figure1). Grice and Segre (2011) defined the skin as the largest organ in the body and estimated a total surface of 1.8 m2 of diverse habitats with a specialized niche of different microorganisms.[79] A total of skin bacterial flora has not been defined yet because of this diversity of niches and the differences observed between individuals.[80,81] However at least 19 bacterial phyla are reported in the commensal bacterial skin flora.[82] Contrary to the GI tract, Actinobacteria is the most dominant phylum in the skin bacteria.[83] It is followed by Firmicutes, Proteobacteria, and Bacteroidetes consecutively.[84] At the genus level, Corynebacterium, Propionibacterium and, Staphylococcus are the most identified.[85, 86]



76 Robert P. Dckson et al., "The Microbiome and the Respiratory Tract," pp. 481-504.

77 Aravind Sundararaman et al., "Role of probiotics to combat viral infections with emphasis on COVID-19," pp. 8089-8104.

78 Robert P. Dckson et al., "The Microbiome and the Respiratory Tract," pp. 481-504.

79 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome," Nature 9, no. 4, 2011. pp. 244-253.

80 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

81 Angela H. Nobbs et al., "Microbiota of the mouth: a blessing or a curse?" pp. 135-165.

82 Ibid.

83 Ibid.

84 Ibid.

85 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

86 Angela H. Nobbs et al., "microbiota of the mouth: a blessing or a curse?" pp. 135-165.

Figure1[87]: Histology of the human skin showing the repartition of the skin microbiota. The concentration of bacterial flora on the skin surface illustrates the protective barrier constituted by the epidermis.

It is the skin surface where the skin microbiome dominates. Also, the microorganisms which inhabit the skin, whatever are transients or residents, differ from a sampling site to another. These differences explain the effects of the surrounding environmental factors on the exposed skin area. Furthermore, the physical and chemical structures of the skin niche of the body have a significant effect on bacterial colonization. For example, Propionibacterium sp dominates the sebaceous sites on the face, back, etc...[88],[89] This is due to the secretion of sebum from the sebaceous glands, which is a lipid-rich substance.[90] The study of P. acnes' genome revealed multiple genes encoding lipases.[91] Thus, this species hydrolyses the skin lipids of the sebum and use the released free fatty acids as a nutrient.[92] These fatty acids also contribute to the maintaining of acidic pH in these microenvironments; thus growth of pathogens like Staphylococcus aureus and streptococcus pyrogenes is inhibited.[93] In the moist regions of the skin such as the gluteal crease, toe webspace, nare and umbilicus, the Corynebacterium species are predominating.[94],[95] On the other hand, the dry microenvironments like the volar forearm, buttock, and hypothenar palm, are predominated by Proteobacteria (especially Alpha group) followed by Bacteroidetes.[96],[97]

The relation between skin bacterial flora and the human host can be beneficial for humans also. Certainly, the role of most of these commensal bacteria remains unknown in the human body but some of them have recently shown a positive relation with the human immunity system. A study on coagulase-negative Staphylococcus isolated from the skin of healthy and atopic dermatitis patients revealed that these organisms are able to produce antibacterial products against the skin pathogen Staphylococcus aureus.[98] Phenol-soluble modulins secreted by Staphylococcus epidermidis can inhibit not only S.aureus but also the Group A Streptococcus. The S.epidermidis co-operate with the

87 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome" pp. 245.

88 Ibid. pp. 244-252

89 Angela H. Nobbs et al., "microbiota of the mouth: a blessing or a curse?", in The human microbiota: how microbial communities affect health and disease, ed. David N. Fredricks (New Jersey, Wiley-Blackwell, 2013), pp. 135-165.

90 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome" pp. 244-253.

91 Ibid.

92 Ibid.

93 Ibid.

94 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome" pp. 244-253.

95 Angela H. Nobbs et al., "Microbiota of the mouth: a blessing or a curse?" pp. 135-165.

96 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

97 Angela H. Nobbs et al., "MICROBIOTA OF THE MOUTH: A BLESSING OR A CURSE?" pp. 135-165.

98 Teruaki Nakatsuji et al., "Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus and are deficient in atopic dermatitis." Science Translational Medicine 9, no. 378, 2017. pp. 1-11.

host AMP (antimicrobial peptides) to enhance the killing of the pathogens.[99],[100] In addition, S.epidermidis has an anti-inflammatory function. It secretes the lipoteichoic acid which induces the inhibition of skin inflammation by activation of TLR2- and TLR3- host cells.[101],[102]

III. Susceptible Human Bacterial Dysbiosis During/ After COVID-19 Pandemic

The novel pandemic virus can express its pathogenicity in hosts' organ microbiota, by dysbiosis of the microbiota or/and possible mutations of its genes.[103] These changes in human microbiota can result from the virulence of the virus as well as the measures taken for the virus treatments and preventions.

The treatment which receives the COVID-19 patients consists of a combination of at least two effective products such as large spectrum antibiotics like vancomycin, cefazolin; and Calcium enhancers.[104] These massive uses of bactericidal products affect the body organs metabolisms since a decrease in the bacterial community of organs is observed that is related to an increase of endotoxins like lipopolysaccharides, inside the different organs.[105] The study standing in Hubei Province, China, demonstrates the consequence of early antibiotic uses for non-severe cases of COVID-19.[106] 20.42% of early antibiotics administered patients have developed secondary bacterial infection opposite to 12.22% of late to non-antibiotics administered patients.[107] This result confirms the dysbiosis of human microbiota during and after the COVID-19 infection. It is also reported that overusing antibiotics causes antibiotic-associated diarrhea (AAD) which can cause Clostridium difficile associated diarrhea (CDAD) in hospitalized patients.[108]

Effects on lung bacterial flora

Huang et al., (2020) have found that 100% of studied patients in their study have developed pneumonia with abnormal observation on chest computed tomography scan.[109] The attack of SARS-CoV-2 on its receptor (ACE II) induces cytokine storm which in

99 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

100 Teruaki Nakatsuji et al., "Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus and are deficient in atopic dermatitis," pp. 1-11.

101 Elizabeth A. Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

102 Yuping Lai., "Activation of TLR2 by a Small Molecule Produced by Staphylococcus epidermidis Increases Antimicrobial Defense against Bacterial Skin Infections." Journal of Investigative Dermatology 130, no. 9, 2020. pp. 2211-2221.

103 Hedayati ChM and Badlou BA, "COVID-19 War, Human Microbiota Function.'' Journal of Internal Medicine and Emergency Research 1, no. 2, 2020. 1-4. https://www.maplespub.com/webroot/files/COVID-19-War-Human-Microbiota-Function_1591950264.pdf.

104 Hedayati ChM and Badlou BA, "COVID-19 War, Human Microbiota Function,'' pp. 1-4.

105 Ibid.

106 Xiaoxv Yin et al., "Evaluation of early antibiotics use in non-severe COVID-19 patients admitted with low risk of bacterial infection." Research Square, 2020.

107 Ibid.

108 Busra AKTAS and Belma ASLIM, "Gut-lung axis and dysbiosis in COVID-19." Turkish Journal of Biology 44, no. 3, 2020. pp. 265-272.

109 Chaolin Huang et al., "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China." pp. 497-506.

turn cause the damage of lungs and multiple organs.[110] The viral RNA enters the T cells for their replications and develops new virions and causes the cell's death.[111] Nasal application of Corynebacterium pseudodiphtheriticium, which is a normal respiratory bacterial flora, on mice has shown an increase of the Toll-like receptor (TLR-3) and improvement of the TNF-, IL-6, IFN-, and IFN- cells; that is thought to be able to boost host defenses against Respiratory Synsytial Virus (RSV) and secondary pneumonia in infant mice.[112],[113] Even if the contribution of lung microbiota against ARDS after novel coronavirus infection is still unknown, these precedent studies show the importance of respiratory tract microbiota for combating viral infection complications by reduction of the cytokine storm. Further, Fan and colleagues have been investigated the microbial community of 20 deceased COVID-19 patients and found that most of them have developed bacterial and fungal infections.[114] Bacterial genera characterized in this study consist of Acinetobacter (80.70%), Chryseobacterium (2.68%), Burkholderia (2.00%), Brevundimonas (1.18%), Sphingobium (0.93%), and Enterobacteriaceae (0.68%) regularly found in all studied cases.[115] Mycobacterium (3.59%) and Prevotella (0.56%) were only detected in two of the 20 subjects.[116] In this study, the lung microbial dysbiosis is marked by the enrichment of OUT in lungs and the domination of Acinetobacter, which holds one of the most antibiotic resistance species (Acinetobacter baumannii), and decreasing of normal lung flora like Prevotella. [117]

Effects on GI tract bacterial flora

SARS-CoV-2 RNA is founding in faecal samples from COVID-19 cases.[118] Manifestation in the GI tract has been observed in some of COVID-19 patients (diarrhae, nausea, ...) and studies in these effects are underway. It is demonstrated in many studies that the low respiratory tract infection affects the GI tract and a disturbance of the intestinal microbiota is observed because of the intestinal-lung axis.[119],[120] Zuo et al., have found the SARS-Cov-2 genome in the faecal samples of 15 hospitalized positive cases of COVID-19, even from the patients who did not show any intestinal infection symptoms.[121] Their results of the bacterial profile of the GI tract of the patients with high SARS-Cov-2 respiratory infection show a higher abundance of opportunistic pathogens such as Collinsella aerofaciens, Collinsella tanakaei, the normal coloniser in the upper respiratory tract, and oral cavity bacteria Streptococcus infantis and, Morganella morganii.[122] Contrary to that, patients with low or none- SARS-Cov-2 infection have shown the presence of a high abundance of SCFAs and tryptophan producer bacteria such as Parabacteroides merdae, Bacteroides stercoris and, Alistipes onderdonkii.[123] The abundance of pathogens in gut microbiota explains the failure of the defense barrier constituted by the normal bacterial flora inhabiting the GI tract. Even if the route of this virus GI tract infections still unknown, a relation is observed between this tract microbiota and the lung microbiota. This relation which is assumed to be via the blood and lymphatic system can explain the evidence of the gastro-intestinal tract SARS-Cov-2 infection.[124]

Dysbiosis of skin bacterial flora

Region of the skin, its chemical attributes, gender, geographical location and race, depth within the epidermis, antibiotic treatment and vaccination, use of cosmetics, age of the individual, and its health status are thought to influence the skin microbiota.[125] It is thought that the mucosal contacts between humans lead to the enrichment of bacterial diversity of the human microbiota which provides immune stimulation.[126] During the delivery, the baby is contaminated by the mother's vaginal microflora like Lactobacillus and Sneathia during vaginal delivery, or by the mother's skin bacteria like Propionibacterium and Staphylococcus in the case of Cesarean section.[127],[128] Soap and hygienic products are considered as potential factors which affect the human skin barrier that could affect the mucosal cells and bacterial flora.[129] Authors suggest that the more acidic character of men's skin and the frequent hand washing of women could be the causes of lower bacterial numbers in women and lower bacterial diversity in men.[130] During this pandemic period, most people regularly use hand sanitizers containing 70-80% alcohols. However, overuse of such products causes skin irritation and the development of disinfectant-resistance bacteria.[131] In addition, these products can inhibit

110 Saroj Khatiwada and Astha Subedi, "Lung microbiome and coronavirus disease 2019 (COVID-19): Possible link and implications," 100073.

111 Ibid.

112 Saroj Khatiwada and Astha Subedi, "Lung microbiome and coronavirus disease 2019 (COVID-19): Possible link and implications," 100073.

113 Paulraj Kanmani et al., "Respiratory Commensal Bacteria Corynebacterium pseudodiphtheriticum Improves Resistance of Infant Mice to Respiratory Syncytial Virus and Streptococcus pneumoniae Superinfection" Frontiers in Microbiology 8, (2017): 1613. Doi: 10.3389/fmicb.2017.01613.

114 Juan Fan et al., "The lung tissue microbiota features of 20 deceased patients with COVID-19" Journal of Infection 81, no.3, 2020. pp. 64-67.

115 Ibid.

116 Ibid.

117 Ibid.

118 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19."

119 Robert P. Dickson et al., "The Microbiome and the Respiratory Tract." pp. 481-504.

120 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19."

121 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19."

122 Tao Zuo et al., "Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19."

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124 Aravind Sundararaman et al., "Role of probiotics to combat viral infections with emphasis on COVID-19," pp. 8089-8104.

125 Anthony M. Cundell, "Microbial Ecology of the Human Skin" Microbial ecology 76, no. 1, 2018 pp.113-120.

126 Célia P. F. Dominigues et al., "The Social Distancing Imposed to Contain COVID-19 Can Affect Our Microbiome: a double-Edged Sword in Human Health." mSphere 5, no. 5, 2020.

127 Elizabeth A Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

128 Mariana Rosenthal et al., "Skin microbiota: Microbial community structure and its potential association with health and disease." Infection, Genetics and Evolution 11, no. 5, 2011. pp. 839-848.

129 Elizabeth A Grice and Julia A. Serge, "The skin microbiome," pp. 244-253.

130 Noah Fierera et al., "The influence of sex, handedness, and washing on the diversity of hand surface bacteria." PNAS 105, no.46 (2008): 17994-19799

131 Chandanapalli Sai Himabindu et al., "Hand sanitizers: is over usage harmful?" pp. 296-300.

the establishment of pathogens but overusing of them provide skin dryness, bleeding, and desiccation; this biological destruction of the skin (considering as a barrier) opens the way to pathogens and toxins to enter the body since incorrectly uses hand sanitizers kill the beneficial bacteria and cause dysbiosis of the skin, gut and other organs microflora.[132],[133] Until now, no study in the microbial dysbiosis in the skin during the SARS-CoV-2 pandemics has been elaborated. But we suggest that contact reduction and regular use of hand sanitizers can affect the skin bacterial flora and develop skin inflammatory disease and allergy.

IV. Conclusion

Since the end of 2019, the SARS-Cov-2 infects progressively every point over the world. Studies are running for further understanding its infection mechanisms, discovering effective vaccine, finding susceptible treatment, and avoiding human health implications during/after this period. This review covers the dysbiosis of the bacterial flora of the skin, the digestive system as well as that of the respiratory system which can be observed during the period of this pandemic. Considering the main role of this flora in the human immune system, this susceptible disturbance can be the origin of other diseases and infections such as skin inflammatory disease, lung injury, AAD, and CDAD. Improvement of the disease preventive methods and treatment is necessary to avoid such disaster to human health. Probiotics administration and a controlled diet could be more effective against this bacterial dysbiosis during and after this pandemic period.

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132 Chandanapalli Sai Himabindu et al., "Hand sanitizers: is over usage harmful?" pp. 296-300.

133 Mariana Rosenthal et al., "Skin microbiota: Microbial community structure and its potential association with health and disease," pp. 839-848.

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One Virus, Countless Consequences

Ghada Tagorti*

Abstract

In late 2019, due to a virus outbreak, the planet began to change, morbidity escalated jeopardizing lives and livelihood, and the crisis mushroomed to touch every aspect of modern life. Although this pandemic namely COVID-19 is considered as a novel experience without any modern precedent, researchers are providing insights to overcome the COVID-19, and predictions to the possible outcomes in the post-COVID-19 era have been assessed. In this regard, we present here an overview of recent studies, highlighting the effects of COVID-19

Özet

2019 yılının sonlarında ortaya çıkan bir virüs salgını tüm gezegeni değiştirmekte; hastalık oranı artmakta, hayatlar ve geçim kaynakları riske girmekte ve bu derin kriz yaşamın her alanına dokunacak şekilde adeta bir mantar gibi büyümektedir. Her ne kadar, COVID-19 modern hayatta daha önce deneyimlenmemiş emsali olmayan bir salgın olsa da, araştırmacılar COVID-19'un üstesinden gelmek ve derinine analiz etmek için tahminler ve değerlendirmeler sunmaktadırlar. Bu bağlamda, bu çalışma yakın zamanda yapılan araştırmalar üzerin-

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on the human body and animals, including the expected consequences in the post-COVID-19 period.

Keywords: *Anemia, Diet, Disorders, Organ Models, Post-COVID-19, Wildlife*

den COVID-19'un insan vücuduna ve hayvanlara etkisini sorgulamaya, aynı zamanda COVID-19 sonrası dönemde neler beklendiğini değerlendirmektedir.

Anahtar kelimeler: *Kansızlık, Diyet, Hastalıklar, Organ Modelleri, COVID-19 Sonrası, Yaban Hayatı*

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Graphical Abstract

I. Introduction

For millennia, humanity has interfered with the ecosystems, to reach the point where 80% of terrestrial and marine regions on the Earth are substantially altered.[1] Besides, only 40% of the forest areas have high landscape-level integrity, whereas the remained area is degraded.[2] This degradation enhances the risk of zoonotic disease outbreaks from wildlife due to biodiversity loss. From 1940 to 2004, around 335 emerging infectious diseases (EIDs) were recorded, and 52% of these EIDs and 72% of the emerging zoonoses originating from wildlife. Further, an increased frequency of outbreaks over time was observed.[3] On the other hand, due to a connected human society, an increase in long-distance transport of disease vectors was facilitated, leading to the rise of human-wild animal interfaces such as markets.[4] Given that, connectivity accelerates, as a result, human-human transition speed up. Interestingly, around 1.7 million viruses from the same viral families are not studied yet, among them an estimated 700,000 viruses in mammals and birds are predicted to possess a zoonotic disease potential.[5] One of them, the severe acute respiratory syndrome coronavirus 2, namely SARS-CoV-2 which is responsible for the pandemic known as coronavirus disease 2019 (COVID-19).

Coronaviruses, which are RNA viruses, were reported from the mid-1960s with two species 229E and OC43, both responsible for the common cold.[6] In 2002, SARS-CoV emerged in China, and studies revolved around pathogenic human coronaviruses.[7] Later, NL63 causing bronchiolitis and HKU1 causing pneumonia were identified.[8] In fact, humans are commonly infected with 229E, NL63, OC43, and HKU1.9 Subsequently, the MERS-CoV were isolated in the Middle East in 2012 with a restricted circulation to specific regions of the world.[10] Until 2019, a new pandemic has sparked with the SARS-CoV-2 to be the seventh coronavirus infecting humans.[11] Although humans confronted coronaviruses, none of them had triggered a pandemic as SARS-CoV-2. However, historically and in more contemporary times, outbreaks such as Spanish flu, Asian flu, Swine flu, SARS, Ebola, Zika, and more pandemics and epidemics have ravaged humanity. For instance, during Spanish flu (1918-1919), 20-50 million death has been recorded, 32 million deaths estimated for the ongoing HIV/AIDS, 18.500 officially recorded in laboratories with 570.000 as estimated death during Swine flu (2009-2010), whereas COVID-19 had registered 932,997 deaths as of 8:30 am 15 September.[12] Unequivocally, pandemics wiped out a huge number of humans and to date, mankind is largely affected.

Even though it is still early to conclude the aftermath of the COVID-19, studies emphasize the importance of preparedness for the predicted outcomes. With this in mind, we attempt to illustrate briefly in this paper the impacts of COVID-19, during and after the pandemic, on human biology, animals in science as well as in wildlife.

II. Post–COVID-19 and Diet Quality

The prevalence of anemia in pregnant women until 2016 has no record of any change in all the regions of the world.[13] As known, the prevalence of anemia in women is correlated with the gross domestic product (GDP) per capita. Surprisingly, a decline in

1 Venter et al., "Sixteen years of change"; Jones et al., "The location and protection".
2 Grantham et al., "Modification of forests".
3 Jones et al., "Global trends in emerging".
4 Tatem, Rogers, and Hay, "Global transport networks".
5 Carroll et al., "The Global Virome Project".
6 Hamre and Procknow, "A new virus isolated"; McIntosh et al., "Recovery in tracheal organ".
7 Drosten et al., "Identification of novel coronavirus".
8 Van der hoek et al., "Identification of new coronavirus"; Woo et al., "Characterization genome"
9 CDC, "Human coronavirus types".
10 Zaki et al., "Isolation of novel coronavirus".
11 Chan et al., "A familial cluster".
12 McMullan et al., "Humans reacted to pandemics"; Worldometers, "Coronavirus".
13 Ritchie and Roser, "Micronutrient Deficiency".

global GDP due to COVID-19 has been recorded.[14] In addition, around a 20% increase in poverty globally with 80 million people in South Africa and 42 million people in South Asia joined the group of the poor.[15] Moreover, during an economic crisis, an increase in micronutrient malnutrition is expected before weight loss, since households sacrifice dietary diversity. In this regard, the change to cheaper and lower quality foods depletes the micronutrient stores in the body and lowered, therefore, the immunity.[16] On the other hand, the availability of nutritious foods (animal source products, fruits, and vegetables) in particular is affected by COVID-19 where the production of these foods is labor-intensive and impacted by social distancing. Moreover, these products are susceptible to perish when markets are disrupted and the first to be dropped from the household menu when incomes fall. For instance, food security and diet quality have worsened in Addis Abba during COVID-19. The average households are less consuming nutritionally beneficial foods, except the richest quintile.[17] The limitations on the movement of goods, especially imported foods, fruits, and vegetables reduced as well as the consumption of healthy food. In Bangladesh, transport costs rise by 20% and labor shortages lead to wastage of milk, poultry, and fish whereas, in Indonesia, a 24% decline for fresh vegetables from March to May 2020 was recorded. Further, of 137 country-food combinations, 111 show price increases where the largest was in Rwanda (19.5%) followed by Tanzania (12.3%), and Mozambique (10.5%). Foods with the greatest increases were cheese (12.8%), onions (10.5%), chicken (10.1%), and oranges (9.5%).[18] This increase is related to some studies done in vitamins as a way to strengthen the immune system to help defeat COVID-19. Consequently, the price of these vitamin sources perceives a dramatic increase. Taking as an example, the vitamin C found in citrus fruits including oranges, limes, and lemons were used in China. Vitamin C is able to contribute to enzymatic function, tissue repair, and immunity. The use of large doses of IV vitamin C (10000-20000 mg/day), delivered over 8 to 10 hours had successfully treated more than 50 patients with moderate to severe COVID-19.[19] On the other hand, vitamin D reduces the risk of microbial infection and death by maintaining tight junctions, thereby the virus is unable to disturb the junction integrity. Moreover, the cellular innate immunity is enhanced by vitamin D through the induction of antimicrobial peptides and in part by reducing the cytokines storm.[20] Therefore, vitamin D possesses an anti-inflammatory and immunomodulatory effect justifying its usage for COVID-19 since SARS-CoV-2 initially uses immune evasion mechanisms leading to cytokines storm.[21] Surprisingly, the vitamin D levels are low in the aging population, especially in Spain, Italy, and Switzerland.[22] Given that, vitamin D concentrations tend

14 IMF, "A Crisis Like No Other".

15 Laborde, Martin, and Vos, "Poverty and food insecurity".

16 Klotz et al., "Nutrition in perfect storm".

17 Hirvonen et al., "Food and nutrition security".

18 GAIN, "Impact on food systems".

19 Cheng, "Intravenous dose of vitamin C".

20 Grant et al., "Vitamin D Supplementation".

21 Jakovac, "COVID-19 and vitamin D".

22 Ilie, Stefanescu, and Smith, "The role of vitamin D".

to decrease with age, which may be significant for COVID-19 since case-fatality rates increase with age.

Despite the high level of public awareness regarding healthy foods benefits, incomes, and food prices restricted access to nutritious food. Furthermore, micronutrient intervention programs and health system are affected during COVID-19 as an example the disruption of tuberculosis therapy have a significant impact on tuberculosis where just with 3-month lock-down a setback of tuberculosis programs to 5-8 years with additional 6.3 million cases and additional 1.4 million deaths by 2025 could be recorded.[23] Another disruption of up to 75% was recorded during the first months of the lock-down in antenatal care programs (ANC) responsible for iron and folic acid accessibility to women.[24] Taken together, COVID-19 negatively affected the diet quality of the population. Considering the previous pandemics, the recovery of health care services might be slow, exacerbating in this way the current scenario. For example, during the first 4 months of the Ebola pandemic in Liberia, a 32.5% decrease in output of ANC services was noted and more than a year was needed to recover the pre-pandemic levels.[25]

As a result, population recovery from anemia after COVID-19 requires considerable time since the social distancing reduced families' incomes, disrupted ongoing health programs and food supplies. This situation may prey on people whose immune systems are already impaired by malnutrition and increases thereby overall morbidity and mortality. On the other hand, malnutrition predisposed the population to whatever infection, while the infection per se will increase malnutrition and death rates, further enhancing vulnerability in a vicious cycle.[26]

III. Post–COVID-19 and Disorders

Acute COVID-19 is not the end, as a post-viral syndrome following the infection has been observed. Strikingly, a scarcity of information has been reported on the persisted symptoms as well as their severity after discharging from the hospital as recovered patients. Interestingly, a study designed in Italy recorded 32% of recovered patients with 1 or 2 persisted symptoms and 55% possessed 3 or even more. The related symptoms compromise fatigue (53.1%), dyspnea (43.4%), joint pain (27.3%), and chest pain (21.7%).[27] In fact, a subgroup of individuals is likely to experience the post-COVID-19 syndrome since the immune heterogeneity in COVID-19 is high with three distinct "immunotypes" emphasizing thereby the different possibilities to succumb to COVID-19 and consequently different clinical outcomes.[28] Additionally, the post-COVID-19 syndrome is quite similar to the post-SARS episode. Both of them are responsible for chronic fatigue syndrome/myalgic encephalomyelitis, a disabling chronic disease considered as a

23 STOPTB partnership, "Devastating Effect of COVID-19".

24 UNICEF, "Situation tracking".

25 Wagenaar et al., "The Ebola virus".

26 Viana, "Anemia and infection".

27 Carfì, Bernabei, and Landi, "Persistent Symptoms in Patients".

28 Mathew et al., "Deep immune profiling".

disorder of the brain with unknown etiology.[29] The SARS studies demonstrated that the virus crossed the blood-brain barrier into the hypothalamus via the olfactory pathway, involving the disturbance of lymphatic drainage along the olfactory nerves. In contrast, the coronavirus points out an entry side independent of neurons.[30] Although anosmia in COVID-19 has been reported, surprisingly nonneuronal cell types were the vulnerable cells.[31] However, a build-up of pro-inflammatory cytokines is observed in both infections, passing in circumventricular organs and giving rise to autonomic dysfunction suggesting in this way the post-viral syndrome.

Currently, sufficient time has not yet elapsed to understand better the post-COVID-19 syndrome but some groups such as the Body Politic COVID-19 reported from 91% of 640 COVID-19 patients exacerbating symptoms, no recovery even after 40 days (Body Politic COVID-19 Support Group, 2020).[32] Moreover, several studies recorded long-term complications including lung scarring, blood clots, and renal failure.[33] Furthermore, scattered reports and a cohort study reported a link between Kawasaki disease (KD) which tends to affect coronary arteries in children, and COVID-19.[34] According to the correlation between KD, influenza, and respiratory enteroviruses, there is speculation that COVID-19 could induce KD.[35] Moreover, an increase in the emergence of KD had occurred just two weeks after the rise of COVID-19 supporting the association between COVID-19 and KD.[36] On top of that, another syndrome was recorded after the onset of coronavirus known as Guillain-Barré syndrome (GBS). This disorder was first described as a form of limb weakness, but nowadays it is considered as a neuromuscular disorder associated with respiratory difficulties. To date, GBS is generally precipitated by an infection such as influenza A, Zika virus, and Epstein-Barr virus.[37] The incubation period, which is defined as the lag time between the exposure of an antecedent infection and the onset of symptoms, is typically 10 to 14 days for GBS.[38] However, GBS symptoms were observed after an interval of 7 days after COVID-19 recovery and without any documentation of an associated infection suggesting in this way the classic pattern of the post-infection.[39] As it seemed GBS is actually caused by an aberrant autoimmune response to an infection and given the fact that SARS-CoV-2 responsible for an excessive immune response with increased pro-inflammatory cytokines such as interleukin-6, the neurological complications are just the consequence of this immune response.[40]

29 Cortes et al., "Myalgic Encephalomyelitis"; Moldofsky and Patcai, "Chronic musculoskeletal".

30 Perrin et al., "Into the looking glass"; Bostancıklıoğlu, "SARS-CoV2 entry".

31 Brann et al., "Non-neuronal expression".

32 Body Politic COVID-19 Support Group, "COVID-19 recovery".

33 Parshley, "Long-term complications".

34 Jones et al., "COVID-19 and Kawasaki Disease"; Rivera-Figueroa et al., "Incomplete Kawasaki Disease"; Schroeder, Wilson, and Ralston, "COVID-19 and Kawasaki Disease".

35 Kim et al., "Evaluation of Kawasaki Disease".

36 Ouldali et al., "Emergence of Kawasaki disease".

37 Wijdicks and Klein, "Guillain-Barré Syndrome".

38 Styczynski et al., "Increased rates Guillain-Barré".

39 Arnaud et al., "Post SARS-CoV-2".

As known, diabetic patients were sensitive to COVID-19 with a high risk of morbidity and mortality since the infection can trigger more stress. Consequently, an increase in the secretion of hormones responsible for hyperglycemia such as glucocorticoids is observed resulting in more diabetic complications.[41] Interestingly, it appears that SARS-CoV-2 can induce diabetes mellitus in healthy patients like enteroviruses, retroviruses, and Epstein-Barr virus which were involved in the development of diabetes.[42] The entrance of coronavirus to the human body is assured through the interaction with the ACE2 receptor. The expression of ACE2 in the endocrine tissue of the pancreas is greater than in the exocrine section. Therefore, the viral damage in the pancreas is more extended in the endocrine tissue, yielding to pancreatic islet damage and causing acute insulin-dependent diabetes, namely type 1 diabetes.[43] Another change could occur in the adrenal gland similar to SARS-CoV where necrosis of the gland and vasculitis in the medulla were recorded.[44]

Hence, COVID-19 fuels a new burden with these long-term outcomes following the post-pandemic, while COVID-19 symptoms are just the tip of the iceberg, the remained complications after recovery could be even more severe. In this regard, efforts to prioritize post-COVID-19 disorders and diseases should be assured.

IV. Post–COVID-19 and Antimicrobial Resistance

The increased focus on infection prevention through hand hygiene and social distancing suggested a reduction in the transmission of disease. However, some negative factors were enhanced. The increased empirical antimicrobial use in acute care, the overcrowding in healthcare services, and the disruption of organizational programs including antimicrobial stewardship were increased.[45] Additionally, the challenge of the high burden of cases and the challenge to differentiate from bacterial infection, and the uncertain rates of attributable co-infection increase the risk of antimicrobial resistance (AMR). According to previous respiratory virus pandemic such as the 2009 H1N1 influenza, co-infection was linked to Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, and aspergillosis.[46] However, little data of co-infection in other coronavirus infections are available to support the prescription of antimicrobial during COVID-19. Interestingly, a lower rate of reported co-infection in COVID-19 (8%) and high rates of antimicrobial use (72%) often with a broad spectrum such as quino-

40 Scheidl et al., "Guillain-Barré syndrome".

41 Wang et al., "Timely blood glucose management".

42 Jaeckel, Manns, and Von Herrath, "Viruses and diabetes".

43 Yang et al., "Binding of SARS coronavirus".

44 Ding et al., "Pathology of SARS".

45 Rawson et al., "Impact on antimicrobial resistance"; Rawson et al, "Antimicrobial use".

46 Randolph et al., "Pediatric Acute Lung Injury".

lones and carbapenems were recorded.[47] In a systematic review about co-infections in COVID-19, 7% of co-infection were bacterial and 3% are viral co-infection.[48] On the other hand, the site of co-infection, the differentiation between settings such as critical and non-critical care, and the attributable risk to COVID-19 is still to be defined. Moreover, due to off-label prescriptions for COVID-19, the community surged, as an example, to the use of hydroxychloroquine/chloroquine in the USA.[49]

Overall, the potential of COVID-19 has been followed by an increase in AMR. Measures and efforts to limit antibiotic treatment after the pandemic should be redoubled, such as reserving antibiotic treatment for severe conditions and control the duration of administration. AMR was a threat before the pandemic that still increasingly emerges and spreads. Additionally, COVID-19 impacts vulnerable populations with inadequate sanitary conditions encouraging the AMR. Without disregarding the fact that the cost of health care is high due to AMR as more expensive drugs are required and endemic infectious diseases could reemerge.[50] Consequently, continued actions are required to cope with the AMR.

V. Post–COVID-19 and Animal Welfare (3rs)

The quest for speedy vaccine/drug discovery raises the need for fast pre-clinical models to assure fast-track clinical testing. In this light, the Cochrane on 19 August 2020 recorded more than 10,000 launched studies, with over 160 vaccines for COVID-19 which are under development (115 in April).[51] The 'covidisation' of research enhanced therefore the awareness of animal use by avoiding and replacing animal tests. First, in order to shortcut the time of drug development as the animal-based tests may be lengthy and would fail due to species specificity or the urge of specific features found only in humans. Additionally, the public is conflicted about animal use in coronavirus-related research. In a recent survey conducted in the United Kingdom, 84% of participants agree that research needs to be done into alternatives than using animals in research.[52] Although statistics on the use of animals for scientific purposes for the year 2020 provided by the Members states are available by the end of 2021, and the European Union report would be ready by the end of 2022, a decrease in animal use was revealed through COVID-19 H2020 projects with only 10 of 100 COVID-19 H2020 projects were conducted on animals.[53] From this point, using animals is the last resort, not a default approach anymore. Furthermore, the increase of global communication and data sharing like the COVID-19 data portal, UK Academy of Medical Sciences COVID-19 Preclinical Drug Development Database, and US National Institute of Health Strategic Plan, may help to reduce the impact of science on animals.

47 Rawson et al., "Bacterial and fungal co-infection".

48 Lansbury et al., "Co-infections in people".

49 Vaduganathan et al., "Prescription Fill Patterns".

50 WHO, "Antimicrobial resistance".

51 Cochrane, "COVID-19 study register"; Thanh et al., "The COVID-19 vaccine".

52 Williams, "Understanding animal research".

53 Desaintes, "Research response".

In this context, non-animal technologies are developed such as the commercial human lung models which were used in some studies for the SARS-CoV-2 pathogenesis as it corroborates the expression of ACE2 in goblet/secretory cells and ciliated cells.[54] Moreover, microfluidic devices with stem cell-derived from human vascular endothelial cells to model COVID-19 associated thrombus formation were used, as well as micro-physiological systems that reproduce the minimal functional entity of the brain.[55] Besides accelerating the drug discovery for COVID-19, this shift in the use of animals would help to confront any viral infections confronted in the future which have species-specific features also by saving on time and cost notably when genetically modified strains are needed to be bred, while human organ models are already appropriate for the discovery of antiviral treatment.[56] Thereby, COVID-19 provided the opportunity to pressure the reduction of animals' usage and to highlight new technologies that have proved to be more suitable for the next generation.

VI. Post–COVID-19 and Wildlife

The COVID-19 is still impacting wildlife. As a result of the reduction of human disturbance, change in the activity of some vertebrate species by venturing into urban areas has been recorded yielding to spatial niche extension.[57] On the other hand, industrial air pollution, particularly nitrogen dioxide, is restricting the abundance and reproduction of aerial insectivorous birds.[58] Like a huge decrease in air pollution during COVID-19 was observed comprising nitrogen dioxide and sulfur dioxide, a large clutch size has been predicted.[59] Further, the decline in manufacturing and production has led to restraining in wildlife trade and also fishing.[60] For instance, Olive Ridley, an endangered sea turtle in India, managed to nest and lay an estimated 60 million eggs after the restrictions on human activities.[61] Presumably, a decrease in road-killing has been observed especially on amphibian populations as the major proportion of fauna casualties on roads.[62] Notwithstanding the positive effects caused by COVID-19, some tangible disadvantages were reported. For example, the poaching of wild animals had increased in India with 88 cases compared to 35 reported cases before the COVID-19 period.[63] Based on these numbers, additional burdens on wildlife conservation are placed. A field that already suffers from inherent constraints like shortage of staff, funds, and even insufficient patrolling infrastructures. Thus, to avoid the loss of benefits following out the previous

54 Pizzorno et al., "Treatment of SARS-CoV-2"; Pruijssers et al., "Remdesivir inhibits SARS-CoV-2"; Sungnak et al., "SARS-CoV-2 entry factors".

55 Lakshmanan et al., "Microfluidic Bleeding Chip"; Bullen et al., "Human Brain Sphere".

56 Busquet et al., "Novel animal-free test".

57 Corlett et al., "Impacts on biodiversity conservation".

58 Newman, Novakova, and McClave, "The influence of industrial air emissions"; Sanderfoot and Holloway, "Air pollution impacts".

59 Muhammad, Long, and Salman, "COVID-19 pandemic and environmental pollution"; Buonocore et al., "Lockdown cleaning the skies".

60 Bates et al., "Global Human Confinement Experiment".

61 Bradford, "Undisturbed sea turtles".

62 Beebee, "Effects of road mortality".

63 Badola, "Indian Wildlife".

management actions achieved in the past years, the establishment of new plans is needed.

VII. Conclusion

The COVID-19 pandemic is above and beyond severe respiratory problems, by affecting all the human body even after recovery and further by influencing human-animal relationship: from animal models to human organ models, as well as impacting the environment such as wildlife activities and breeding success. Although the impact varies from one region to another, health crises, poverty, inequalities, interruption of previous programs were observed on a global scale. Without urgent responses, deaths soar and the suffering may endanger human and animals' lives. Therefore, immediate responses should be undertaken to support particularly vulnerable groups, through the development of response plans to the post-COVID-19 era and meanwhile to protect mother nature and its creatures for a safe future.

Author Statements

The authors would like to state that there is no financial interests or connections that might raise the question of bias in the work reported or the conclusions, implications, or opinions stated.

Sources of Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure of The Conflict of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Beyond COVID-19: Strategic Priorities for Healthcare, Disease Surveillance, and Vaccines

Abednego Nzyuko Masai*

Abstract

The COVID-19 pandemic has significantly affected the health systems in both developed and developing countries. It has revealed some of the failures of current health systems. It has challenged policymakers to come up with innovative disease surveillance methods, resilient health systems that can rapidly adapt to changes in epidemics, and health policies that ensure vaccines are accessible to the vulnerable and marginalized people in society. While countries try to control the spread of the SARS-CoV-2 virus through several measures, the question of the impact of these interventions on other respiratory infections, ac-

Özet

COVID-19 pandemisi hem gelişmiş hem de gelişmekte olan ülkelerdeki sağlık sistemlerini önemli ölçüde etkilemiştir. Bu pandemi, mevcut sağlık sistemlerinin bazı başarısızlıklarını ortaya koymuştur. Ayrıca politikacıların, yenilikçi hastalık sürveyans yöntemleri, salgın hastalıklardaki değişikliklere hızla uyum sağlayabilen esnek sağlık sistemleri ve toplumda savunmasız kişilerin aşı almalarını sağlayan sağlık politikalarını bulmalarını teşvik etmiştir. Ülkeler, SARS-CoV-2 virüsünün yayılmasını çeşitli önlemlerle kontrol etmeye çalışırken, bu müdahalelerin diğer solunum yolu enfeksiyonları üzerindeki etkisi, kaliteli

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cess to quality and affordable healthcare, distribution of future COVID-19 vaccines to low and middle-income countries, and disease surveillance beyond COVID-19 pandemic emerged. This review critically explores the status of health systems, coronavirus disease surveillance, COVID-19 vaccine development, and the changes in the distribution of influenza among other respiratory infections during the pandemic. The author draws lessons from the COVID-19 pandemic to show the need to improve current public health systems, which will increase preparedness for future pandemics and protect the health of the global population. The paper concludes that countries should learn from the threat caused by the coronavirus pandemic and strategize on better ways for managing potential future epidemics in the post-COVID-19 period.

Keywords: *COVID-19, Disease Surveillance, Health System, Health Policy, Influenza, Post-COVID-19 era, SARS-CoV-2, Vaccine*

ve uygun fiyatlı sağlık hizmetlerine erişim, gelecekteki COVID-19 aşılarının düşük ve orta gelirli ülkelere dağıtılması ve COVID-19 pandemisinden sonra bulaşıcı hastalık sürveyansı soruları ortaya çıkmıştır. Bu derleme, sağlık sistemlerinin durumunu, koronavirüs hastalığı sürveyansını, COVID-19 aşısı geliştirmeyi ve pandemi sırasında diğer solunum yolu enfeksiyonları arasında influenzanın dağılımındaki değişiklikleri incelemektedir. Yazar, gelecekteki salgınlara karşı hazırlığı artıracak ve küresel nüfusun sağlığını koruyacak olan mevcut halk sağlığı sistemlerini iyileştirmek gerektiğini göstermek için COVID-19 salgınından dersler çıkarmaktadır. Bu makale, ülkelerin koronavirüs salgınının yol açtığı krizden ders almaları ve COVID-19 pandeminin sonrası salgınları daha iyi yönetme yolları üzerinde stratejiler geliştirilmesi gerektiği sonucuna varmaktadır.

Anahtar kelimeler: *COVID-19, Hastalık Sürveyansı, Sağlık Sistemi, Sağlık Politikası, Influenza, COVID-19 sonrası dönem, SARS-CoV-2, Aşı*

*

I. Introduction

Since its emergence, coronavirus disease 2019 (COVID-19) has affected the daily life of nearly all of the human population. In December 2019, clinicians observed that clusters of patients in Wuhan city located in Hubei province of China showed symptoms of severe acute respiratory symptoms with pneumonia of unknown aetiology[1]. Sequencing of the viral genome isolated from patients' samples showed that the virus was different from SARS-CoV and MERS-CoV viruses, which caused the SARS outbreak in 2003 and the MERS outbreak in 2012. In the past two decades, three coronaviruses have emerged in the human population, causing a high alert in global public health.

The WHO declared COVID-19 as a Public Health Emergency of International Concern (PHEIC) and issued temporary recommendations under the International Health Regulation act (IRH) in January 2020. These recommendations urged countries to mitigate the spread of COVID-19 disease, contribute to international response through communication and collaboration, increase knowledge of the novel coronavirus disease, and advance research. WHO announced the disease as a global pandemic in March 2020 and strongly recommended countries take urgent measures to control its rapid spread.

1 Zhu et al. "A Novel Coronavirus from Patients with Pneumonia in China, 2019.". N Engl J Med 382, no. 8, 2020, pp. 727-33.

The COVID-19 pandemic has affected both developed and developing countries, with the number of confirmed cases rising from less than one million in February 2020 to more than one hundred and forty million cases and three million deaths in April 2021. The rapid spread of the novel SARS-CoV-2 virus with the resulting hospitalizations and deaths has strained existing health systems and unexpectedly overburdened even countries with stable healthcare infrastructure and resources[2]. The COVID-19 pandemic has been the deadliest global event to occur so far in the 21st century, disrupting economic, social, cultural, and political activities.

Perhaps the gravity of the disruption caused by the COVID-19 pandemic is the motivating factor for researchers globally continuously working to develop a vaccine against the virus and add to the ever-emerging knowledge of the COVID-19 disease. Indeed, this pandemic has opened debates on the resilience of health systems to deadly infections that cause mass hospitalizations and deaths, the existence of sensitive surveillance systems that can detect and contain outbreaks early, and personal protective measures against infections of public health concern. Governments and non-governmental health agencies should address these issues to prepare for pandemics in the future and protect the healthcare of the global population beyond the COVID-19 pandemic.

II. Method

An in-depth review of existing literature from both LMICs and HICs was conducted between August and October 2020 to investigate measures to mitigate the impact of the coronavirus pandemic, changes in the distribution of other respiratory infections, and distribution of coronavirus vaccines. The literature was searched and extracted from databases such as Pubmed, Science Direct, PLOS, and Cochrane as well as web search engines such as Google Scholar. For the national reports and data, an authentic government website, development agencies, and organizations websites, which include WHO, CDC, Ministry of Health (MoH) websites were visited. References mentioned in key review papers were also accessed. The main keywords related to the study aims, that is, 'disease surveillance', 'coronavirus pandemic', 'vaccine development', 'health systems', and 'preparedness' were combined with Boolean operators 'AND' and 'OR' to narrow the search and produce conclusive evidence.

2 Munster et al. "A Novel Coronavirus Emerging in China - Key Questions for Impact Assessment." N Engl J Med 382, no. 8, 2020, pp. 692-94.

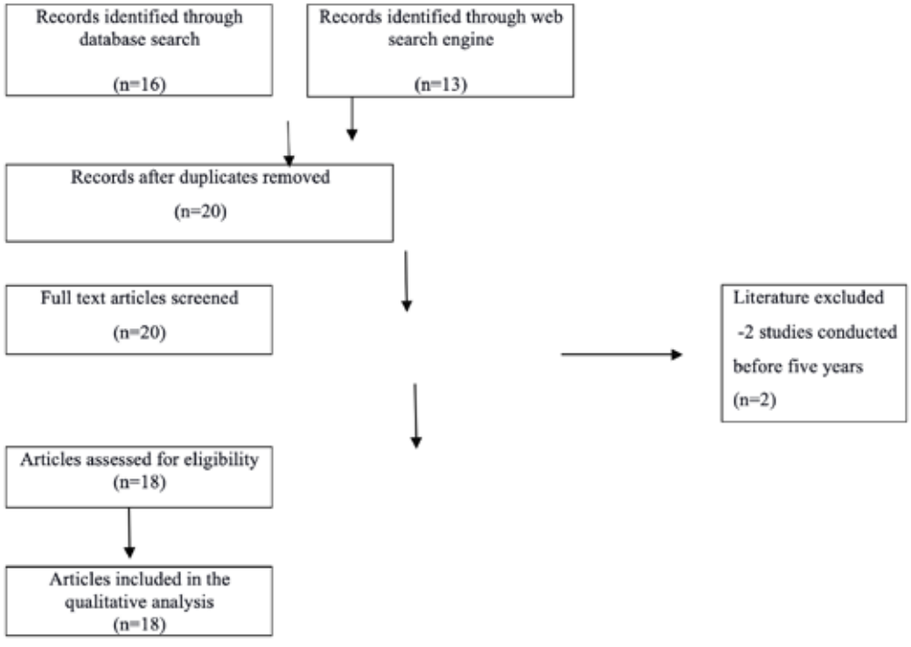

Figure 1. Study selection and characteristics

III. Results

Impact of COVID-19 Pandemic on Health Systems

COVID-19 pandemic has affected countries differently. While the health systems in some countries were resilient to the effects caused by the coronavirus pandemic, others were overburdened. The COVID-19 pandemic has reminded policymakers of the need for planning for major healthcare emergencies and strengthening the health systems. After the emergence of the novel coronavirus, countries invested in building hospitals and quarantine facilities, purchasing personal protective measures (PPEs) for frontline healthcare workers, and mobilizing healthcare workers to collaborate in managing the rising cases of confirmed COVID-19 infections. For example, China built two hospitals in Wuhan city in 10 days to cater to patients diagnosed with the COVID-19 disease[3] and Turkey built two hospitals with a 1000-bed capacity each in Istanbul amid the COVID-19 pandemic[4].

Conversely, low and middle-income countries that could not establish such mega hospitals and healthcare infrastructure to cope with the COVID-19 pandemic depended on donations and loans from developed countries, multinational organizations, and philanthropists to contain the spread of the SARS-CoV-2 virus. The lack of established healthcare infrastructure and insufficient personal protective equipment (PPEs) for frontline healthcare workers has raised fears of a potential increase in the number of coronavirus infections in these countries. For example, healthcare workers in some countries went for strikes demanding better working conditions and lack of PPEs while others fled when patients suspected of coronavirus visited the hospitals.

Therefore, countries should invest more in the health sector and formulate policies to reduce any misappropriation of allocated resources. Investing in healthcare infrastructure and public health systems enables countries to experience a reduced impact of outbreaks and emergencies in the future.

As observed, marginalized individuals that lacked adequate healthcare insurance were disproportionately affected by the coronavirus pandemic[5], which opened the debate on universal health coverage (UHC). This Sustainable Development Goal target 3.8 protects all citizens from financial burdens when seeking healthcare. Some countries incorporated COVID-19 testing, hospitalization, and treatment into national healthcare insurance. For example, Turkey included COVID-19 testing into the national insurance (SGK), and Spain nationalized all private hospitals, making them accessible to the public and healthcare workers[6].

Countries should learn from the COVID-19 pandemic on the need to introduce and expand universal health coverage to all citizens in the post-COVID-19 era. As governments around the world feel the economic impact of the COVID-19 pandemic, people without health insurance are the most hit economically. Every country should promote access to healthcare as a fundamental human right. More so during the 21st century when health emergencies and disasters risk undermining global efforts to promote human health and increase life expectancy.

3 Williams, Sophie. "Coronavirus: How Can China Build a Hospital So Quickly?", BBC News accessed 12.09.2020. (https://www.bbc.com/news/world-asia-china-51245156).

4 Zontur and Aydin. "Turkey to Build 2 More Hospitals Amid Virus Pandemic." Anadolu Agency news. accessed 12.09.2020 (https://www.aa.com.tr/en/latest-on-coronavirus-outbreak/).

5 Shadmi et al. "Health equity and COVID-19: global perspectives". Int J Equity Health. 2020;19(1):104, 2020.

6 San Juan, David Michael. "Responding to COVID-19 through Socialist (ic) Measures: A Preliminary Review." Available at SSRN 3559398 (2020).

The need to strengthen existing disease surveillance systems and establish new ones

COVID-19 disease surveillance has played an essential role in detecting infection hotspots, monitoring changes in the pandemic, identifying populations at the highest risk, and planning for future epidemics. Building surveillance systems that can identify asymptomatic individuals is essential to reduce the spread of the SARS-CoV-2 virus, especially when fears of a more deadly third wave are looming. In the post-COVID-19 era, international organizations such as the World Health Organization should encourage member countries to collaborate in establishing new and strengthening existing surveillance systems, which can detect outbreaks early. Timely identification and containment of future epidemics can be made possible by real-time identification of emerging and re-emerging infectious diseases.

Countries have used innovative surveillance methods to track COVID-19 hotspots. For example, some countries have used the detection of the SARS-CoV-2 virus in the sewers to assess the level of infections in the population[7]. This method enabled the identification of COVID-19 infection hotspots seven days before they were reported.

Moreover, several counties used digital information to track COVID-19 infections. For example, in China, people used a mobile application to input their information about their COVID-19 infection status[8]. After the spread of COVID-19 around the world, more countries have tracked coronavirus infections using digital information surveillance systems[9].

This form of surveillance has been used in the past to track epidemics. For example, Cambridge University created a mobile phone application called FluPhone to monitor flu infections[10]. Furthermore, mobile phone data was used during the Ebola outbreak that occurred in West Africa during the 2014 – 2016 period[11]. Employing digital mobile applications has proved to be useful during epidemics. They are cost-effective, time-efficient, and provide real-time monitoring of infections, unlike traditional surveillance systems through hospital records, telephone calls, and home visits.

The use of big data to monitor infections during epidemics has received criticism over privacy concerns. In the post-COVID period, the use of big data and digital information surveillance methods will continue to draw global attention to their importance versus

7 La Rosa, et al. "First Detection of Sars-Cov-2 in Untreated Wastewaters in Italy." [In eng]. Sci Total Environ, 2020 pp.736.

8 Huang Y., Sun M. , and Sui Y. "How Digital Contact Tracing Slowed COVID-19 in East Asia." Havard Business Review. Accessed 12.09.2020 (https://hbr.org/2020/04/how-digital-contact-tracing-slowed-COVID-19-in-east-asia)

9 European Union. " Tracking Mobile Devices to Fight Coronavirus." Accessed 13.09.2020 (https://www.europarl.europa.eu/RegData/etudes/BRIE/2020/649384/EPRS_BRI (2020)649384_EN.pdf

10 University of Cambridge. "FluPhone: Disease Tracking by App." Accessed.13.09.2020 (https://www.cam.ac.uk/research/news/fluphone-disease-tracking-by-app)

11 Erikson, S. L. "Cell Phones ≠ Self and Other Problems with Big Data Detection and Containment During Epidemics." [In eng]. Med Anthropol Q 32, no. 3, 2018, pp. 315-39.

privacy infringement. Therefore, countries and international organizations should formulate national and international policies on access to people's personal information during the epidemic and other emergencies.

Personal protective measures against COVID-19 and prevention of transmission of other respiratory infections

After the SARS-CoV-2 virus emerged in Wuhan in late December and began spreading to different regions, countries enforced community measures to prevent the spread of the virus and advised citizens to use personal protective measures against the coronavirus disease. Protective measures such as social distancing, wearing facemasks, hand hygiene, school closure, and restriction of mass gatherings were effective in lowering the epidemic curve. Countries that moved swiftly to adopt and enforce these measures reduced the further spread of the SARS-CoV-2 virus. In contrast, countries that adopted these measures after the virus had already spread in the population reported higher numbers of COVID-19 cases, hospitalizations, and COVID-19-related fatalities.

The effectiveness of non-pharmaceutical measures in preventing transmission of COVID-19 disease has caused researchers to investigate the potential impact of these measures on the transmission of other respiratory infections. For example, influenza cases during the 2019-2020 flu season were lower after the novel SARS-CoV-2 virus emerged, and people began to use personal protective measures[12],[13]. Indeed, the transmission of both the SARS-CoV-2 virus and influenza virus is majorly through the respiratory route, and efforts to prevent the spread of one disease can potentially prevent transmission of the other. Studies are underway to provide further evidence of the effect of preventive measures against COVID-19 in preventing influenza, influenza-like illnesses, and other respiratory infections.

Therefore, the voluntary use of personal protective measures such as facemasks and hand hygiene during flu season should be encouraged beyond the COVID-19 pandemic to prevent the spread of other respiratory infections, which continue to cause morbidity and mortality globally. According to the Centres for Disease Control and Prevention (CDC), influenza alone caused more than twenty-four thousand deaths in the United States during the 2019-2020 flu season. Thus, personal protective measures have the potential of complementing the annual influenza vaccine available for the circulating influenza virus strain.

COVID-19 Vaccine Development and Access

Although non-pharmaceutical measures such as social distancing, wearing facemasks, hand hygiene, contact tracing, and quarantine of infected individuals have mitigated the impact of COVID-19, a safe and effective vaccine is necessary to end this pandemic. To date, there is no effective targeted treatment for COVID-19 disease, and researchers

12 Itaya, Furuse, and Jindai. "Does COVID-19 Infection Impact on the Trend of Seasonal Influenza Infection? 11 Countries and Regions, from 2014 to 2020." Int J Infect Dis 97, 2020, pp. 78-80.

13 Centers for Disease Control and Prevention. "2019-2020 U.S. Flu Season: Preliminary Burden Estimates." Accessed 13.09.2020. (https://www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm)

around the world are continuously working to develop a safe and effective vaccine. Developing an effective vaccine during previous epidemics took several years. For example, the vaccine against the Ebola virus was licensed by the European Union five years after the virus emerged in West Africa in 2014[14]. However, several pharmaceutical companies have developed COVID-19 vaccine candidates ten months after COVID-19 disease emerged[15]. This success is due to international collaboration and improved technology in vaccine development. Indeed, after the sequence of the SARS-CoV-2 viral genome was shared in January 2020, researchers around the world began studies to produce a vaccine. As of March 2021, several vaccines have been approved for mass administration. Resource-rich countries donated billions of dollars to the development of COVID-19 vaccines and purchased the first doses of successful vaccines[16]. On the other hand, some low and middle-income countries, which cannot purchase the COVID-19 vaccines, have collaborated with countries and companies producing the vaccines by participating in clinical trials to secure their share of vaccine doses if the clinical trials produced positive outcomes.

However, the majority of low and middle-income countries face uncertainty in the distribution of a successful vaccine and rely on international organizations such as the World Health Organization to lobby for their vaccine acquisition. For example, the WHO called for equitable distribution and access to future COVID-19 vaccines. Therefore, stakeholders need to look at distribution and access to COVID-19 vaccines holistically and formulate international policies and agreements early to protect populations living in low and middle-income countries from the potential lack of access to the future COVID-19 vaccine.

IV. Conclusion

The COVID-19 pandemic has negatively affected nearly all sectors globally. It has served as a wake-up call for countries to prioritize healthcare and ensure that citizens are protected from potential future disasters. Furthermore, the pandemic has revealed inadequacies of current healthcare and surveillance systems set up by governments and challenged researchers to come up with innovative methods of detecting and containing future epidemics. Governments should consider the health of citizens as national security and treat any threats to national and global public health as an emergency, requiring immediate attention. Health systems during the post-COVID-19 periods ought to be more resilient, accessible by the marginalized members of the community, and affordable. Governments should take drastic measures to protect the health of the global population during and beyond the COVID-19 pandemic. This paper, therefore, recommends the following short, medium-term, and long-term measures that will enable a better healthcare delivery system, disease surveillance, and vaccine access during and after the coronavirus pandemic.

1. Strengthening existing and developing new public health systems. Robust primary healthcare systems protect communities from diseases and potential disasters. Lack of streamlined public health systems during the COVID-19 pandemic has caused the SARS-CoV-2 virus to spread undetected in communities resulting in untimely government response. Consequently, massive infections and hospitalizations due to coronavirus disease were reported. The government investment in the health system would mean that there would be timely detection and containment of epidemics as well as healthcare of the population.

2. Ensure universal healthcare to all. Community access to quality and affordable healthcare ought to be a priority of all governments. During the COVID-19 pandemic, people without healthcare insurance have been the hardest hit. Furthermore, countries, where all citizens had access to universal healthcare care, experienced a lower negative impact of the pandemic when compared to countries where healthcare was unaffordable to the majority of the population. This long-term measure will improve the health and well-being of the global population.

3. Improve infectious disease surveillance systems. Surveillance of infectious disease ensures early detection and containment of outbreaks and monitoring of trends in the transmission of disease. For example, countries such as China, Austria, UK, and South Korea have used big data to track COVID-19 infection hotspots in real-time. However, national and international policies and frameworks should be formulated to protect the privacy of citizens and ensure that governments do not use personal information of citizens for purposes other than disease surveillance.

4. Accessibility of the future COVID-19 vaccine. The WHO has emphasized the need for fair distribution of the vaccine. International policies that ensure low and middle-income countries access the coronavirus vaccine ought to be formulated early. Moreover, governments should conduct campaigns to increase public confidence in the future COVID-19 vaccine and protect citizens from the potential financial exploitations in receiving the vaccine.

5. Promote community health by encouraging voluntary personal protective measures against respiratory infections beyond the COVID-19 pandemic. Researchers have shown that measures such as hand hygiene, wearing a face mask and social distancing reduce the incidence of respiratory infections that still cause morbidity and mortality in communities. People should use these measures voluntarily during certain circumstances to protect themselves and prevent the transmission of respiratory infections. This personal responsibility will prevent infections, hospitalizations, and deaths associated with respiratory infections.

14 European Union. "Vaccine against Ebola: Commission grants first-ever market authorization." Accessed 13.09.2020 (https://ec.europa.eu/commission/presscorner/detail/en/ip_19_6246)

15 Corum et al. "Coronavirus Vaccine Tracker." The New York Times. Accessed 13.09.2020 (https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html)

16 Koirala et al. "Vaccines for COVID-19: The Current State of Play." [In eng]. Paediatr Respir Rev 35, 2020, pp. 43-49.

6. This brief paper sought to examine the status of health systems, coronavirus disease surveillance, and COVID-19 vaccine access during and beyond the pandemic. It examined the shortcomings of most health systems in dealing with this pandemic. Moreover, it investigated the developments made in the COVID-19 vaccine clinical trials. It also showed some of the surveillance methods used during the pandemic to track infection hotspots. Finally, the paper examined the impact of personal protective measures against COVID-19 on other respiratory infections. The author argues that lessons can be learned from the current pandemic to improve the status of health systems, access to healthcare and vaccines, and disease surveillance during and beyond the coronavirus pandemic. For good national and global health, the health of individuals must be well protected from all current and future threats.

Guidelines and regulations: All the procedures including design, analysis, interpretation, and reporting of the study findings were performed according to the scientific guidelines

Competing interests: The author declare no conflicts of interest.

Authorship contributions: ANM designed the study, analyzed the findings, prepared, and revised the manuscript

Funding: The author did not receive any funding for this research.

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Study of Molecular Docking And Evaluation of Adme Properties of Obtained Compounds Such as Podofilox as Glucocorticoid Receptor's Activator Which is Effective in the Treatment of COVID-19

Zahra Shahpar*

Abstract

The present study aimed to determine the appropriate compounds as glucocorticoid receptor activators in glucocorticoid therapy in the treatment of patients with coronavirus pneumonia 2019 (COVID-19) And determining Podofilox as the best compound among the studied compounds.

Materials and methods: This research was conducted in a descriptive-analytical manner. To investigate how ligands bind to the active site of the target glucocorticoid receptor (GR), especially the Podofilox ligand. Initially, the three-dimensional structure of the target was analyzed using Chemira software and optimized in terms of energy.

Özet

Bu çalışma, koronavirüs pnömonisi 2019 (COVID-19) hastalarının tedavisinde glukokortikoid tedavisinde glukokortikoid reseptör aktivatörleri olarak uygun bileşikleri belirlemeyi ve incelenen bileşikler arasında en iyi bileşik olarak Podofilox'u belirlemeyi amaçlamaktadır.

Materyaller ve yöntemler: Bu araştırma betimsel-analitik bir şekilde yürütülmüştür. Ligandların hedef glukokortikoid reseptörünün (GR) aktif bölgesine, özellikle de Podofilox ligandına nasıl bağlandığını araştırmak. Başlangıçta hedefin üç boyutlu yapısı Chemira yazılımı kullanılarak analiz edildi ve enerji açısından optimize edildi.

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Docking studies were performed using auto dock_vina software and docking results were analyzed using molegro virtual docker software. In the final stage, after selecting Podofilox as a ligand, we obtain the ADME properties of the Podofilox compound.

Research Findings: Based on the results of docking, the best compound suitable for connecting to the target Podofilox the best docking results were related to this compound. This combined with the most negative level of binding energy showed a greater tendency to bind to the active site of the target glucocorticoid receptor (GR).

Discussion: Finally, according to the results of docking and ADME studies, it can be concluded that Podofilox can be one of the GCR target activators and help in the treatment stage of COVID-19

Keywords: *Molecular Docking, COVID-19 Disease, Target, Ligand, Compound*

Yerleştirme çalışmaları auto dock_vina yazılımı kullanılarak gerçekleştirildi ve yerleştirme sonuçları molegro sanal docker yazılımı kullanılarak analiz edildi. Son aşamada, bir ligand olarak Podofilox'u seçtikten sonra, Podofilox bileşiğinin ADME özelliklerini elde ederiz.

Araştırma Bulguları: Yerleştirme sonuçlarına göre, hedef Podofilox'a bağlanmak için en uygun bileşik, en iyi yerleştirme sonuçları bu bileşikle ilgiliydi

Bu, en negatif bağlanma enerjisi seviyesiyle birleştirildiğinde, hedef glukokortikoid reseptörünün (GR) aktif bölgesine bağlanma konusunda daha büyük bir eğilim gösterdi.

Tartışma: Son olarak, yerleştirme ve ADME çalışmalarının sonuçlarına göre, Podofilox'un GCR hedef aktivatörlerinden biri olabileceği ve COVID 19'un tedavi aşamasında yardımcı olabileceği sonucuna varılabilir.

Anahtar kelimeler: *Moleküler Yerleştirme, COVID-19, Hedef, Ligand, Bileşik*

*

I. Introduction

In December 2019, an outbreak of pneumonia caused by a novel coronavirus occurred in Wuhan, Hubei province, and has spread rapidly throughout China, with an ongoing risk of a pandemic1. After virus identification and isolation, the pathogen for this pneumonia was originally called 2019 novel coronavirus (2019-nCoV)2 but has subsequently been officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the WHO.

No therapies have been shown effective except dexamethasone, a glucocorticoid that was recently proved to be the first life-saving drug in this disease. Remarkably, around 20% of infected people develop a severe form of COVID-19, giving rise to respiratory and multi-organ failures requiring sub-intensive and intensive care interventions. This phenomenon is due to an excessive immune response that damages pulmonary alveoli, leading to a cytokine and chemokine storm with systemic effects. Indeed, glucocorticoids' role in regulating this immune response is controversial, and they have been used in clinical practice in a variety of countries, even without a previous clear consensus on their evidence-based benefit. Indeed, around 20% of infected patients develop Acute Respiratory Distress Syndrome (ARDS)

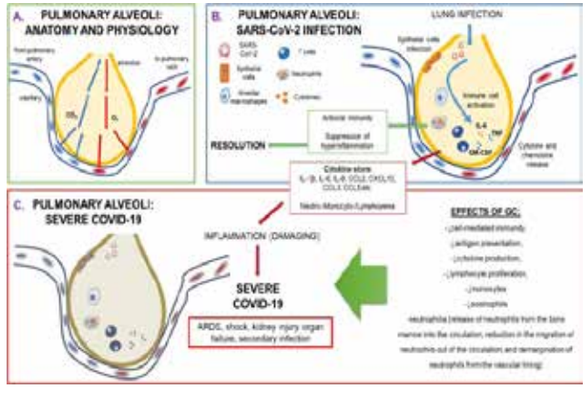


Fig. 1. Physiology and pathophysiology of pulmonary alveoli during SARS-CoV-2 infection

The genomic mechanism of action is mediated by the GC receptor (GCR) that generates the majority of anti-inflammatory and immunosuppressive effects. GCR is localized within the cytoplasm, and the complex generated after its binding with the GC translocates into the nucleus, where it inhibits the transcription of the genes involved in the activation of leukocytes and the regulation of the function of epithelial, stromal, and endothelial cells.

This generates a reduction of pro-inflammatory cytokines, chemokines, and molecules of cellular adhesion and of other enzymes that are involved in the inflammatory response. Specifically, the effects are a reduction of the recruitment of white blood cells (including monocytes-macrophages but excluding neutrophils) into affected areas, further inhibiting the release of chemotactic signals, and the expression of cytokines regulating the function of granulocyte monocyte-colony stimulating factor (GM-CSF)) and fibroblast proliferation.

Therefore, we can reduce the inflammatory effects in the body by activating the GCR target by a ligand that has the best docking and ADME results, and the studies performed can have an impact on the fight against COVID-19.

One of the promising technologies in the process of drug development and expansion is drug-assisted drug exploration.

Given that bioinformatics and information technology are advancing at an unexpected pace today, their importance in the fields of medicine, biotechnology and pharmacology can not be denied, Therefore, at present, almost traditional methods of drug synthesis are abandoned, and through computer and bioinformatics calculations with the least

cost, the drug is designed and its performance in the computer environment is examined, and finally, if appropriate, leading to drug synthesis in It becomes a laboratory environment.

A prime example of the importance of using computers in drug design is a 2010 study by Rahrig et al. In this work, using docking, dioxygenase inhibitors were developed, which are 2, 3 new for indoleamine enzyme involved in cancer.

As a result of using computer methods, it is possible to study the interaction of chemical compounds with proteins before conducting experimental experiments, and after selecting the compounds that are most likely to bind to the target, they can be tested in the laboratory or the system. Examined live. How the ligand binds to the target structure is studied to design new ligands with a greater tendency to react with this molecule. This method is used when the large structural details of the target molecule are available, the docking process leads to an understanding of the relationship between the activity structure of known ligands and the level of their molecular interaction with the active site of the target.

This computational study aims to design an inhibitor with higher inhibitory power than other previous inhibitors by molecular docking.

II. Materials and Methods

In this study, computer methods such as docking have been used to discover new compounds. To investigate and identify the connection of exactly 22 compounds to the active site of GCR. Before docking, you must first determine the best active position in the GCR target. For this purpose, we referred to the UNIPROT database.(http://www.uniprot.org/)

Among the different parts of the third structure based on the criteria for selecting the structure, namely: We chose the lowest resolution, the highest sequence, the lowest number of chains for the best part. This part of the target, which is itself a protein called 4UDD, was selected as the best part of the target, and studies on the third structure of 4UDD were selected.

We were also able to check the 3D structure and complete specifications of the 4UDD from the RCSB PDB database. From the structures, we chose 4UDD, which is a single chain with a resolution of 1.80 A and a suitable number of amino acids. Also in the 4UDD structure, the R-value free criterion is equal to 0.224 A and the R-value work criterion is equal to 0.213 A. Both criteria are close to each other and also close to the resolution criterion which is equal to 1.80 A. (RCSB PDB, http://rcsb.org)

In the next step, the third structure of 4UDD, which was taken from the PDB database, was evaluated in the Procheck errat database based on the criteria of the Ramachandran diagram.

According to Ramachandran criteria, the 4UDD 3D structure needs to be optimized. We use the RAMACHANDRAN PLOT criterion to confirm whether the selected 3D structure of 4UDD has a suitable structure or not. For this purpose, we enter the PDB format of the 4UDD target protein in the PROCHECK ERRAT database and analyze the results of the Ramachandran diagram.

The Ramachandran diagram shows the psi and phi angles for the placement of amino acids. This diagram shows the permitted areas in red color. Amino acids in red areas give the protein a more favorable structure. Therefore, by holding the 4UDD sequence in Fasta format from the PDB database, we were able to optimize the 4UDD 3D structure in the SWISS-MODEL database.

(http://swissmodel.expasy.org/.)

After reviewing the structures based on the overlap with other templates and also reviewing the best GMQE and QMEAN, we selected the most suitable 3D structure for 4UDD.

We were able to get the structure in the right proportion from the Ramachandran diagram.

Then the 3D structure of 4UDD in terms of druggability in the database (https: // www.zbh.uni -hamburg.de) was reviewed and the results were obtained based on the following table. According to the results in the table below, two packets of the 4UDD target have a druggability score above 80%and The best score is for p1, which is equal to 86%.

Name	Volume	Surface	Drug score
	A^3	A^2	
P_0	1509.44	1494.3	0.81
P_1	497.66	609.39	0.86
P_2	153.6	340.49	0.24
P_3	120.38	311.38	0.25
P_4	117.5	277.92	0.26

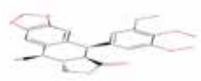
Table 1: Based on this table, the druggability of 4udd protein is examined and according to the data, based on this protein, it has 5 packets to receive ligand, which is the best position in terms of drug reception, position p0 with 81% and position P1 with 86%.

In the next step in the library of chemical compounds, we looked for suitable compounds to replace as ligands for this purpose, we used the zinc15 database (http://zinc15.docking.org.)

From the total of 3155 combinations found for the 4UDD target, we were able to reduce the number of combinations to 22 by the in vivo and biogenic filters in this database.

In these filters, we used in vivo and biogenic filters. In vivo refers to when research or work is done with or within an entire, living organism. Examples can include studies in animal models or human clinical trials and a biogenic substance is a product made by or of life forms. The term encompasses constituents, secretions, and metabolites of plants or animals. In the context of molecular biology, biogenic substances are referred to as biomolecules.

Nomber	**Mol Formula**	**logP**	**Weight (kda)**
1	C22H28O3 	4.063	340.463
2	C20H24O2 	3.613	296.41
3	C21H28O2 	3.883	312.453
4	C20H30O2 	4.269	302.458
5	C21H28O5 	1.558	360.45
6	C24H32O4S 	4.852	416.583

7	C22H22O8 	2.409	414.41
8	C22H29FO5 	1.896	392.467
9	C23H30O6 	2.561	402.487
10	C22H30O5 	1.804	374.477
11	C23H29ClO4 	4.752	404.934
12	C21H28O2 	3.883	312.453
13	C22H27NO2 	4.221	337.463
14	C25H31F3O5S 	4.43	500.579
15	C24H30F2O6 	2.367	452.494

16	C23H31FO6 	2.445	422.493
17	C21H30O2 	4.724	314.469
18	C24H34O4 	4.655	386.532
19	C21H30O3 	3.838	330.468
20	C21H30O5 	1.782	362.466
21	C21H28O2 	4.644	312.453
22	C19H28O2 	3.879	288.431

Table 2: This table shows the composition information we obtained from the zinc15 database. New DOCX Document.docx

Name	Chemical Formula	Weight(kda)
Amcinonide	$C_{28}H_{35}FO_7$	502.5717
Betamethasone	$C_{22}H_{29}FO_5$	392.4611
Prednisone	$C_{21}H_{26}O_5$	358.4281

Table 3: In this data section, we selected 3 drugs related to the GCR target that has been approved by the FDA and recently used for COVID-19 as a benchmark and shown in the table above.1.docx

To test the results of the compounds, we use three drugs that have already been approved by the FDA for the 4UDD target. We also used 3 FDA-approved drugs for GCR protein to test the test and listed their properties in the table above.

The two-dimensional structure of the desired ligands is then plotted by ChemBioDraw Ultra to minimize the energy of the molecules.

The conformers of all 22 compounds with the lowest energy were then transferred to the docking stage.

In the next step, using chimera software, we removed cofactors and solvent molecules, water, and ions from the 4UDD protein structure, minimized the structure energy, and finally optimized the target structure for docking operations. For example, in the preparation of molecules, by reducing the energy, we were able to reduce the energy from [90.88]kcal/mol to [50.146] kcal/mol by bringing the residues closer to the ligand.

After removing unnecessary parts in the target and optimizing the target and ligands we started the docking operation. After removing unnecessary parts in the target and optimizing the target and ligands we started the docking operation perform docking operations using Autodock_vina Software.

A feature of good software is having high accuracy to get a reliable result as well as high speed. Compared to docking software, this program almost doubles the speed of the 4-molecule autodock, as well as improves the accuracy of the pairing mode predictions.

The binding of the molecules was simulated with Autodock_vina software with 73% accuracy[19][20]. Since the structure of the target is balanced at 310 ° K and was at its most stable, and the simulation of the connection by applying the flexibility of the target receiver is very costly in terms of time and computation. The molecular structure of the receptor can be assumed to be flexible and rigid.

In the docking step, we entered 22 ligands of Table 2 and also the drugs mentioned for the test in Table 4 into the Docking software. Then the docking results were checked by MVD software. Each of the ligands can have different binding energy to the target in different states, called poses, in different directions. Poses show different modes of attachment of ligands to the target and may have several similarities.

Ligands posed together, in which case their best energy is displayed along with the number of repetitions in another column. The results were about 115 poses for 22 ligands in Table 2 and their binding energy. As mentioned earlier, the best energy is the lowest energy.

Gibbs free energy is a thermodynamic quantity that indicates the degree to which a reaction occurs spontaneously. It is possible to perform a thermodynamic process when the Gibbs free energy changes are negative

After examining the docking energy of 22 ligands in Table 2 and examining the energy of 115 different poses of the ligands, we selected 12 of their most negative energies which are shown in the table below:

Ligand's name	Docking energy (kcal/mol)
[00]ZINC000001849528	_ 114.696
[01]ZINC000001849528	_ 98.326
[00]ZINC000003814395	_ 103.598
[00]ZINC000003861599	_ 123.477
[01]ZINC000003861599	_ 120.345
[03]ZINC000003861599	_ 119.627
[02]ZINC000003861599	_ 116.502
[00]ZINC000003861806(Podofilox)	_ 131.569
[01]ZINC000003861806	_ 128.690
[00]ZINC000003881958	- 110.367
[00]ZINC000003977981	- 98.693
[00]ZINC000019132424	- 100.232

Table 4: The results of docking poses of the compounds in Table 2 are shown above along with their docking energy. The best pose is marked in yellow, which corresponds to one of the x poses 2.docx

Then docking of 3 drugs approved in Table 3was performed. From the 35 poses created, we selected 3 of the most negative energies which are shown in the table below:

Ligand's name	Docking energy(kcal/mol)
Amcinonide	_ 110.239
Betamethasone	_ 108.830
Prednisone	_ 106.932

Table 5: This table shows the docking results of the 3 drugs we selected in Table 3 for the test, along with their docking energy.3.docx

The best-medicated pose is Amcinonide and is about [-110.239] kcal/ mol While the best poses of the ligands in Table 2 are related to the ligand [00] ZINC000003861806

By entering this code in the ZINC15 database, we were able to obtain the information and name of this combination. Its name is (Podofilox) and its docking energy is about [- 131.569] kcal/mol. Also, the energy of the remaining poses of the ligands in Table 2 is more negative than the most negative energy of the poses of the drug ligands in Table 3 that mentioned earlier, the best energy is the lowest energy, which not only makes the connection operational but also gives the structure stability. Up to this point, considering that the docking energy of the test ligands was more appropriate and smaller than the confirmation ligands, it can be expected that the test ligand and target binding is a suitable bond.

In selecting the appropriate ligand, the properties of pharmaceutical compounds must be considered!

The term ADME should be considered. ADME is the abbreviation for Absorption, Distribution, Metabolism, and Excretion. Pharmacokinetics is a specific branch of pharmacology that studies what the body does to a drug. Pharmacokinetic studies evaluate:

- The rate that a chemical is absorbed and distributed
- The rate and pathways of drug metabolism and excretion
- The plasma concentration of a drug over time

ADME is the four steps of pharmacokinetics. Let us break down what each of these steps involves.

The first indicator is the polar surface area, abbreviated TPSA

If TPSA is <140 A2, the drug is suitable for absorption in the digestive tract, and if TPSA is <70 A2, the drug is suitable for absorption from the blood-brain barrier.

The next indicator is lipophilicity

The partition coefficient, P, is a measure of the differential solubility of a compound in two immiscible solvents. The most commonly used solvent system is octan-1-oil/water. The partition coefficient is the descriptor of lipophilicity for neutral compounds, or where the compound exists in a single form.

LogP = log10 (Partition Coefficient) P=(Compound octand)/(Compound water)

A negative value for logP means the compound has a higher affinity for the aqueous phase (it is more hydrophilic); when logP = 0 the compound is equally partitioned between the lipid and aqueous phases; a positive value for logP denotes a higher concentration in the lipid phase (i.e., the compound is more lipophilic). LogP = 1 means there is a 10:1 partitioning in Organic: Aqueous phases.

The more fat-friendly the drug, the higher it is absorbed in the intestine. It has high metabolite power and little drug interaction so it has little excretion by the kidneys Instead, the more ambitious the drug, the lower the absorption but the greater the dispersing power Stable or low metabolites and therefore have high renal excretion

The next indicator is the solubility of the drug

Based on the relationship between solubility and lipophilicity are related to each other

Log s = 0.5 _ 0.01 × (m.p C0 _ 25) _ Log p

We will have solubility based on the ruler

Insoluble < -10 < poorly < -6 < moderately < -4 <soluble < -2 <very <0 < highly

Due to the calculated cLogP amount distribution of more than 3000 drugs available in the cLogP market should not be more than 5, Because by increasing it, all the pharmacophore properties of the drug decrease.

Solubility also affects the absorption and distribution of the drug. The estimated solubility (LogS) of 80% of the drugs on the market is greater than -4.

Naturally, the most suitable case is the most optimal and economical model, so in choosing the drug, we usually look for the most solvent one. Finally, the last index is

the SA score, which means synthetic accessibility score, meaning that the drug must be easily synthesized or the raw materials of the drug must be available. According to the mentioned explanations, we determine the properties of selected ligands and confirmation ligands.

To obtain the ADME results of the selected compounds with the most negative docking energy, we used the Admetsar database.

After reviewing the criteria of Lipinski's law No. 5, we exclude several compounds that have a TPSA> 70, because according to the rules mentioned above, compounds with this property can cross the blood-brain barrier.

We selected the best combinations according to Lipinski's conditions and displayed them in the table in pink.

Ligand's name	TPSA	Log $P_{o/w}$	Log S	Synthetic accessibility
ZINC1849528	43.37 Å²	3.90	-4.11	5.08
ZINC3814395	37.30 Å²	3.71	-3.81	5.12
ZINC3861599	85.74 Å²	3.84	-4.14	5.94
ZINC3861806 (Podofilox)	92.68 Å²	2.33	-3.71	4.64
ZINC3881958	46.26 Å²	3.90	-4.41	5.50
ZINC3977981	93.06 Å²	2.64	-4.08	6.02
ZINC19132424	34.14 Å²	4.03	-4.26	4.79
Amcinonide	99.13 Å²	3.48	-4.94	6.58
Betamethasone	94.83 Å²	2.14	-3.36	5.47
Prednisone	91.67 Å²	1.84	-2.85	5.13

Table 6: In this table, the ADME properties of the combinations from Tables 2 and 3 that had the best docking energy were selected. After reviewing the ADME properties of the combinations, we selected the best combinations and displayed them in pink4.docx

According to what can be seen in the table above, the ADME properties of compound Podofilox have similar properties to the three drugs in Table 4 and even have better

docking energy than these three drugs, so it can be concluded that compound Podofilox can be one of the activating ligands of GCR target Be.

III. Discussion and Results

Since the outbreak of the corona-virus pandemic, more than 100 articles have been published to investigate the effects of different drugs and compounds on the virus. The method of drug design with bioinformatics tools underlies the design of most drugs and vaccines, so it is recognized as one of the stages of pharmacy. If we want to look at the issue from a comparative point of view, we can change the software or databases used in this discussion. In addition, because the coronavirus pandemic is a new pandemic, the study of compounds and drugs at the bioinformatics level was compared as much as possible in terms of methods and materials. Molecular docking is one of the key methods of computational chemistry that is commonly used in the drug discovery process. The minimum amount of energy or optimization is an important technique in molecular bonding calculations. Complex optimization allows the ligand to gain the least energy position at the active site of the protein. Using molecular docking, information can be obtained such as where the ligand binds to the protein, the role of each of the protein amino acids, or the ligand atoms in the interaction and binding energies. It is also possible to evaluate the interaction of two proteins with each other or with this technique. Ligand DNA is performed by finding the best orientation of the ligand towards the active site of the receptor and estimating the binding energy of two important aspects of the algorithm.

The research findings show that according to Table 6, the best compounds are shown in pink, of which 3 are related to the compounds in Table 3 and 3 are related to the drugs in Table 4, although all 3 drugs in Table 4 are among the best ligands. However, compound Podofilox in Table 3 has both better docking energy and more suitable Lipinski properties than drugs approved for the GCR target. Although bioinformatics calculations are the first step for drug design and the drug designed by bioinformatics must go through clinical stages and be approved by various tests, but in the computer design phase of the drug, according to text information, tables and references, it can be concluded that combination Podofilox, it could be the next drug for the GCR target and be effective against COVID-19 disease.

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Antiviral Drugs and Antiviral Properties Used in the Treatment of COVID-19

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Abstract

The COVID-19 pandemic, which has spread all over the world and dragged many people to death, has been continuing for at least 9 months since its inception. At this time, the researchers have not found a new effective drug against SARS CoV-2. Some pre-existing drugs are used in the treatment of COVID-19, including some antivirals. It is aimed to explain only the antiviral effects of drugs against COVID-19 with this study. Remdesivir acts against COVID-19 by causing premature termination of the RNA chain of the virus. Favipiravir, which inhibits RNA-dependent RNA polymerase, is highly effective against COVID-19. Lopinavir / Ritonavir inhibitors the protease enzymes of the virus, furthermore Ritonavir increases the half-life of Lopinavir. Ribavirin induces the genome mutation of the virus

Özet

COVİD-19 salgını başlamasının üzerinden bir seneden fazla vakit geçmesine rağmen hala hızla yayılmaya devam etmektedir. Bu süre zarfında SARS CoV-2'ye karşı etkili yeni bir ilaç geliştirilememiştir. Bazı antivirallar dahil önceden bulunan bazı ilaçlar COVİD-19 tedavisinde kullanılmaktadır. Bu derlemede sadece COVİD-19'a karşı antiviral etki gösteren ilaçların değerlendirilmesi amaçlanmıştır. Remdesivir, COVİD-19'a karşı virüsün RNA zincirinin erken sonlandırılmasına neden olarak etki göstermektedir. RNA'ya bağlı RNA polimerazi inhibe eden favipiravir, COVİD-19'a karşı oldukça etkilidir. Lopinavir/ Ritonavir virüsün proteaz enzimlerini engellemekte, ayrıca Ritonavir, Lopinavir'in yarılanma ömrünü artırmaktadır. Ribavirin virüsün genom mutasyonunu indüklemekte ve normal replikasyonunu inhibe etmekte ve RNA'ya

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and inhibitors of normal replication and inhibitors of RNA-dependent RNA polymerase. Interferon exerts antiviral effects on various cell types and through an adaptive immune response. Chloroquine and Hydroxychloroquine inhibitor pH-dependent viral replication by increasing the endosomal pH, thus preventing or slowing the spread of the virus to other host cells. Azithromycin increased hydroxychloroquine's antiviral effect against COVID-19. Ivermectin has been identified as an inhibitor of the interaction of human immunodeficiency virus-1 (HIV-1) with the integral protein and importin IMP) α/β1 heterodimer responsible for nuclear import. Nitazoxanide acts by inhibiting the N protein expression of the virus; suppressing pro-inflammatory cytokines and the production of IL 6; preventing the replication of DNA and RNA viruses. As a result; Remdesivir, Favipiravir, Lopinavir/Ritonavir, and Ribavirin; Chloroquine and hydroxychloroquine, the drugs for malaria; Azithromycin in the macrolide antibacterial group showed a positive antiviral effect both pre-clinically and clinically against COVID-19. It is thought that ivermectin and nitazoxanide can be effective against COVID-19 based on antiviral effects and preclinical studies.

Keywords: *COVID-19, SARS CoV-2, Remdesivir, Favirpiravir, Chloroquine, Hydroxychloroquine*

bağımlı RNA polimerazı da engellemektedir. İnterferonlar, çeşitli hücre tiplerinde adaptif bağışıklık tepkisi aracılığı ile antiviral etki göstermektedir. Klorokin ve Hidroksiklorokin, endozomal pH'yı artırarak pH'ya bağımlı viral replikasyonu inhibe etmekte ve böylece virüsün başka konak hücrelere yayılmasına engel olmakta veya yavaşlatmaktadır ve Tümör Nekroz Faktör α (TNF-α) ve IL6 salınımını baskılayarak sitokin fırtınasını engellemektedir. Azitromisin COVİD-19 hastalarda hidroksiklorokin ile kombine kullanıldığında antiviral etkisini artırmıştır. Nitazoksanid, virüsün N protein ekspresyonunu inhibe ederek; proinflamatuvar sitokinleri ve interlokin 6'nin üretimini baskılayarak; RNA ve DNA virüslerin replikasyonunu engelleyerek etki göstermektedir. Sonuç olarak incelenmiş çalışmalara ve antiviral özelliklere göre; remdesivir, favipiravir, lopinavir/ritonavir ve ribavirin; sıtma ilacı olan klorokin ve hidroksiklorokin; azitromisin hem preklinik ve hem klinik olarak COVİD-19'a karşı olumlu antiviral etki göstermiştir. Ivermektin ve nitazoksanidin ise antiviral etki mekanizması ve preklinik çalışmalar esas alınarak COVİD-19'a karşı etkili olabileceği düşünülmektedir

Anahtar kelimeler: *COVID-19, SARS CoV-2, Remdesivir, Favirpiravir, Chloroquine, Hydroxychloroquine*

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I. Introduction

The novel type of coronavirus (SARS-Cov-2) that causes serious respiratory tract infection first started in Wuhan, China in December 2019 and spread almost all over the world in a short time. In February 2020, it was officially named COVID-19 by WHO. According to the WHO report, it is said to be of animal origin and is generally transmitted from human to human by droplets.

The virus isolated from COVID-19patients belongs to the beta coronavirus genus, which causes severe acute respiratory syndrome (SARS-Cov) and Middle East respiratory syndrome (MERS-Cov) from simple cold sores. Although asymptomatic, COVID-19patients have mild symptoms, fever, cough, shortness of breath, diarrhea, headache, muscle and joint pain. Severe cases can result in pneumonia, severe respiratory failure, renal failure and death. The unknown characteristics of the disease make it difficult to prevent and treat the pandemic with certainty.

At least a year after the onset of the epidemic, there is still no definitive treatment. However, some pre-existing drugs and treatment methods are being tried and used to reduce the activity of the virus, minimize and improve the damage it causes and treat the symptoms. In this review, it is aimed to evaluate pharmacologically the antiviral properties of drugs used in COVID-19 disease. Antiviral, some antimalarial and antibacterial, some anti-inflammatory drugs, ACEi drugs and some biological agents are used in the treatment of COVID-19. In this review, only antiviral effective drugs used in the treatment of COVID-19 are discussed under the headings of RNA-dependent RNA polymerase inhibitors, Protease promoters, Ribavirin, Interferons, Chloroquine, Hydroxychloroquine, Azithromycin, Ivermectin and Nitazoxanide.

II. RNA-Dependent RNA Polymerase Inhibitors

Remdesivir

Remdesivir is nucleoside analogue antiviral drug. İt inhibits the replication of the virus by inhibiting RNA-dependent RNA polymerase enzyme. In other words, it binds to the RNA chain of the virus and causes early termination of the RNA chain of the virus[1]. Remdesivir is known as an experimental drug that exhibits antiviral activity against RNA viruses, including SARS and MERS. Remdesivir provided rapid recovery in COVID-19 patients in some precautionary and clinical studies. Based on this preliminary evidence, the FDA approved the use of remdesivir in the treatment of hospitalized COVID-19patients on May 01, 2020[2].

Wang et al. concluded that remdesivir binds to RNA of viruses, including SARS and MERS, causing early termination of the RNA chain of the virus[3]. Jean TP et al. proved that remdesivir induced replication of SAR-COV and MERS-Cov viruses in human airway epithelial cell cultures. In addition, in this study, remdesivir was found to have a broad-spectrum antiviral effect against coronaviruses circulating in human lung cells. Remdesivir significantly reduced the viral load of SARS-Cov virus in its prophylactic and therapeutic use in the mouse model[4]. Elfiky et al. demonstrated that remdesivir binds to RNA-dependent RNA polymerase enzyme for a long time and frequently compared to other drugs and also suggested that GTP may be a new target for SARS-Cov-2 inhibition[5].

1 Meda Venkatasubbaiah, P. Dwarakanadha Reddy and Suggala V. Satyanarayana, "Literature-based review of the drugs used for the treatment of COVID-19," Current medicine research and practice, 10/3 (2020): 101, accessed July 10, 2020,

2 Nikita Mehta et al., "Pharmacotherapy in COVID-19; A narrative review for emergency providers," The American journal of emergency medicine 38/7 (2020):1489.

3 Manli Wang et al., "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro," Cell research 30/3 (2020):269.

4 Shio Shin Jean et al., "Treatment options for COVID-19: The reality and challenges," Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi 53/3 (2020): 436.

5 Abdo A Elfiky, "Ribavirin, Remdesivir, Sofosbuvir, Galidesivir, and Tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): A molecular docking study," Life sciences 253 (2020): 117592.

According to Holshue et al., a 35-year-old COVID-19 severe patient was administered intravenous remdesivir and continued until discharge. On the 10th day, the virus load decreased in the respiratory fluid of the patient and the COVID-19 test was negative on the 12th day. During this time, the patient also recovered clinically[6]. In a randomized, double-blind, placebo-controlled, and multicenter study in 10 hospitals in Hubi, China, 158 of 237 patients with COVID-19 positive pneumonia were administered 100mg remdesivir intravenously every day for 10 days starting with 200mg on the first day, and the remaining patients were given placebo, lopinavir-ritonavir, interferons, and corticosteroids. There was no statistically significant difference in the healing of the patients in two groups. However, there was a numerical acceleration in the clinical recovery of patients receiving remdesivir compared to patients receiving placebo. Further studies are needed to confirm these effects of the drug. However, since SARS-Cov-2 is not a clear active liaison agent, remdesivir is used in the treatment of COVID-19 based on these studies.

The most common side effects of remdesivir are digestive system disorders, transaminase level increase and infusion site reaction. It also stands out as a problem that it is not everywhere in the world and it is expensive[7].

Favipiravir (FPV)

Favipiravir is a nucleoside analogue RNA-dependent RNA polymerase inhibitor antiviral initially designed for the treatment of RNA viruses such as Ebola and influenza[8]. It was approved for influenza infection in Japan in 2014. Favipraivir directly inhibits the replication and transcription of the virus, leading to incorrect binding in newly developing vRNA in the virus. Or RNA inhibits the fusion of nucleotides by binding to the active division of polymerase, thereby preventing the proliferation and transcription of the virus[9]. Approved for COVID-19 treatment in China in March 2020[10].

In a NHP model study by Madelain et al., favipiravir was found to have viral clearance and adaptive donation response. Accordingly, it is said that it may be an option in the treatment of emerging viral diseases.

Preliminary results of clinical trials in China have shown that favipiravir has promising potential in the treatment of SARS-CoV-2. In a study conducted by Shenzhen's 3rd public hospital in Guangdong, China, the COVID-19 test positive of 35 COVID-19 patients who received favipiravir was negative after four days of treatment and the treatment

6 Michelle L Holshue et al., "First Case of 2019 Novel Coronavirus in the United Statesi," The New England journal of medicine 382/10 (2020): 932.

7 Yeming Wang et al., "Remdesivir in adults with severe COVID-19: a randomized, double-blind, placebo-controlled, multicenter trial," Lancet (London, England) 395/10236(2020): 1572–73.

8 Yan-Rong Guo et al., "The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status," Military Medical Research 7/1 (2020):11.

9 Venkatasubbaiah, Reddy and Satyanarayana, "Literature-based review of the drugs used for the treatment of COVID-19," 106.

10 Wang et al, "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro," 271.

of COVID-19 patients who did not receive favipiravir lasted 11 days. In an open-label comparative controlled study by Cia et al., a group of COVID-19 patients received two doses of 600mg FPV orally every day for 14 days starting with two doses of 1600mg favipiravir on the first day, and another group of COVID-19 patients received two doses of lopinavir (LPV) 400mg and ritonavir (RTV) 100mg daily for 14 days starting on the same day. Both groups of patients received two daily doses of INF- 60μg by inhalation[11]. After 14 days, the efficacy of the treatment was evaluated in terms of viral clearance and chest tomography improvement, and it was found that viral clearance accelerated, and chest tomography improved in patients treated with FPV compared to patients receiving LPV/RTV[12]. Based on these studies, FPV is used in the treatment of COVID-19 patients in accordance with the COVID-19 treatment algorithm of each country. However, more extensive studies are needed, and clinical trials are currently underway worldwide.

Abnormal transaminases, psychiatric symptoms, gastrointestinal discomfort and elevated uric acid in serum are known to be the most common side effects of FPV[13]. FPV has a safer and more positive profile in terms of serious undesirable etiquette. In addition, it is not clear whether it has side effects such as hyper uremia, teratogenicity and QTC lengthening. Therefore, FPV is a reliable and tolerable drug when used for a short time. Chronic use should be used with caution.

III. Protease Inhibitors

Lopinavir-Ritonavir are protease inhibitor antiviral drugs. When both are used in combination, its antiviral activity increases even more. The LPV/RTV combination is typically used in the treatment of HIV. It has also been reported that LPV is effective against coronavirus. LPV and RTV act by inhibiting protease enzymes of the virus[14]. In addition, ritonavir inhibits the metabolism of lopinavir by inhibiting cytochrome P450 and increase half-life.

In a comparative study in mice, LPV/RTV reduced MERS-CoV virus load and improved lung function[15].

According to a 2004 study, viral load decreased, peripheral lymphocyte counts increased, adverse events and death decreased in SARS-CoV patients receiving LPV/RTV and ribavirin in combination with a nucleoside analogue. Patients treated with this combination needed less corticosteroid medication than patients receiving riba-

11 Vincent Madilian et al., "Modeling Favipiravir Antiviral Efficacy Against Emerging Viruses: From Animal Studies to Clinical Trials," CPT: pharmacometrics & systems pharmacology 9/5 (2020): 259.

12 Wang et al., "Remdesivir in adults with severe COVID-19: a randomized, double-blind, placebo-controlled, multicenter trial," 1573.

13 Qingxian Cai et al., "Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study," Engineering (Beijing, China) 6/10 (2020): 1192.

14 C M Chu et al., "Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings," Thorax 59/3(2004): 254.

15 Maria L. Agostini et al., "Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease," mBio 9/2 (2018): 21.

virin alone and the risk of nosocomial infection was reduced[16]. According to the case report published by Han et al., a 47-year-old male COVID-19 patient treated with LPV/RTV 400mg/100mg, methylprednisolone 40mg and recombinant human interferon α 2b 10 million IU recovered in 10 days and the COVID-19 test was negative[17]. In another study, 9 COVID-19 patients who received 400mg/100mg LPV/RTV daily recovered after 4-11 days of treatment and the COVID-19 test was negative. In a randomized, controlled open-label study in China, the mean age of 199 COVID-19 patients aged 49-68 years decreased the viral load of 99 patients in the LPV/RTV group receiving 400mg/100mg LPV/RTV daily and 100 patients in the standard group by the same proportion. More than 64 clinical trials are currently being conducted on this combination worldwide.

The Ministry of Health/Directorate General of Health Services of India has recommended the combination of LPV/RTV for the clinical management of COVID-19 patients at the following doses. LPV200mg/RTV50mg, 2 tablets twice a day LPV400mg/RTV100mg/5ml suspension should be taken twice a day for 14 days or up to 7 days after the symptoms have passed[18].

The Spanish Association of Hospital Pharmacy also recommended LPV/RTV alone or in combination for the antiviral treatment of COVID-19 patients. Accordingly, LPV400mg/RTV200mg should be taken orally every 12 hours or by patients with LPV/RTV+ interferon α 2B COVID-19. Interferon α-2b should be taken twice daily from 100000-200000 IU/kg nebulization route for mild cases and 200000-400000 IU/kg for severe cases for 5-7 days. In addition, 250mcg of interferon beta 1B should be administered subcutaneously every 48 hours for 14 days[19]. Gastrointestinal disorders, metabolic and nutritional disorders, skin and nervous system disorders are the negative effects of LPV/RTV.

IV. Ribavirin

Ribavirine is a guanosine analogue. It is a wide-spectrum antiviral drug. Initially only approved for the treatment of severe respiratory syncytial virus (RSV) in children. Then, the combination of interferon α and ribavirin was also found to be effective against hepatitis C virus[20]. RSV, including hepatitis C, is used in the treatment of viral infections such as influenza (A and B) and viral hemorrhagic fever. Ribavirin induces genome mutation and inhibits normal replication of the virus by combining and inhibiting the virus with RNA.

16 Chu vd., "Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings," 255.

17 Bin Cao et al., "A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe COVID-19," The New England journal of medicine 382/19 (2020):1788.

18 "Guidelines on Clinical Management of COVID-19," last aptade March 17, 2020, https://www.aiims.edu/images/pdf/.

19 "Hospital pharmacy procedures for the management of antiviral treatment in the new coronavirus SARS-CoV-2 disease (COVID-19|," last aptade March 19, 2020, https://www.eahp.eu/sites/default/files/hospital.

20 Venkatasubbaiah, Reddy and Satyanarayana, "Literature-based review of the drugs used for the treatment of COVID-19," 106.

Ribavirin also inhibits RNA-dependent RNA polymerase[21]. The antiviral activity of ribavirin against SARS-CoV was estimated in vitro at a concentration of 50 mcg/mL[22].

According to the study conducted by Wu C et al. (Docking Study) in 2020, that ribavirin may be a strong SARS Plpr inhibitor because it binds to the active site of PLpr(Papain-like Protease) with low energy[23]. In a comprehensive review, viral replication increased while suppressing proinflammatory responses in the ribavirin mouse model[24]. Ribavirin inhibited IL4 production in Th2 cells in vitro and in vivo and showed a positive effect on interferon's in Th1 cells. In addition, while protecting Th1 cytokines, macrophage inhibited proinflammatory cytokines and Th2 cytokines[25].

In a retrospective study, the mean age was 45 years; 126 of 144 SARS patients received a loading dose of 2g IV ribavirin administered intravenously at 1g every 6 hours and 500mg every 8 hours on days 5.6.7 for 4 days. 74% of the patients recovered and were discharged until the 14th day after the treatment. However, hemolysis developed in approximately 50% and hemoglobin level decreased[26]. Ribavirin has been tested in combination with LPV/RTV for COVID-19. However, because ribavirin reduces hemoglobin levels, it may cause adverse effects in patients with respiratory distress[27].

V. Interferons

IFN α/β are immunomodulatory agents with broad-spectrum antiviral activity. It exhibits antiviral activity through an adaptive immune response in various cell types. Human can produce 13 types of IFN α and only one type of IFN β[28]. Type 1 IFNs are approved for the treatment of some cancers, autoimmune diseases and some viral infections (hepatitis B and hepatitis C)[29].

21 Helen S T e, Glenn Randall and Donald M Jensen, "Mechanism of action of ribavirin in the treatment of chronic hepatitis C," Gastroenterology & hepatology 3/3 (2007): 219–21.

22 Jaspher Chan et al., "Treatment With Lopinavir/Ritonavir or Interferon-β1b Improves Outcome of MERS-CoV Infection in a Nonhuman Primate Model of Common Marmoset," The Journal of infectious diseases 212/12(2015): 1908.

23 Canrong Wu et al., "Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods," Acta pharmaceutica Sinica. B 10/5 (2020):768.

24 Vincent C. C. Cheng et al., "Severe acute respiratory syndrome coronavirus as an agent of emerging and reemerging infection," Clinical microbiology reviews 20/4(2007):666.

25 Qin Ning et al., "Ribavirin inhibits viral-induced macrophage production of TNF, IL-1, the procoagulant fgl2 prothrombinase and preserves Th1 cytokine production but inhibits Th2 cytokine response," Journal of immunology 160/7(1998): 3487–3493.

26 Christopher M. Booth et al., "Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area," JAMA 289/21(2003): 287.

27 Miguel Angel Martinez, "Compounds with Therapeutic Potential against Novel Respiratory 2019 Coronavirus," Antimicrobial agents and chemotherapy 64/5(2020): 20.

28 Sidney Pestka, Christopher D Krause and Mark R Walter, "Interferons, interferon-like cytokines, and their receptors," Immunological reviews 202(2004): 15.

29 Emily Mantlo et al., "Antiviral activities of type I interferons to SARS-CoV-2 infection," Antiviral research 179 (2020:104811.

Type 1 IFNs provided clinical improvement in MERS-CoV-infected marmoses[30]. According to the study of Mantlo et al., SARS-CoV-2 cell culture was found to be highly sensitive to both IFN α and IFN, inhibiting the replication of SARS-CoV-2 in vitro. This concentration is also clinically achievable in patients. Based on this evidence, it is suggested that IFN/IFN alone or in combination with other antiviral drugs may be an option in the treatment of COVID-19 patients.

VI. Chloroquine

Chloroquine is an approved antimalarial drug for the treatment of malaria and prophylaxis; intestinal amebiasis. It is also used in the treatment of various rheumatic diseases and for the prophylaxis of Zika virus. According to in vitro and clinical applications, chloroquine is said to be effective against SARS CoV-1 and SARS CoV-2.

Chloroquine inhibits pH-dependent viral replication by increasing endosomal pH, thereby preventing or slowing the spread of the virus to other host cells. Chloroquine has also been reported to have an immunomodulatory effect by suppressing the release of Tumor Necrosis Factor (TNF) and IL6. This suppression can help prevent cytokine storm in COVID-19 patients[31]. According to data from various preclinical studies, chloroquine is known to be useful in the control of human coronavirus infection with the following mechanisms. Protease enzyme inhibition of SARS CoVs; inhibition of biosynthesis of sialic acid; HcoV-OC43 inhibition in HERT-18 cells; activation of protein kinase (MAPK) and extracellular signal-regulated kinase (ERK) enzymes activated by P38 mitogen at coronavirus 299E in human lung epithelial cells; inhibition of viral spread in cell culture by increasing endosomal pH; interference with terminal glycosylation of ACE2 receptor; engaging replication of SARS CoV in vero E6 cells. Wu et al. (docking study) estimated that chloroquine has therapeutic potency in the treatment of COVID-19 and stated that it may be an option in the treatment of these patients[32].

Chloroquine has been useful in controlling pneumonia in COVID-19 patients receiving 500mg chloroquine every 12 hours for 10 days. In another study, chloroquine was found to be superior to other treatments in reducing the severity of pneumonia in COVID-19 patients in terms of both efficacy and safety. In a multicenter clinical study conducted with more than 100 patients in China, chloroquine was found to be effective against pneumonia in COVID-19 patients[33]. Based on this evidence, the Chinese government has approved the use of chloroquine for the treatment of COVID-19 patients, among other treatments. However, chloroquine is known to have negative effects on hematological, hepatic, and renal systems. Chloroquine has also been shown to cause

30 Wang et al, "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro," 271.

31 Mehta et al, "Pharmacotherapy in COVID-19; A narrative review for emergency providers," 1450.

32 Wu et al., "Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods," 769.

33 Jianjun Goa, Zhenxue Tian and Xu yang, "Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies," Bioscience trends 14/1(2020): 72.

QTC prolongation along with ventricular dysrhythmia. The American Academy of Ophthalmology stated that chloroquine can cause retinopathy when used for a long time. Another common side effect of chloroquine is skin disorders. Chloroquine is available in various formulations worldwide with the price of the thigh. Chloroquine is also used in the treatment of COVID-19 within the framework of COVID-19 treatment detection developed in many countries.

VII. Hydroxychloroquine

Hydroxychloroquine has been introduced for uncomplicated malaria treatment and prophylaxis. It is also used in the treatment of rheumatoid arthritis, chronic discoid lupus erythematosus and systemic lupus erythematosus. Hydroxychloroquine also acts by controlling the cytokine storm in advanced phases in COVID-19 patients such as chloroquine. In vitro studies have reported that hydroxychloroquine is stronger than chloroquine and has little drug-drug interaction potential. In the in vitro pharmacokinetic model, hydroxy chloroquine was found to be superior to chloroquine in its ability to inhibit SARS CoV-2[34].

Christophe et al. reported that the antiviral activity of hydroxy chloroquine was stronger than that of chloroquine in a comparative Vero cell culture study.

According to a study conducted in India, the likelihood of being infected with COVID-19 was reduced in healthcare professionals who received hydroxychloroquine prophylactically compared to healthcare professionals who did not receive hydroxychloroquine[35]. In another study, the incidence of COVID-19 infection decreased after an average of 6 weeks of follow-up in healthcare professionals receiving hydroxychloroquine prophylactically in AIIMS, New Delhi. According to the data of recent studies, hydroxychloroquine has been shown to be a more effective; tolerable; reliable drug compared to chloroquine. Chloroquine and hydroxychloroquine are recommended for the treatment of moderate COVID-19 patients and hospitalized COVID-19 patients in combination with azithromycin, considering their easier and wider accessibility compared to antiviral drugs. Each country uses hydroxychloroquine in the treatment of COVID-19 in accordance with its ownCOVID-19 treatment algorithm.

VIII. Azithromycin

In fact, azithromycin is an antibacterial drug from the bacteriostatically acting macrolide group. However, according to new studies, it has also been known to have an antiviral effect. In an in vitro study, azithromycin showed an effect against Ebola virus. Azithromycin is also thought to have a good potential in preventing severe respiratory infections.

34 Xueting Yao et al., "In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)," Clinical infectious diseases: an official publication of the Infectious Diseases Society of America 71/15(2020): 736.

35 Christophe Biot et al., "Design and synthesis of hydroxyferroquine derivatives with antimalarial and antiviral activities," Journal of medicinal chemistry 49/9(2006):2846.

In one study, 20 COVID-19 patients with severe conditions were given 200 mg hydrocylchloroquine every hour and 500 mg azitromycin every day for the first day of treatment, resulting in increased antiviral strength of azithromycin and hydroxychloroquine. This combination has shown good results in the treatment of COVID-19 in the clinic. The combination of azithromycin and hydroxychloroquine is said to be an alternative to antiviral drugs such as remdesivir in the treatment of CVOD-19 patients.

IX. Other Antiviral Drugs to Sars-Cov-2

In this context, Ivermectin and Nitazoxanide showed a promising effect against COVID-19.

Ivermectin

Ivermectin is an FDA-approved broad-spectrum anti-parasitic drug. It has also been shown to have a wide antiviral effect in recent years. In vitro, ivermectin has been identified as an inhibitor of the interaction of the integral protein of human immunodeficiency virus-1 (HIV-1) and the import responsible for nuclear entry (IMP) α/β 1 heterodimerin[36]. Ivermectin has been shown to inhibit the nuclear entry of the virus and the replication of HIV-1[37]. Ivermectin has been known to inhibit nuclear entry into viral proteins including Simia Virus (SV40), major tumor antigen (T-ag), and Dang Virus(DENV), non-structural protein 5. In particular, this inhibition has been reported to restrict RNA virus infections including DNV 1-4; West Nile Virus; Venezuelan Horse Encephalitis Virus (VEEV) and Influenza[38]. Ivermectin has also shown a similar effect to DNA viruses such as pseudo rabies (PRV). SARS Cov-2, which causes severe acute respiratory syndrome that burns your world in November, is also a single-stranded RNA virus.

Studies on the proteins of SARS CoVs have shown that IMP α/β 1 has a potential role in signal-induced nucleusitoplasmic closure of SARS CoV's nucleucapside protein during infection. Furthermore, the adjunct protein of SARS CoV antagonized the antiviral activity of the transcription factor STAT1 by isolating IMP α/β 1 in the ER/ Goli membrane of ORF6 viruses. Based on these reports, it is thought that ivermectin is theoretically effective on SARA CoV-2[39]. According to data from preclinical studies, ivermectin reduced the RNA of the virus in Vero-hSLM cells at 48 hours, inhibiting nuclear entry and DNA polymerase in BoHV-1 and inhibiting virus replication. In addition, ivermectin inhibited the introduction and spread of DNA polymerase UL42 into the nucleus of

36 Leon Caly et al., "The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro." Antiviral research 178(2020): 104787.

37 Kylie M. Wagstaff et al., "Ivermectin is a specific inhibitor of importin α/β-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus," The Biochemical journal 443/3 (2012): 852.

38 Carlos Chaccour et al., "The SARS-CoV-2 Ivermectin Navarra-ISGlobal Trial (SAINT) to Evaluate the Potential of Ivermectin to Reduce COVID-19 Transmission in low risk, non-severe COVID-19 patients in the first 48 hours after symptoms onset: A structured summary of a study protocol for a randomized control pilot trial," Trials 21/1 (2020): 498.

39 Caly et al., "The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro." 1047.

pseudorabies viruses. Many clinical studies are ongoing on whether ivermectin is effective against COVID-19.

Nitazoxanide

Nitazoxanide is a broad-spectrum ant parasitic and antiviral prod rug used in fluenza patients. After ingestion, rapidly converted to active metabolites (tizoxanide and tizoxanide- conjugates)[40]. Preclinical studies have shown an effect against MERS CoV and other coronaviruses. Nitazoxanide acts by inhibiting N protein exploration of the virus; suppressing the production of proinflammatory cytokines and interlocin 6; inhibiting the replication of RNA and DNA viruses 1. Nitazoxanide increased the production of INF α and INF β.

Symptoms were found to be reduced in uncomplicated acute flu patients when nitazoxanide 500 mg daily was administered for 5 days. This dose is thought to reduce morbidity and mortality in COVID-19 patients when used in combination with azithromycin. On March 9, 2020, French scientists suggested examining whether nitazoxanide was effective against COVID-19, but then it was ignored. A study published on March 15, 2020 suggested that nitazoxanide may be effective when used with hydroxychloroquine in COVID-19 patients. Many clinical studies are ongoing worldwide on this subject.

X. Discussion

In order to control and treat rapidly spreading diseases such as COVID-19, it is necessary to try existing drugs; to develop new special drug molecules; to develop vaccines against the disease. However, it is not possible and easy to develop new drugs and new vaccines in a short time. In addition to new drug and vaccine studies for the treatment and control of COVID-19, some pre-existing drugs were thought to be effective against SARS CoV-2 according to the mechanism of action, and preclinical and clinical studies were conducted. Even if it is low, these drugs provide an important contribution to the treatment of COVID-19.

Remdesivir was approved for use in COVID-19 patients on May 1, 2020. Remdesivir binds RNA viruses including SARS and MERS to the RNA chain, causing early termination of the RNA chain of the virus. Remdesivir is extensively and frequently bound to RNA-dependent RNA polymerase enzyme of the novel coronavirus compared to other drugs. In addition, it is recommended that GTP may be a new one for SARS-Cov-2 failure. It has been reported to be effective against SARA Cov-2 in many pre-clinical and clinical studies.

In March 2020, the use of favipiravir in the treatment of COVID-19 was approved by the Chinese state. Favipiravir directly inhibits the replication and transcription of the virus by causing false binding in newly developing vRNA in the virus. Or RNA inhibits

40 Mina T Kelleni, "Nitazoxanide/azithromycin combination for COVID-19: A suggested new protocol for early management," Pharmacological research 157(2020): 104874.

the fusion of nucleocytes by binding to the active division of polymerase, thereby engaging the proliferation and transcription of the virus. Favipiravir helped accelerate viral clearance and improve chest tomography in COVID-19 patients compared to Lopinavir/ Ritonavir.

Lopinavir/ Ritonavir acts by inhibiting protease enzymes of the virus. In addition, ritonavir inhibits the metabolism of lopinavir by inhibiting cytochrome P450 and strengthens the effect of prolonging half-life. In addition to preclinical evidence, Lopinavir/ Ritonavir reduced viral load and reduced recovery time in COVID-19 patients in clinical trials.

Ribavirin combines with and inhibits RNA of the virus, inducing genome mutation and inhibiting normal replication of the virus, and inhibiting RNA-dependent RNA polymerase. Ribavirin inhibited IL4 production in Th2 cells in vitro and in vivo and showed a positive effect on interferons in Th1 cells. Ribavirin showed significant and promising antiviral activity in SARS-Cov patients for 14 days, while it showed serious side effects such as hemolysis in 50% of patients. It is also tried in combination with Lopinavir/ Ritonavir for the treatment of COVID-19.

Interferons exhibit antiviral activity through an adaptive immune response in various cell types. SARS-CoV-2 was found to be highly susceptible to both IFN α and IFN β in cell culture, inhibiting replication of IFN α and IFN β SARS-CoV-2 in vitro. This concentration is also clinically achievable in patients.

Chloroquine and Hydroxychloroquine inhibit pH-dependent viral replication by increasing endosomal pH, thereby preventing or slowing the spread of the virus to other host cells. It has also been reported to have an immunomodulatory effect by suppressing tumor necrosis factor α (TNF-α) and IL6 release. This suppression prevents cytokine storm in COVID-19 patients. Hydroxychloroquine is stronger than chloroquine and has little drug-drug interaction potential. In the in vitro pharmacokinetic model, hydroxy chloroquine was found to be superior to chloroquine in its ability to inhibit SARS CoV-2. According to the data of recent studies, hydroxychloroquine has been shown to be a more effective; tolerable; reliable drug compared to chloroquine. In addition, both Chloroquine and hydroxychloroquine have easier and wider accessibility compared to antiviral drugs.

Azithromycin is an antibacterial drug from the bacteriostatically acting macrolide group, as well as showing antiviral effect. It increased its antiviral effect when used in combination with hydroxychloroquine in COVID-19 patients. Azithromycin-hydroxychlorine combination is a strong alternative to antiviral drugs such as remdesivir in the treatment of COVID-19 in terms of both accessibility and price.

Finally, ivermectin and nitazoxanide, which are anti-parasites but also show a broad-spectrum antiviral effect, are thought to be effective against COVID-19 considering the antiviral mechanisms of action.

XI. Conclusion

In conclusion, according to the antiviral properties evaluated in the absence, the mechanisms of action and the results of the studies, remdesivir, favirpiravir, lopinavir/ ritonavir and ribavirin were found to have quite antiviral effects against SARS CoV-2. In addition, the malaria drug chloroquine and hydroxychloroquine showed a positive antiviral effect against COVID-19 both preclinically and clinically. Ivermectin and nitazoxanide are thought to be effective against COVID-19 based on the antiviral mechanism of action and preclinical studies. However, all of these drugs are not 100% effective.

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Pathogenicity, Therapeutic Candidates and Vaccines of Novel Coronavirus Disease (COVID-19): A Literature Review

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Abstract

A severe acute respiratory syndrome, caused by an extremely contagious novel coronavirus (SARS-CoV-2), has been widely spreading worldwide since it was first reported in late December 2019 in Wuhan, China. On March 11, 2020, the coronavirus disease (COVID-19) was officially announced as a global pandemic by the World Health Organization (WHO). As of August 1, 2020, WHO data demonstrated over 17.3 million confirmed cases and over 675000 deaths globally because of COVID-19. SARS-CoV-2 is a β-coronavirus that is analogous to severe acute respiratory syndrome coronavirus (SARS-CoV) and

Özet

Son derece bulaşıcı bir koronavirüsün (SARS-CoV-2) neden olduğu şiddetli akut solunum sendromu, ilk olarak Aralık 2019'un sonunda Çin'in Wuhan şehrinde bildirilmiştir. 11 Mart 2020 tarihinde koronavirüs hastalığı (COVID-19) Dünya Sağlık Örgütü (WHO) tarafından resmen küresel bir pandemi olarak ilan edilmiştir. WHO, 1 Ağustos 2020'ye kadar dünya çapında COVID-19 nedeniyle 17,3 milyondan fazla doğrulanmış vaka ve 675.000'den fazla ölüm olduğunu açıklamıştır. SARS-CoV-2, şiddetli akut solunum sendromu koronavirüsüne (SARS-CoV) ve Orta Doğu solunum sendromu koronavirüsüne (MERS-CoV)

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Middle East respiratory syndrome coronavirus (MERS-CoV). The genetic material of SARS-CoV-2 is highly matching with bat coronaviruses, suggesting that the bat is its reservoir host. SARS-CoV-2 chiefly spreads through direct human-to-human transmission by inhalation of infectious respiratory droplets or direct contact, as well as touching contaminated surfaces. The clinical characteristics of COVID-19 patients commonly include fever, myalgia cough, dyspnea, and bilateral lung infiltrates on chest scanning. The elderly and individuals with comorbidities, such as hypertension, diabetes, and cardiovascular diseases, are extremely vulnerable to infection and disease severity which may be associated with cytokine storm that induces acute respiratory distress syndrome (ARDS). Angiotensin-converting enzyme 2 (ACE2) is the basic receptor for SARS-CoV-2 to enter host cells. To date, there are limited therapeutic approaches for COVID-19. Several potential drugs and vaccines are being rapidly developed and investigated for their efficacy in the treatment of COVID-19. In this review, the latest information on the transmission routes, risk factors, pathogenesis and immune responses, clinical features, diagnosis, and treatment of COVID-19 are all reviewed, as well as discussing the drugs with possible clinical benefits and vaccine advancements to fight this viral outbreak.

Keywords: *COVID-19, SARS-CoV-2, Pathogenesis, Pandemic*

benzer bir koronavirüstür. SARS-CoV-2'nin genetik materyali yarasa koronavirüsleriyle oldukça uyumludur ve bu da yarasanın rezervuar barındırıcısı olduğunu düşündürmektedir. SARS-CoV-2, bulaşıcı solunum damlacıklarının solunması, kontamine yüzeylere veya doğrudan temas yoluyla insandan insana bulaşarak yayılmaktadır. COVID-19 hastalarının ana klinik özellikleri ateş, kas ağrısı, öksürük, nefes darlığı ve göğüs taramasında bilateral akciğer infiltrasyonunu içermektedir. Yaşlılar ve hipertansiyon, diyabet, kardiyovasküler hastalıkları gibi komorbiditeleri olan bireyler, enfeksiyon ve hastalık şiddetine karşı aşırı derecede savunmasızdır. Hastalık şiddeti, akut solunum sıkıntısı sendromuna (ARDS) neden olan sitokin fırtınası ile ilişkili olabilir. Anjiyotensin dönüştürücü enzim 2 (ACE2), SARS-CoV-2'nin konakçı hücrelere girmesi için temel reseptördür. Bugüne kadar, COVID-19 için sınırlı terapötik yaklaşımlar vardır. Çeşitli potansiyel ilaçlar ve aşılar hızla geliştirilmekte ve COVID-19 tedavisindeki etkinlikleri açısından araştırılmaktadır. Bu çalışmada, COVID-19 salgınıyla savaşmak için olası klinik faydaları olan ilaçları ve aşıdaki ilerlemeleri tartışmanın yanı sıra COVID-19'un bulaşma yolları, risk faktörleri, patogenezi ve bağışıklık tepkileri, klinik özellikleri, teşhisi ve tedavisi ile ilgili tespit edilen bilgiler gözden geçirilmiştir.

Anahtar kelimeler: *COVID-19, SARS-CoV-2, Patogenez, Pandemi*

I. Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a zoonotic virus that was originally transmitted from bats to humans then from person to person who is in direct contact with each other[1]. SARS-CoV-2 is a greatly pathogenic, human-infecting Betacorona virus with a positive-sense single-stranded RNA (+ssRNS)[2]. The number of infected individuals has been rapidly growing worldwide. By August 1, 2020, a total of 17,396,943 confirmed cases of coronavirus disease (COVID-19) have been reported to the WHO. Of these cases, 675,060 deaths have been informed (3.9% mortality)[3]. The purpose of this work is to summarize the recent understanding of the newly emerged COVID-19, including transmission, risk factors, pathogenesis, symptoms, diagnosis, and treatment, as well as repurposed drugs and vaccine development.

II. Transmission

SARS-CoV-2 has multiple routes of transmission which causes its fast-spreading rate. Direct Person to person transmission is the major route and occurs among close contacts either by direct contact or via inhaling respiratory droplets from an infected person who coughs, sneezes, or talks[4].

SARS-CoV-2 may spread through Airborne transmission, particularly within crowded and stuffy places where droplet nuclei having a diameter less than 5μm are suspended in the air for long distances (>1 m) and periods; hence, inhalation of infectious dose from these droplets can cause infection.

Fomites are a source of SARS-CoV-2 transmission since it is variably stable on different surfaces with 3 hours on the copper, 24 hours on paperboard, and up to 2-3 days on steel and plastic surfaces. Infection may occur by touching the virus-contaminated objects and contacting the mucosa in the nose, mouth, or eyes[5].

SARS-CoV-2 can spread through the fecal-oral route as it induces gastrointestinal symptoms like vomiting, diarrhea, and abdominal pain in a significant proportion of COVID-19 patients[6]. Moreover, the virus has been isolated and cultured successfully from a stool specimen of a SARS-CoV-2 patient[7]. Also, positive SARS-CoV-2 stool samples of children were seen even after testing negative from specimens of the respi-

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3 World Health Organization, "Coronavirus Disease 2019 (COVID-19): Situation Report, 194," (2020).

4 Jasper Fuk-Woo Chan et al., "A Familial Cluster of Pneumonia Associated with the 2019 Novel Coronavirus Indicating Person-to-Person Transmission: A Study of a Family Cluster," The Lancet 395, no. 10223 (2020).

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6 Jonathan Kopel et al., "Clinical Insights into the Gastrointestinal Manifestations of COVID-19," Digestive diseases and sciences 65, no. 7 (2020).

7 JingCheng Zhang, SaiBin Wang, and YaDong Xue, "Fecal Specimen Diagnosis 2019 Novel Coronavirus-Infected Pneumonia," Journal of medical virology 92, no. 6 (2020).

ratory tract[8]. There are many concerns that SARS-CoV-2 may spread via contaminated water consumption, especially in countries with a large population and weak sewage treatment systems[9].

SARS-CoV-2 can enter the body through ocular tissue causing viral conjunctivitis that abates before the onset of COVID-19 symptoms., both ACE2 and TMPRSS2, which are key factors in SARS-CoV-2 pathogenicity, are expressed in eyes[10]. Therefore, strong recommendations for the medical staff to wear protective goggles to reduce occupational exposure to the virus[11].

III. Risk Factors

Age and sex are important factors as most of the patients were adult males with a median age between 49 and 56 years[12],[13],[14]. In other studies, infection of children occurred, but clinical manifestations were milder mainly without fever and pneumonia[15],[16].

Individuals with comorbidities such as hypertension, cardiovascular diseases, diabetes, cerebrovascular diseases, malignancy, and fungal or bacterial confections are more vulnerable to be infected with SARS-CoV-2 and develop severe symptoms. These comorbidities lead to subsequent poor prognosis, progression to severe condition that requires respiratory support or admission to intensive care unit (ICU), and high mortality rate[17],[18],[19],[20],[21].

8 Y. Xu et al., "Characteristics of Pediatric Sars-Cov-2 Infection and Potential Evidence for Persistent Fecal Viral Shedding," Nat Med 26, no. 4 (2020).

9 Gourav Dhar Bhowmick et al., "Coronavirus Disease 2019 (COVID-19) Outbreak: Some Serious Consequences with Urban and Rural Water Cycle," npj Clean Water 3, no. 1 (2020).no. 1 (2020

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11 S. Schnichels et al., "[Can Sars-Cov-2 Infect the Eye?-an Overview of the Receptor Status in Ocular Tissue]," Ophthalmologe 117, no. 7 (2020).

12 N. Chen et al., "Epidemiological and Clinical Characteristics of 99 Cases of 2019 Novel Coronavirus Pneumonia in Wuhan, China: A Descriptive Study," Lancet 395, no. 10223 (2020).

13 D. Wang et al., "Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China," Jama 323, no. 11 (2020).

14 C. Huang et al., "Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China," Lancet 395, no. 10223 (2020).

15 Chan et al., "A Familial Cluster of Pneumonia Associated with the 2019 Novel Coronavirus Indicating Person-to-Person Transmission: A Study of a Family Cluster.

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17 Chen et al., "Epidemiological and Clinical Characteristics of 99 Cases of 2019 Novel Coronavirus Pneumonia in Wuhan, China: A Descriptive Study."

18 Wang et al., "Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China."

19 Chan et al., "A Familial Cluster of Pneumonia Associated with the 2019 Novel Coronavirus Indicating Person-to-Person Transmission: A Study of a Family Cluster."

20 Y. D. Peng et al., "[Clinical Characteristics and Outcomes of 112 Cardiovascular Disease Patients Infected by 2019-Ncov]," Zhonghua Xin Xue Guan Bing Za Zhi 48, no. 0 (2020).

21 K. Liu et al., "Clinical Characteristics of Novel Coronavirus Cases in Tertiary Hospitals in Hubei Province," Chin Med J (Engl) 133, no. 9 (2020).

Obese patients with COVID-19 have a high mortality rate[22] due to the negative effect of obesity on immunity by disrupting T-cells functions[23] and altering the mechanical function of chest wall causing poor ventilation as a result of fat accumulation in the mediastinum, abdominal and thoracic cavities, leading to intensifying the acute respiratory distress and pneumonia[24]. Also, smoking augments the severity of acute respiratory distress in hospitalized COVID-19 patients[25].

A recent study that included 1980 COVID-19 cases in Italy and Spain found that genetics and blood groups may be determinants of COVID-19 vulnerability and severity. People with blood type A are more susceptible to be infected with SARS-CoV-2 and at higher risk of severe illness. In contrast, individuals with blood group O have a lower risk of developing severe symptoms[26].

COVID-19 patients with compromised immune systems are more likely to become severely ill and stay infectious longer than others[27].

IV. Pathogenesis

SARS-CoV-2 entry into cells is chiefly mediated through endocytosis. Angiotensin-converting enzyme 2 (ACE2) is the necessary functional transmembrane receptor for SARS-CoV2 entry into human cells[28],[29],[30]. ACE2 is highly expressed in ciliated cells of the respiratory epithelium and alveolar cells, as well as myocardiocytes, kidney cells, and vascular endothelium[31].

The main physiological role of ACE2 is in cardiovascular system (CVS) regulation via metabolism and controlling of the Renin-Angiotensin system (RAS) by regulating An-

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29 W. Li et al., "Angiotensin-Converting Enzyme 2 Is a Functional Receptor for the Sars Coronavirus," Nature 426, no. 6965 (2003).

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31 I. Hamming et al., "Tissue Distribution of Ace2 Protein, the Functional Receptor for Sars Coronavirus. A First Step in Understanding Sars Pathogenesis," J Pathol 203, no. 2 (2004).

giotensin 2 (Ang2) and a sequence of biochemical pathways that balance vasodilation, vasoconstriction, anti-fibrosis, and anti-inflammatory response in endothelial cells[32].

The large spike protein of SARS-CoV2, which is crucial for cellular entry and infection, has 2 major subunits. The S1 subunit comprises receptor-binding domain (RBD), which is responsible for recognition and attachment to ACE2 receptors, and S2 subunit that is basic in host cell membrane fusion and endocytosis[33]

Host cell protease activation is an important determinant of SARS-CoV2 pathogenesis. Transmembrane protease serine 2 (TMPRSS2) and lysosomal cathepsins activate SARS-CoV-2 viral entry. TMPRSS2 cleaves ACE2, promoting the cell`s viral uptake. TMPRSS2 also cleaves the spike protein of SARS-CoV-2, activating it for endocytosis[34]. Moreover, Furin enhances SARS-CoV-2 entry by prior spike protein pre-activation during viral packaging. Accordingly, improving the viral entry into cells with low expression of TMPRSS2 and lysosomal cathepsins[35].

The interaction between viral spike protein and membrane-bound ACE2 leads to internalization of ACE2 via endocytosis; thus, downregulation of ACE2 expression in lung tissues and loss of its cardioprotective role in the RAS system; consequently, vascular hemostasis deteriorates and Nitric Oxide (NO) production is reduced, along with elevation of proinflammatory and procoagulatory factors in lungs which trigger inflammatory lesions, alveolar wall thickening, and bleeding[36].

SARS-CoV-2 evades the immune surveillance so that infects host cells without being efficiently monitored by antiviral immunity. Mechanisms of immune evasion include hiding RBD through conformational masking[37]. Furthermore, expression of a protein, which is encoded from open reading frame 8 (ORF8), that links with MHC-I molecules and down-regulates their surface expression on various cell types disrupting antigen presentation; hence, it weakens detection and elimination of infected cells by cytotoxic T lymphocytes[38].

Due to the massive activation of the immune system by SARS-CoV-2 a cytokine storm occurs. Proinflammatory cytokines such as interleukin (IL)-1, IL2, IL6, IL7, IL12, IL-17,

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34 Hoffmann et al., "Sars-Cov-2 Cell Entry Depends on Ace2 and Tmprss2 and Is Blocked by a Clinically Proven Protease Inhibitor."

35 Jian Shang et al., "Cell Entry Mechanisms of Sars-Cov-2," Proceedings of the National Academy of Sciences 117, no. 21 (2020).

36 P. Verdecchia et al., "The Pivotal Link between Ace2 Deficiency and Sars-Cov-2 Infection," Eur J Intern Med 76 (2020).

37 Shang et al., "Cell Entry Mechanisms of Sars-Cov-2."

38 Yiwen Zhang et al., "The Orf8 Protein of Sars-Cov-2 Mediates Immune Evasion through Potently Downregulating Mhc-I," bioRxiv (2020).

tumor necrosis factor-α (TNF-α), interferon-gamma (IFNγ), IFNγ-induced protein 10 (IP10), macrophage inflammatory proteins1A (MIP1A), Granulocyte colony-stimulating factor (GCSF), granulocyte-macrophage colony-stimulating factor (GM-CSF) and monocyte chemoattractant protein-1 (MCP1) are dramatically elevated and exaggerate pneumonia and lung injury[39],[40],[41]. CD4+ and CD8+ T cells, in Pneumonic COVID-19 Patients, have a higher capability to secrete in- vitro IL-17, which reinforces the inflammatory response, and to activate neutrophils that migrate to the lung and seriously aggravate the pathogenesis of COVID-19[42]. Massive inflammatory cytokine release, endothelial dysfunction, and hypoxia predispose COVID-19 patients to hemostatic disorders such as disseminated intravascular coagulation (DIC), venous thromboembolism, and myocardial infarction[43].

V. Clinical Features

The clinical manifestations of COVID-19 are divided according to its severity into several categories[44]:

Mild disease: occurs in 80% of cases who experience no pneumonia. signs of upper respiratory tract viral infection, such as mild fever, dry cough, sore throat, nasal congestion, headache, and myalgia are seen[45]. Also loss of taste and/or smell, which could be utilized to differentiate between influenza and COVID-19 infection[46]. Moreover, diarrhea and vomiting are usually found. More serious symptoms, such as dyspnea, are absent.

Moderate disease: in addition to the previous signs excessive coughing, shortness of breath, and tachypnea are observed, but with no signs of severe pneumonia.

Severe disease: occurs in nearly 14% of cases. Symptoms include acute dyspnea and tachypnea with respiratory frequency ≥ 30/min, blood oxygen saturation (SpO2) ≤ 90 on room air, and the ratio between partial pressure of oxygen and fraction of inspired oxygen (PaO2/FiO2) < 300 mmHg.

39 Huang et al., "Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China."

40 Evangelos J Giamarellos-Bourboulis et al., "Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure," Cell host & microbe (2020).

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44 Marco Cascella et al., "Features, Evaluation and Treatment Coronavirus (COVID-19)," in Statpearls [Internet] (StatPearls Publishing, 2020).

45 Michael C. Grant et al., "The Prevalence of Symptoms in 24,410 Adults Infected by the Novel Coronavirus (Sars-Cov-2; COVID-19): A Systematic Review and Meta-Analysis of 148 Studies from 9 Countries," PloS one 15, no. 6 (2020).

46 Akosua Adom Agyeman et al., "Smell and Taste Dysfunction in Patients with COVID-19: A Systematic Review and Meta-Analysis" (paper presented at the Mayo Clinic Proceedings, 2020).

Critical disease: develops in nearly 5% of patients and includes severe pneumonia associated with acute respiratory failure that requires ICU admission, sepsis, and multiple organ dysfunction (MOD)[47].

Acute Respiratory Distress Syndrome (ARDS)

ARDS is a sign of serious respiratory failure and results from the damage of the alveolar epithelial cells by SARS-CoV-2[48]. According to PaO2/FiO2 ratio ARDS is Mild when 200 mmHg < PaO2/FiO2 ≤ 300 mmHg, moderate when 100 mmHg < PaO2/FiO2 ≤ 200 mmHg, and Severe when PaO2/FiO2 ≤ 100 mmHg[49].

Septic shock

It may occur in the critical cases of COVID-19 patients, indicating higher mortality and is characterized by multiorgan involvement, including respiratory manifestations such as severe dyspnea and hypoxemia, as well as extrapulmonary manifestations[50] such as renal impairment with reduced urine output, tachycardia, coagulopathy, mediastinal lymphadenopathy[51], thrombocytopenia, gastrointestinal complications, liver dysfunction, and neurological abnormalities such as altered mental status. The SOFA "Sequential Organ Failure Assessment" score is used to estimate the rate of organ failure in ICUs and the corresponding prognostic value to forecast ICU mortality by analyzing lab outcomes and clinical data[52].

VI. Diagnosis of COVID-19

Laboratory diagnosis

The standard confirmation method of COVID-19 infection is real-time reverse-transcription polymerase chain reaction (rRT-PCR)[53],[54] . Samples are collected mainly from the upper respiratory tract such as nasopharyngeal and oropharyngeal swabs or lower respiratory tract such as sputum or endotracheal aspirates[55]. Also, amniotic fluid and cord blood specimens can be used in pregnant women for the diagnosis of SARS-CoV-2 infection with rRT-PCR[56]. Complete blood count and inflammatory biomarkers determination are very useful for COVID-19 diagnosis and progression prediction. Lymphopenia is the most noticeable laboratory finding[57], together with leukopenia, thrombocytopenia, and elevated transaminases[58]. Inflammatory markers such as IL6, CRP, and ESR are also increased[59]. Interestingly, elevated levels of neutrophil-to-lymphocyte ratio (NLR)[60], VEGF-D[61], and more than fourfold increase in D-dimer[62] indicate a critical illness and MOD.

Clinical diagnosis

COVID-19 can be clinically diagnosed based on symptoms, exposures, and scanning of the chest[63]. Chest computed tomography (CT) in early infection shows bilateral multilobar ground-glass opacities with peripheral, asymmetric, and posterior distribution. Subpleural dominance, lobular septal thickening with variable alveolar filling, and consolidation may be seen with disease progression[64].

VII. Treatment

Treatment of COVID-19 varies according to the phase of the illness[65]. Three stages present, the mild, pulmonary, and inflammatory phases. In the Mild phase, the patient simply needs symptomatic treatment and self-isolation.

The second phase is the pulmonary phase in which Patients require hospitalization and exhibit fever, bilateral pulmonary consolidations, and hypoxemia. If oxygen levels fluctuate, external oxygen may be given.

47 Zunyou Wu and Jennifer M. McGoogan, "Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention," JAMA 323, no. 13 (2020).

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55 Ibid.

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58 Brandon Michael Henry et al., "Hematologic, Biochemical and Immune Biomarker Abnormalities Associated with Severe Illness and Mortality in Coronavirus Disease 2019 (COVID-19): A Meta-Analysis," Clinical Chemistry and Laboratory Medicine (CCLM) 58, no. 7 (2020).

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62 L. Zhang et al., "D-Dimer Levels on Admission to Predict in-Hospital Mortality in Patients with COVID-19," J Thromb Haemost 18, no. 6 (2020).

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64 Sana Salehi et al., "Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients," American Journal of Roentgenology 215, no. 1 (2020).

65 Centers for Disease Control and Prevention CDC, "Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)," CDC, https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html.

The third phase is the inflammatory phase, which has the most severe complications of COVID-19 such as ARDS, and MOD. The patients are admitted to ICU, and the treatment strategy involves electrolyte balancing, hydration, and stabilizing the functioning internal systems. All clinical parameters and vital signs are closely monitored[66]. No effective therapies have been proven yet for COVID-19. However, a considerable number of promising therapeutic agents are provided by the growing understanding of SARS-CoV-2 virology.

VIII. Drugs with Prospective Clinical Benefits

Drugs with antiviral activity

Hydroxychloroquine (HCQ)

HCQ alters endocytosis of SARS-CoV-2 into cells by elevating the pH of endosomes and lysosomes[67], inhibition of N-glycosylation of host receptors, and decreasing its binding ability and proteolytic processing. HCQ may also prevent the formation of mature virions; consequently, impairing recognition of viral antigens by antigen-presenting cells (APCs). Moreover, HCQ can impair the release of IL-6, IL-1beta, and TNF-alfa; thus, it has an immunomodulatory effect and reduces the severity of the disease[68]. HCQ also shows anti-thrombotic properties via interfering with platelet aggregation and blood clotting proteins[69]. The association between HCQ and Azithromycin has resulted in significant viral load reduction in some patients, but worries about prolonged QT interval arise with this combination[70]. Recently many clinical trials of HCQ have been stopped as no significant benefits for severe COVID-19 cases were observed[71,72]. A new trial has been launched to treat COVID-19 outpatients with HCQ (NCT04466540)[73] .

66 Cascella et al., "Features, Evaluation and Treatment Coronavirus (COVID-19)."

67 Eugenia Quiros Roldan et al., "The Possible Mechanisms of Action of 4-Aminoquinolines (Chloroquine/Hydroxychloroquine) against Sars-Cov-2 Infection (COVID-19): A Role for Iron Homeostasis?," Pharmacological Research 158 (2020).

68 Christian A. Devaux et al., "New Insights on the Antiviral Effects of Chloroquine against Coronavirus: What to Expect for COVID-19?," International Journal of Antimicrobial Agents 55, no. 5 (2020).

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70 Philippe Gautret et al., "Hydroxychloroquine and Azithromycin as a Treatment of COVID-19: Results of an Open-Label Non-Randomized Clinical Trial," International Journal of Antimicrobial Agents 56, no. 1 (2020).

71 World Health Organization (WHO), "Who Discontinues Hydroxychloroquine and Lopinavir/Ritonavir Treatment Arms for COVID-19," World Health Organization, https://www.who.int/news-room/detail/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-COVID-19.

72 National Institutes of Health (NIH), "Nih Halts Clinical Trial of Hydroxychloroquine: Study Shows Treatment Does No Harm, but Provides No Benefit," National Institutes of Health (NIH), https://www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine.

73 ClinicalTrials.gov, https://clinicaltrials.gov/.

Remdesivir

Remdesivir is a promising antiviral agent against SARS-CoV-2. It is an adenosine nucleotide analogue that inhibits virus replication by inhibiting the RNA-dependent RNA polymerase (RdRp)[74]. Successful case reports of Remdesivir for COVID-19 have been reported[75]. A randomized double-blind Phase 3 clinical trial involving 1063 patients and comparing Remdesivir with the standard of care is being conducted by The National Institute of Health (NCT04280705)[76] . Hospitalized patients with severe pneumonia who received Remdesivir had a better recovery than similar patients who received a placebo[77].

Lopinavir/Ritonavir (LPV/r)

Lopinavir is an approved antiretroviral drug by the Food and Drug Administration (FDA) to treat HIV infection by acting as a protease inhibitor, used in oral combination with ritonavir which acts as a booster by inhibiting cytochrome P450 to increase blood concentration and duration of action of Lopinavir[78]. LPV/r showed an in-vitro antiviral effect against other coronaviruses through inhibition of 3-chymotrypsin-like protease[79]. An open-label randomized clinical trial involving 199 patients with severe COVID-19 showed No significant results from the treatment of COVID-19 with LPV/r in China (ChiCTR2000029308)[80].

Favipiravir

It is an antiviral agent approved for the treatment of re-emerging pandemic influenza in China and Japan. A prodrug of a purine nucleotide. The active form selectively inhibits RdRp of RNA viruses, preventing viral replication[81]. The preliminary results from one of the clinical trials showed that the group of COVID-19 cases treated with favipiravir is significantly superior to the control group that was treated with arbidol[82].

74 Calvin J. Gordon et al., "Remdesivir Is a Direct-Acting Antiviral That Inhibits Rna-Dependent Rna Polymerase from Severe Acute Respiratory Syndrome Coronavirus 2 with High Potency," Journal of Biological Chemistry 295, no. 20 (2020).

75 Stephanie A. Kujawski et al., "First 12 Patients with Coronavirus Disease 2019 (COVID-19) in the United States," medRxiv (2020).

76 ClinicalTrials.gov.

77 J. D. Goldman et al., "Remdesivir for 5 or 10 Days in Patients with Severe COVID-19," N Engl J Med (2020).

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82 Chang Chen et al., "Favipiravir Versus Arbidol for COVID-19: A Randomized Clinical Trial," medRxiv (2020).

Anticytokines

Tocilizumab, Sarilumab, and Fingolimod

Tocilizumab is a monoclonal antibody that targets IL-6 receptors as COVID-19 complications and lung injuries are mainly associated with elevated IL-6[83]. Common adverse effects of Tocilizumab include increasing in upper respiratory tract infection, hypertension, and hepatotoxicity[84]. (NCT04317092) is a running clinical trial to assess Tocilizumab for COVID-19 treatment[85].

Similar monoclonal antibodies that are IL-6 receptor antagonists include Sarilumab and Fingolimod. (NCT04315298) and (NCT04280588) are ongoing clinical trials for assessing their efficacy in COVID-19 treatment respectively[86].

Canakinumab and Emapalumab

Canakinumab is a monoclonal antibody that targets IL-1 receptors. It is being tested for COVID-19 pneumonia in phase 2 clinical trial (NCT04362813)[87]. Emapalumab is a monoclonal antibody that inhibits inflammatory signals mediated by interferon-gamma by binding to it and preventing its binding to cell surface receptors. Emapalumab is being tested in combination with Anakinra, which is an IL-1 antagonist, in phase 2 clinical trial) for COVID-19 management (NCT04339712[88].

Mavrilimumab and Gimsilumab

They are monoclonal antibodies against GM-CSF; thus, improving the hyperinflammatory state of COVID-19 patients[89]. Gimsilumab is being evaluated for its efficacy and safety in the treatment of COVID-19 cases with ARDS (NCT04351243)[90]. In a recent study Mavrilimumab has improved the clinical picture in non-mechanically ventilated patients with severe COVID-19 pneumonia compared with standard care by blocking GM-CSF receptor-α[91], while for assessing its efficacy and safety in severe COVID-19 pneumonia, a phase 2 clinical trial is ongoing (NCT04397497)[92] .

83 Giamarellos-Bourboulis et al., "Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure."

84 James M. Sanders et al., "Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review," JAMA 323, no. 18 (2020).

85 ClinicalTrials.gov.

86 Ibid.

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89 Aldo Bonaventura et al., "Targeting Gm-Csf in COVID-19 Pneumonia: Rationale and Strategies," Frontiers in Immunology 11, no. 1625 (2020).

90 ClinicalTrials.gov.

91 Giacomo De Luca et al., "Gm-Csf Blockade with Mavrilimumab in Severe COVID-19 Pneumonia and Systemic Hyperinflammation: A Single-Centre, Prospective Cohort Study," The Lancet Rheumatology (2020).

92 ClinicalTrials.gov.

Baricitinib

Baricitinib has anti-inflammatory activity by acting as Janus Kinase (JAK) inhibitor and thus preventing cytokine release. Also, it has an antiviral effect by disrupting AP2-associated protein kinase (AAK1) which is a regulator of viral entry by endocytosis[93]. In an open-label pilot study, the treatment of COVID-19 patients with Baricitinib combined with LPV/r showed a significant improvement in clinical outcomes and laboratory parameters, moreover, the majority of Baricitinib treated patients were discharged from the hospital[94]. Baricitinib is appropriate for the early phases of the infection to prevent viral entry into the cells, and in the advanced stages to act as an anti-inflammatory. A phase 3 clinical trial has been launched to test its efficiency in COVID-19 treatment (NCT04340232)[95] .

Ruxolitinib

It is a cytokine release inhibitor by selective inhibition of JAK1 and JAK2[96]. In a single-blind randomized controlled trial, patients who were treated with Ruxolitinib experienced faster clinical improvement[97]. In a pilot study, Ruxolitinib therapy for COVID-19 patients with hyper inflammation was safe and significantly effective[98]. A phase 2 clinical trial has been started to investigate its efficacy in the management of hyperinflammatory state and improving lung function in COVID-19 cases (NCT04338958)[99].

Blood derived products

Convalescent plasma transfusion (CPT)

CPT therapy can decrease the mortality rate in severe COVID-19 patients, and protect susceptible individuals such as health care workers from SARS-CoV-2 infection due to its content of neutralizing antibodies to the virus. Convalescent plasma (CP) is collected from recovered individuals 2-3 weeks after infection. A single recovered individual donation can be used for the treatment of 2-3 recipients[100]. Possible side effects associated with CPT therapy are allergic reactions, transfusion-associated circulatory overload (TACO), and transfusion-related acute lung injury (TRALI)[101]. Multiple studies

93 P. Richardson et al., "Baricitinib as Potential Treatment for 2019-Ncov Acute Respiratory Disease," Lancet 395, no. 10223 (2020).

94 Fabrizio Cantini et al., "Baricitinib Therapy in COVID-19: A Pilot Study on Safety and Clinical Impact," The Journal of infection 81, no. 2 (2020).

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96 R. A. Mesa, "Ruxolitinib, a Selective Jak1 and Jak2 Inhibitor for the Treatment of Myeloproliferative Neoplasms and Psoriasis," IDrugs 13, no. 6 (2010).

97 Yang Cao et al., "Ruxolitinib in Treatment of Severe Coronavirus Disease 2019 (COVID-19): A multicenter, Single-Blind, Randomized Controlled Trial," Journal of Allergy and Clinical Immunology 146, no. 1 (2020).

98 F. La Rosée et al., "The Janus Kinase 1/2 Inhibitor Ruxolitinib in COVID-19 with Severe Systemic Hyperinflammation," Leukemia 34, no. 7 (2020).

99 ClinicalTrials.gov.

100 X. Wang et al., "Neutralizing Antibodies Responses to Sars-Cov-2 in COVID-19 Inpatients and Convalescent Patients," Clin Infect Dis (2020).

101 Shiyao Pei et al., "Convalescent Plasma to Treat COVID-19: Chinese Strategy and Experiences," medRxiv (2020).

have reported its efficacy in prophylaxis and treatment of SARS-CoV-2 severe infections[102]. Furthermore, a recent interventional clinical study, including 5000 hospitalized and severely ill COVID-19 patients who were treated with CPT, has reported high safety and effectiveness in improving their clinical outcomes (NCT04338360)[103].

Mesenchymal stem cells (MSCs)

MSCs are multipotent stem cells that present in most human tissues, including the umbilical cord. MSCs could be used to reduce lung damage and inhibit the severe inflammation induced by SARS-CoV-2. Moreover, MSCs are deficient in ACE2 receptors that are essential for the virus to enter the cell[104]. A pilot study of intravenous MSCs transplantation reported that MSCs were safe and effective in treating patients with COVID-19 pneumonia, especially for the patients in critically severe cases[105]. An ongoing clinical trial is assessing the efficacy of MSCs as an adjunct therapy to standard supportive care for patients with moderate or severe COVID-19 (NCT04444271)[106].

Other medications

Corticosteroids

Glucocorticoids may mitigate lung damage caused by hyper inflammation, thereby reducing ARDS and mortality. Dexamethasone is given in a daily single dose of 6 mg for up to 10 days. It was found to be effective for the treatment of COVID-19 patients who are receiving mechanical ventilation and patients who require supplemental oxygen, but who are not mechanically ventilated. It has no usefulness for patients who do not require supplemental oxygen or respiratory support[107].

Low molecular weight heparin (LMWH)

Due to the endothelial damage and cytokine storm, systemic coagulopathy and DIC are associated with a high death rate in COVID-19 patients[108]. Therefore, LMWH is given to patients with elevated D-dimer. In- addition to its anticoagulation effect, LMWH has also anti-inflammatory[109] and antiviral activities[110]. International Society on Thrombosis

102 Michael J Joyner et al., "Effect of Convalescent Plasma on Mortality among Hospitalized Patients with COVID-19: Initial Three-Month Experience," ibid.

103 M. J. Joyner et al., "Early Safety Indicators of COVID-19 Convalescent Plasma in 5000 Patients," J Clin Invest (2020).

104 A. K. Shetty, "Mesenchymal Stem Cell Infusion Shows Promise for Combating Coronavirus (COVID-19)-Induced Pneumonia," Aging Dis 11, no. 2 (2020).

105 Z. Leng et al., "Transplantation of Ace2(-) Mesenchymal Stem Cells Improves the Outcome of Patients with COVID-19 Pneumonia," ibid.

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107 P. Horby et al., "Dexamethasone in Hospitalized Patients with COVID-19 - Preliminary Report," N Engl J Med (2020).

108 Tang et al., "Abnormal Coagulation Parameters Are Associated with Poor Prognosis in Patients with Novel Coronavirus Pneumonia."

109 Timothy Poterucha, Peter Libby, and Samuel Goldhaber, "More Than an Anticoagulant: Do Heparins Have Direct Anti-Inflammatory Effects?," Thrombosis and haemostasis 117 (2015).

110 D. Shukla and P. G. Spear, "Herpesviruses and Heparan Sulfate: An Intimate Relationship in Aid of Viral Entry," The Journal of clinical investigation 108, no. 4 (2001).

and Haemostasis (ISTH) and the American Society of Haematology recommends that hospitalized COVID-19 patients should be given thrombo-prophylactic medications[111]. Enoxaparin is being assessed for its therapeutic efficacy in inhibiting coagulopathy and DIC in severe COVID-19 hospitalized patients in a randomized phase 3 clinical trial (NCT04345848)[112].

Nitric oxide gas

Nitric oxide (NO) inhalation can be beneficial for COVID-19 patients because NO increases oxygen supply to the lungs, and inhibits the formation of clots. A previous study showed that severely ill COVID-19 patients can be treated with NO-gas inhalation since it prevented the progression of ARDS in COVID-19 cases[113]. (NCT04338828) and (NCT04388683) are ongoing randomized controlled phase 2 clinical trials to determine NO efficacy in preventing the progression of ARDS and improving the clinical outcomes in patients with COVID-19[114].

Traditional Chinese medicine (TCM)

TCM has Antiviral, anti-inflammation, immune regulation, and organ protection features due to its rich content of various active ingredients. TCM for COVID-19 has shown significant therapeutic effectiveness. Quercetin, isorhamnetin, kaempferol, luteolin, baicalein, naringenin, and wogonin are the principal active constituents of Chinese medicines for the treatment of COVID-19 by targeting AEC2 and 3CL protein, inhibiting inflammatory mediators, and suppressing free radicals[115].

Vitamin C (ascorbic acid)

Ascorbic acid is a potent antioxidant with anti-inflammatory properties, affects cellular immunity and vascular stability. Conditions of oxidative stress such as severe infections and sepsis that are caused by SARS-CoV-2 may require more vitamin C intake[116].

Vitamin D3

Vitamin D3 supplementation may limit fatal adverse effects such as ARDS in severe COVID-19 cases due to its immunomodulatory and antioxidant effects[117,118]. However, a recent study on the association between Vitamin D levels and COVID-19 infection in UK

111 Jecko Thachil et al., "Isth Interim Guidance on Recognition and Management of Coagulopathy in COVID-19," Journal of Thrombosis and Haemostasis 18, no. 5 (2020).

112 ClinicalTrials.gov.

113 Raj Parikh et al., "Inhaled Nitric Oxide Treatment in Spontaneously Breathing COVID-19 Patients," Therapeutic Advances in Respiratory Disease 14 (2020).

114 ClinicalTrials.gov.

115 Y. F. Huang et al., "Review on the Potential Action Mechanisms of Chinese Medicines in Treating Coronavirus Disease 2019 (COVID-19)," Pharmacol Res 158 (2020).

116 X. B. Wei et al., "Efficacy of Vitamin C in Patients with Sepsis: An Updated Meta-Analysis," Eur J Pharmacol 868 (2020).

117 Kim C. Ohaegbulam et al., "Vitamin D Supplementation in COVID-19 Patients: A Clinical Case Series," American Journal of Therapeutics Publish Ahead of Print (9000).

118 Adrian R. Martineau and Nita G. Forouhi, "Vitamin D for COVID-19: A Case to Answer?," The Lancet Diabetes & Endocrinology 8, no. 9 (2020).

Biobank participants has found no positive association between them[119]. An observational clinical trial in Bursa City Hospital is being conducted to determine if blood levels of 25-hydroxy vitamin D are associated with the incidence and severity of COVID-19 disease (NCT04394390). Another ongoing clinical trial hypothesized that high doses of vitamin D3 can Improve the clinical Outcomes of COVID-19 Patients (NCT04411446)[120].

IX. Vaccines

To date, industry and academic institutions are developing about 167 vaccine candidates, with 28 vaccine candidates in the clinical evaluation and 139 in the preclinical stage[121]. A wide variety of technologies are used, including live attenuated, inactivated, viral vectored, virus-like particles (VLPs), DNA / RNA-based, and protein-based vaccines.

RNA vaccines

Moderna and Pfizer companies have developed 2 SARS-CoV-2 mRNA vaccines[122]. The vaccines comprise fragments of messenger ribonucleic acid (mRNA)[123], which encodes protein S of SARS-CoV-2. After injection into the body, immune cells begin to translate it into viral proteins that act as antigens to be identified by other immune cells. The 2 vaccines are being tested in the third phase of clinical trials [(NCT04470427),(NCT04368728)][124] .

DNA vaccines

The viral DNA encoding the viral proteins is introduced into a suitable microorganism via a plasmid or viral vector. DNA is expressed and translated into immunogenic proteins. Inovio Pharmaceuticals and International Vaccine Institute have developed a new DNA vaccine to prevent SARS-COV-2 infection[125]. The DNA encodes the S glycoprotein of SARS-CoV-2, and it is being assessed for its efficacy, safety, and tolerability in a second phase clinical trial (NCT04447781)[126] .

Protein subunits

Subunit vaccines contain definite antigenic epitopes of the virus that can elicit an immune response. They are produced mainly by recombinant DNA technology. The antigens are generally combined with protein fragments to improve its immunogenicity[127]. An adjuvanted recombinant protein (RBD-Dimer) vaccine has been developed to prevent SARS-CoV-2 infection and it has reached phase 2 of clinical trials (NCT04466085)[128],[129].

119 Claire E. Hastie et al., "Vitamin D Concentrations and COVID-19 Infection in Uk Biobank," Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14, no. 4 (2020).

120 ClinicalTrials.gov.

121 World Health Organization (WHO), "Draft Landscape of COVID-19 Candidate Vaccines," World Health Organization (WHO), https://www.who.int/docs/default-source/coronaviruse/novel-coronavirus-landscape-COVID-19-(2).pdf?sfvrsn=8eed631e_1&download=true.

122 Ibid.

123 T. Kramps and J. Probst, "Messenger Rna-Based Vaccines: Progress, Challenges, Applications," Wiley Interdiscip Rev RNA 4, no. 6 (2013).

124 ClinicalTrials.gov.

125 (WHO), "Draft Landscape of COVID-19 Candidate Vaccines".

126 ClinicalTrials.gov.

Viral vector-based vaccines

It depends on the delivery of a viral gene into the cell by using the genome of another virus. After the expression of the gene in the human cell. Produced antigens induce an immune response[130]. AZD1222 is a promising non-replicating viral vector SARS-CoV-2 vaccine developed by Oxford University and AstraZeneca Company[131].it is being investigated in the third phase trials for its safety, immunogenicity, and efficacy (NCT04516746)[132].

Virus-like particles (VLPs) vaccines

They are non-pathogenic fragments that almost resemble viruses, but without carrying viral genetic material. VLPs are safer, more durable, and easier to synthesize, also can stimulate better immune responses than other vaccines[133]. An example is Plant-derived VLP that has been developed by Medicago Inc. for COVID-19 prevention[134]. It is being tested in first phase clinical trials (NCT04450004)[135].

Live attenuated vaccine

It is produced by decreasing the virulence of the virus while keeping it alive. mutation can rarely occur causing virulence reversal, therefore, it is contraindicated in immunocompromised patients[136]. A SARS-CoV-2 live attenuated vaccine was produced by codon deoptimization by Mehmet Ali Aydinlar University and Acıbadem Labmed Health Services. It is currently in the preclinical phase[137].

Inactivated viral vaccines

SARS-CoV-2 is deactivated by chemical or physical procedures. This vaccine type has lower efficacy than other types, therefore, it is usually a multi-dose vaccine[138]. Many

127 Parismita Kalita et al., "Design of a Peptide-Based Subunit Vaccine against Novel Coronavirus Sars-Cov-2," Microbial pathogenesis 145 (2020).

128 ClinicalTrials.gov.

129 (WHO), "Draft Landscape of COVID-19 Candidate Vaccines".

130 Youngjoo Choi and Jun Chang, "Viral Vectors for Vaccine Applications," Clin Exp Vaccine Res 2, no. 2 (2013).

131 (WHO), "Draft Landscape of COVID-19 Candidate Vaccines".

132 ClinicalTrials.gov.

133 B. V. Syomin and Y. V. Ilyin, "Virus-Like Particles as an Instrument of Vaccine Production," Molecular biology 53, no. 3 (2019).

134 (WHO), "Draft Landscape of COVID-19 Candidate Vaccines".

135 ClinicalTrials.gov.

136 A. S. Lauring, J. O. Jones, and R. Andino, "Rationalizing the Development of Live Attenuated Virus Vaccines," Nat Biotechnol 28, no. 6 (2010).

137 (WHO), "Draft Landscape of COVID-19 Candidate Vaccines".

138 U.S. Department of Health & Human Services, "Vaccine Types," https://www.vaccines.gov/basics/types.

inactivated SARS-CoV-2 vaccines are being investigated for their safety and efficacy, one example is Sinovac's COVID-19 inactivated vaccine which is in the third phase of clinical trials (NCT04456595)[139].

X. Conclusion

In conclusion, SARS-CoV-2 is a --coronavirus is a very contagious novel coronavirus (SARS-CoV-2) that has been widely spreading worldwide. SARS-CoV-2 chiefly spreads through direct human-to-human transmission by inhalation of infectious respiratory droplets or direct contact. Clinical characteristics of COVID-19 patients commonly include fever, myalgia cough, and dyspnea. The elderly and individuals with comorbidities, such as hypertension, diabetes, and cardiovascular diseases, are extremely vulnerable to infection and disease severity which may be associated with cytokine storm that induces acute respiratory distress syndrome (ARDS). Angiotensin-converting enzyme 2 (ACE2) is the basic receptor for SARS-CoV-2 to enter host cells. To date, there are limited therapeutic approaches for COVID-19. Several potential drugs and vaccines are being extensively developed and investigated for their efficacy in the treatment of COVID-19. There are no approved efficient medications for COVID-19 and all of the current followed protocols are mainly the management of symptoms and viral infection's sequences. Therefore, prevention and control measures such as wearing face masks and social distancing must be taken as they are the currently available options we can utilize for COVID-19 containment.

139 ClinicalTrials.gov.

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Efficiency of Preventive and Control Measures of COVID-19

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Abstract

Background and objective: COVID-19 emerged in Wuhan, China in December 2019. The situation with this virus is evolving rapidly, and to date, there are no clinically approved antiviral drugs or vaccines for this infection. So, this paper aims to provide the efficiency of the available non-pharmaceutical interventions for COVID-19 to maximize health gain under budget constraints with feasible measures.

Methodology: publicly available information on COVID-19 and similar infection epidemics, such as SARS, MERS, and Influenza was reviewed to identi-

Özet

Arka plan ve amaç: COVID-19, Aralık 2019'da Çin'in Wuhan kentinde ortaya çıktı. Bu virüsle ilgili durum hızla gelişiyor ve bugüne kadar bu enfeksiyon için klinik olarak onaylanmış antiviral ilaç veya aşı mevcut değil. Bu nedenle bu makale, uygulanabilir önlemlerle bütçe kısıtlamaları altında sağlık kazanımını en üst düzeye çıkarmak için COVID-19'la mücadeleye yönelik mevcut farmasötik olmayan müdahalelerin verimliliğini sağlamayı amaçlamaktadır.

Metodoloji: COVID-19 ve SARS, MERS ve İnfluenza gibi benzer enfeksiyon salgınları hakkında halka açık bilgiler, COVID-19 önleyici ve kontrol tedbirlerinin

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fy the contents related to the efficiency of preventive and control measures of COVID-19. The period of the study was from February to July 2020, Sciencedirect database was searched using the keywords "novel coronavirus", "2019 novel coronavirus", "2019-nCoV" or "COVID-19".

Results: Single non-pharmaceutical public health measures need some improvements to be more efficient and to be used in balance with other public health measures to limit the impact of the epidemic efficiently. The development of novel diagnostic assays and defining the animal source may ensure high-efficiency rates. But these are not enough to find a vaccine or antiviral drugs. "One Health" teams and international cooperation may improve the general efficiency of public health measures.

Conclusion: for efficiency of COVID-19 preventive and control measures, Single non-pharmaceutical public health measures should be improved and used in balance. Vaccine and antiviral drugs should be prepared and made accessible immediately. "One Health" teams and global collaborations should be applied.

Keywords: *Efficiency, COVID-19; Preventive and Control Measures*

verimliliği ile ilgili içerikleri belirlemek için gözden geçirildi. Çalışma zamanı Şubat-Temmuz 2020 arasındaydı, Sciencedirect veri tabanı "yeni koronavirüs", "2019 yeni koronavirüs", "2019-nCoV" veya "COVID-19" anahtar kelimeleri kullanılarak arandı.

Bulgular: Tekli farmasötik olmayan halk sağlığı önlemlerinin, salgının etkisini verimli bir şekilde sınırlandırmak için uygulanan tedbirlerin daha verimli olması için bazı iyileştirmeler ve bunların diğer halk sağlığı önlemleriyle denge içinde kullanılmasına ihtiyacı vardır. Yeni teşhis yöntemlerinin geliştirilmesi ve hayvan kaynağının tanımlanması, yüksek verimlilik oranları sağlayabilir. Ancak bunlar aşı veya antiviral ilaç bulmak için yeterli değildir. "Tek Sağlık" ekipleri ve uluslararası işbirliği, halk sağlığı önlemlerinin genel etkinliğini artırabilir.

Sonuç: COVID-19'u önlemeye ve kontrol altına almaya yönelik tedbirlerin etkinliği için, Farmasötik olmayan tekli halk sağlığı tedbirleri iyileştirilmeli ve dengeli kullanılmalıdır. Aşı ve antiviral ilaçlar hazırlanmalı ve hemen erişilebilir hale getirilmelidir. "Tek Sağlık" ekipleri ve küresel işbirlikleri uygulanmalıdır.

Anahtar kelimeler: *COVID-19, Küresel Ekonomi, Eğitim, Gıda Güvenliği, Çözümler*

*

I. Introduction

Since the emergence of COVID-19 in December 2019 in China, the situation with this disease is evolving. COVID-19 infection reached over 1 million and deaths over 50 thousand at the time of writing on April 2, 2020. Now the epidemic in almost all countries has become pandemic as declared by WHO on March 11, 2020. This infection also caused a high economic impact.

The coronaviruses belong to the family coronaviridae, subfamily Coronavirinae and genera betacoronavirus. Coronaviruses were so named because of the unusually large

club-shaped peplomers projecting from the envelope, which give the appearance of a solar corona. The virion is spherical and can range in size from 60 to 220 nm. It has a tubular nucleocapsid which composed of two proteins, N & M and a very large heavily glycosylated envelope glycoprotein S. The genome consists of a single linear molecule of ssRNA of positive polarity, about 30kb in size, which is 5` capped and 3` polyadenylated and is infectious. The family coronaviridae includes over a dozen major host-specific pathogens of mammals and birds[1]. Although most human coronavirus infections are mild, the epidemics of the two betacoronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), have caused more than 10000 cumulative cases in the past two decades, with mortality rates of 10% for SARS-CoV and 37% for MERS-CoV[2]. In December 2019, a novel coronavirus (2019-nCoV) was first isolated from three patients with pneumonia, connected to the cluster of acute respiratory illness cases from Wuhan, China, and genetically closely related to SARS-CoV, which spread in China in 2003[3].

Epidemiologically, 2019-nCoV is highly infectious, with a general incubation period after infection of 4-8 days. All age groups are susceptible to the virus, of which elderly patients with comorbidities are more likely to experience severe illness[4]. The people who are asymptomatic and in the incubation period may be the source of infection, which is of critical significance to the epidemic prevention and control, respiratory droplets (aerosols) are the major route of transmission by contact over a short distance (1.5 m) and through fomites contaminated by said aerosols. The host factor is not fully understood [5].

Common symptoms at the onset of illness are fever, dry cough, and myalgia or fatigue[6]. Less common symptoms are sputum production, headache, haemoptysis, and diarrhoea. Some laboratory tests could provide some hints about the early forms of the disease, such as lymphopenia. Complications included acute respiratory distress syndrome, RNAaemia, acute cardiac injury, and secondary infection. Patients develop acute respiratory distress syndrome, have a high likelihood of admission to intensive care, and might die[7]. The diagnosis is based on the epidemiological risks, clinical fea-

1 David OW and Frank JF, "Medical virology"; Fourth Edition. (New Mexico: Albuquerque, 1994) pp. 451-452.

2 Chaolin Huang et al, "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China". Lancet 395 2020, pp. 497.

3 Agoritsa Baka et al, Risk assessment: Outbreak of acute respiratory syndrome associated with a novel coronavirus, China: first local transmission in the EU/EEA-third update 31 January 2020 (ECDC, 2020): 2. Available online at http://www.ecdc.europa.eu/en/publications-data/risk-assessment-outbreak-acute-respiratory-syndrome-associated--novel-1

4 Q. Han et al. "Corornavirus 2019-nCoV: A brief perspective from the front line", Journal of Infection, 2020:2.

5 Trilla "A. one world, one health: the novel coronavirus COVID-19 epidemic". Med Clin (Barc) 154. 2020: pp. 175.

6 Han et al., "Coronavirus 2019-nCoV, 2; Huang et al, Clinical features of patients", pp. 500.

7 Ibid

tures, and laboratory tests[8]. Although several therapeutic options have experimented in 2019-nCoV infected patients, there are still no specific therapies[9]. Also, there is currently no vaccine to protect against COVID-19. The best way to prevent infection is to take everyday preventive actions, like avoiding close contact with people who are sick and washing hands often[10].

Historically, believed that public health interventions delay the international spread of pandemics, but do not stop them; delaying disease spread can flatten the epidemiological peak, thus distributing cases over a longer period of time. Having fewer people ill at a given time increases the likelihood that medical and other essential services can be maintained and reduces patient surge capacity needs, as interventions are instituted, some cases of illness will be delayed and others are prevented[11]. However, preventing the transmission of infectious diseases is a core goal of contemporary public health and infection prevention and control[12]. For example, the use of traditional non-medical public health measures to contain an infectious disease outbreak; those decreasing contact between infectious and susceptible people, such as travel restriction, quarantine, and increased social distance, and those decreasing effective contact, like washing hands and wearing masks. The likelihood of these measures working depends on the characteristics of the disease and the affected population. This includes the mode of transmission, incubation period, degree of infectiousness, the age group most affected, and contact behavior of the population[13].

COVID-19 is an emerging public health problem of international concern posing a high risk to countries with vulnerable health systems, as declared by WHO On 30th January 2020, and stated that the ability to control local transmission depends on the application of the principles of rapid identification, prevention, and control, followed by patient isolation, rapid diagnosis, and contact tracing[14]. Strategic objectives of WHO include means of ascertaining clinical severity and the extent of transmission, and optimizing treatment options. A key goal is to minimize the economic impact of the virus and counter misinformation on a global scale. In light of this, various bodies have committed to making articles pertaining to

8 X. Li et al, "Molecular immune pathogenesis and diagnosis of COVID-19, Journal of Pharmaceutical Analysis., 2020;

9 Ibid

10 Centers for Disease Prevention and Control, What you need to know about coronavirus disease 2019 (COVID-19), last modified March 3, 2020: 1. Available online at http://www.cdc.gov< 2019-...pdfCOVID-19 fact sheet - cdc

11 Bruce W. Clements and Julie Ann P. Casani, "Pandemic Influenza in Disasters and Public Health; Planning and Response." 2nd Edition, ed. Bruce W. Clements and Julie Ann P. Casani. Elsevier Inc., 2016, pp. 397-405.

12 R. Barratt, R.Z.Shaban and G.L.Gilbert, "Clinician perceptions of respiratory infection risk; a rationale for research in to mask use in routine practice", Infection, Disease and Health 24 2019: pp. 170.

13 Richard. D. Smith, "Responding to global infectious disease outbreaks: lessons from SARS on the role of risk perception, communication and management", Social Science & Medicine 63, 2006, pp. 3115–3116.

14 Laura N. Purcell and Anthony G. Charles, An Invited Commentary on "World Health Organization declares global emergency: A review of the 2019 novel Coronavirus (COVID-19): Emergency or new reality?" International Journal of Surgery 76, 2020: pp. 111.; Catrin Sohrabi, et al. "Review World Health Organization declares global emergency: A review of the 2019 novel coronavirus" (COVID-19), International Journal of Surgery 76, 2020. pp. 71.

COVID-19 immediately available via open access to support a unified global response[15]. So this study aims to provide the efficiency of the available preventive and control measures for limiting the epidemic, then increase their efficiency, or find alternatives and assist health authorities and people strengthen their capacity to respond to this health disaster and remain prepared for future pandemics by helping them prioritize the selection of interventions that maximize health gain under budget constraints with feasible measures.

II. Methodology

The study was a review of publicly available information and studies on the interventions for the outbreak of the disease in December 2019 and previous studies on similar infection epidemics, such as SARS, MERS and Influenza. The study period was from March to July, Sciencedirect database was searched for articles published in English-language, using the keywords "novel coronavirus", "2019 novel coronavirus", "2019-nCoV" or "COVID-19", and taken search results that were deemed important. About 120 number of literature from these search results, and some text books, articles and WHO reports were reviewed. The results of the search were first screened by title and abstract, and then the full texts of relevant articles were examined. References were selected critically by identifying the contents related to the efficiency of preventive and control measures of COVID-19. Then, the efficiency was analyzed by efficacy, saving cost and the feasibility of the measures. Efficacy was the main parameter that judges efficiency. There may be limited information about the efficiency of COVID-19 outbreak preventive and control measures; given this limitation, the study was revised based on the information that become available. Ethical approval or individual consent was not applicable, as this is a review and discussion paper.

III. Results

Public health measures need to be used in balance to limit the impact of the epidemic efficiently[16]. For single measures: travel control is more efficient than travel restriction, as travel ban and restriction may impose a significant economic burden above the direct costs of the infectious outbreak[17]. In travel control, travelers must be educated and encouraged to adopt preventive and control measures when traveling, with governments' suspension of travel when there is a high peak of the epidemic[18]. Screening passengers may be more efficient in the early stage of the outbreak at which no more cases in a specific country, exit screening is slightly more efficient, and the influenza vaccine may save some costs for entry screening and increase the efficiency[19]. Repeating and using

15 Ibid

16 Clements and Casani, Disasters and Public Health, pp. 405.

17 David L Heymann et al, Global health security: the wider lessons from the west African Ebola virus disease epidemic, Lancet 385 2015, pp. 1897.; Aidan Findlater and Isaac I. Bogoch. "Human Mobility and Global Spread of Infectious Diseases: A Focus on Air Travel. Trends in Prasitology" 34 No.9, 2018, pp. 779.; Marius Gilbert et al, "Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study". Lancet 395, 2020. Pp. 875.

18 18 Heymann et al, Global health security, pp. 1897.

19 Annelies Wilder-Smith, The severe acute respiratory syndrome: Impact on travel and tourism, Travel Medicine and Infectious Disease 4 (2006): pp. 56.; Annelies Wilder-Smith, "Tourism and SARS" in Tour-

different samples for RT-qPCR and combining them with Computed Tomography scans in the diagnosis of suspected individuals may enhance the efficiency of the diagnosis measure[20]. Deployment of drugs and deployment, training and control of health workers would be efficient[21]. Quarantine needs to be fully implemented; otherwise, it will be less efficient, but this may cost much amount that some low economic countries cannot afford[22]. Also, social distancing may cost invisibly by opportunity cost. However, using social distancing measures judiciously without delay may be efficient, and other restrictive measures such as isolation and quarantine would boost its efficiency[23]. Compliance with some lifestyle and behavioral changes would be efficient, and people must be educated to help them comply[24]. Hand hygiene would be the most efficient when used correctly and through systemic strategies, including access to the appropriate supplies and community education[25]. Wearing medical masks by healthy people in the community setting is not efficient, but using them by symptomatic patients and their contacts or healthcare workers may be efficient. Healthy people must use non-medical masks for potential source control in areas with the known or suspected widespread transmission or no capacity to implement other containment measures, but vulnerable populations must use medical masks to protect themselves. Cloth masks are less efficient for them[26], and healthcare workers must use respirators instead of medical masks in case of aerosol-generating procedures[27]. Dissemination of timely and clear health information through various channels may show efficiency[28]. Vector control is less efficient unless we identify the host and

ism in Turbulent Times, ed. Jeff Wilks, Donna Pendergast and Peter Leggat (Elsevier Ltd. 2016), pp. 57.

20 D. Chen et al, Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report, International Journal of Infectious Diseases 2020: pp. 7.; C Xie et al, Comparison of different samples for 2019 novel coronavirus detection by nucleic acid amplification tests, International Journal of Infectious Diseases 2020. pp. 3.

21 C. Burdet et al, Need for integrative thinking to fight against emerging infectious diseases. Proceedings of the 5th seminar on emerging infectious diseases, March 22, 2016 – current trends and proposals, Epidemiology and Public Health Journal 66, 2018. pp. 87.

22 Tang et al, An updated estimation of the risk of transmission of the novel coronavirus (2019-nCoV). Infectious Disease Modeling, 2020. pp. 253.; S. Khan et al, Novel coronavirus, poor quarantine, and the risk of pandemic, Journal of Hospital Infection, 2020. pp. 1.

23 Clements and Casani. Disasters and Public Health, 405; Khan S. et al, Novel coronavirus, 2.

24 Jane Dawson et al, Coronavirus SARS-CoV-2 outbreak: Information and interim guidance for pharmacists and the pharmacy workforce, FIP Health Advisory, 2020. pp. 13.; OW and JF, Medical virology, pp. 303; Yongshi Yang et al, The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China, Journal of Autoimmunity, 2020. pp. 13.; Smith, Responding to global infectious disease outbreaks, pp. 3116.

25 Alexandra Peteres et al, The economics of infection prevention: why it is crucial to invest in hand hygiene and nurses during the novel coronavirus pandemic. J Infect 2020. pp. 1.; Dawson et al, Coronavirus SARS-CoV-2 outbreak, pp. 12.

26 World Health Organization. Advice on the use of masks in the context of COVID-19: Interim guidance 6 April 2020: 1-3. Available online at https://www.who.int/publications-detail/advice-on-the-use-of-masks-the-community-during-home-care-and-inhealth-care-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak.

27 Ibid; World Health Organization. Coronavirus disease 2019 (COVID-19), Situation Report-66, 26 March 2020: 1. Available online at https://www.who.int/publications-detail/infection-Prevention-and-Control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125

28 Xingchen Pan et al, Lessons learned from the 2019-nCoV epidemic on prevention of future infectious diseases, Microbes and Infection 22, 2020. Pp. 89.; Smith, Responding to global infectious disease outbreaks, pp. 3120.

intermediate host[29]. "One Health" teams and international cooperation may improve the general efficiency of public health measures[30].

IV. Discussion

There are a variety of community measures that can be taken during a pandemic to reduce the risk of exposure and subsequent results, but a balance is needed when taking interventions because no intervention is without some economic or social cost[31]. Some studies found that only public health interventions blocking over 60% of transmission would be really effective in controlling and containing the coronavirus outbreak[32].

There is strong evidence of the inefficiency of travel restriction[33]. The revised International Health Regulations (IHR) recommends travel and trade restrictions only when these are deemed necessary, as people have demand for risk experience like their demand for preventive care[34]. So travel control is more efficient than travel restriction. One of the ways of travel control is that travelers must leave travel unless is necessary and adopt other preventive and control measures when it is necessary and must have a valid certificate of Influenza virus vaccination to rule out the differential diagnosis and seek immediate care if symptoms appear[35]. Governments must also encourage travelers for that and suspend migration at times of high peak of epidemic[36].

One of the alternatives for traffic restriction may be screening passengers for early detection of symptomatic patients to prevent the exportation of the disease, but it does not detect asymptomatic patients, so its effectiveness is limited[37]. Screening at entry points is costly and has a low yield, so it is not efficient[38]. Screening at exit points is slighter efficient, as the costs of traveling will not spend. Also, the Influenza vaccine will save some costs, as some costs like diagnostic and quarantine costs will be saved and lower discourage of travel for those unwilling to risk travel for the chance of being quarantined. By analogy with SARS, one may argue that entry screening is justified in light of the major economic, social and international impact that even a single imported

29 Trilla. one world, one health, 175; Zhipeng Zhang et al, Emergence of SARS-like Coronavirus in China: An Update, Journal of Infection, 2020. pp. 7.

30 B.D. Anderson and G.C. Gray, Pathogenesis and Immunology, Emerging and Reemerging Infectious Diseases, in Encyclopedia of Microbiology, 4th Edition, ed. Jonathan Cohen William Powderly Steven Opa Elsevier, 2014. pp. 120.

31 Clements and Casani. Disasters and Public Health, pp. 405.

32 Tang et al, An updated estimation, pp. 253.

33 Heymann et al, Global health security, pp. 1897; Findlater and Bogoch, Human Mobility, pp. 779; Gilbert et al, Preparedness and vulnerability, pp. 875.

34 Latin-American society for Travel Medicine (SLAMVI). The next big threat to global health; 2019 novel coronavirus (2019-nCoV): What advice can we give to travellers? – Interim recommendations January 2020, from the Latin-American society for Travel Medicine (SLAMVI), Travel Medicine and Infectious Disease 33, 2020. pp. 2.

35 Ibid; Baka et al, Outbreak of acute respiratory syndrome, 6.

36 Heymann et al, Global health security, 1897.

37 Findlater and Bogoch. Human Mobility,779; Baka et al, Outbreak of acute respiratory syndrome, 3-4;

38 Baka et al, Outbreak of acute respiratory syndrome, pp. 6; Wilder-Smith, The severe acute respiratory syndrome, pp. 56; Wilder-Smith, Tourism and SARS, pp. 57.

SARS case may have. However, new imported SARS cases need not lead to major outbreaks if systems are in place to identify and isolate them efficiently. Rather than investing in airport screening measures to detect rare infectious diseases[39]. So screening may be efficient in the early stage of the outbreak and no more cases in a specific country. But during the outbreak, investing in other measures, such as monitoring and isolation is more important.

Diagnosis of suspected travelers is more effective than travel restriction[40]; generally, early identification could be a crucial step in proper treatment and control as early as possible[41]. But the most common for the diagnosis of COVID-19 is RT-qPCR method, and the false-negative result of this method is very high[42], it might be better to make a diagnosis combining the Computed Tomography scans and the nucleic acid detection together[43]. A study suggests that both nasopharyngeal and oropharyngeal swabs test of SARS-CoV-2 RNA should be performed to reduce the false-negative rate, more tests, more specimens, and more methods could be considered[44]. Thus, repeating, using different samples, and combining with Computed Tomography scans might be better to reduce false negatives, but will also remain less efficient for the same reason, until accurate, rapid, and cheap tests are obtained.

Treatment of confirmed patients is secondary to the need to control the disease; nevertheless, patient care can change the evolution of an epidemic; prompt treatments in the appropriate health facilities with highly trained professionals may relieve patients as well as prevent transmission to healthy people effectively[45]. Patients with mild symptoms may be given care in the home as hospitals may be full, in isolation to reduce the risk of further transmission[46]. Unfortunately, the absence of specific treatment makes the condition very saddening; instead, there are some helpful medicines with the need for close monitoring. Therefore, deployment of drugs and deploying, training, and controlling health workers would be efficient, as it may save time for treatment and increase the effectiveness of treatment procedures. But more research should be done to produce medicines or develop vaccines.

Quarantine of the exposed persons to monitor their symptoms and ensure early detection of cases proved very effective in stopping or reducing the entry of pandemics into

39 Ibid; Wilder-Smith, The severe acute respiratory syndrome, pp. 56.

40 Heymann et al, Global health security, 1896.

41 M.G. Hemida and M.M. Ba Abduallah, The SARS-CoV-2 outbreak from a one health perspective, One Health, 2019. pp. 10.

42 L. Bai et al, Chinese experts' consensus on the Internet of Things-aided diagnosis and treatment of coronavirus disease 2019, Clinical eHealth, 2020. pp. 7.; Li et al, Molecular immune pathogenesis, 8.

43 Xie et al, Comparison of different samples, pp. 3.

44 Chen et al, Recurrence of positive SARS-CoV-2, pp. 7.

45 Burdet et al, Need for integrative thinking, pp. 87.

46 Yang et al, The deadly coronaviruses, pp. 10.

a country[47]. However, quarantine needs to be fully implemented; otherwise, it will be less effective. A study has estimated that only a quarantine rate of infectious population higher than 90% would enable the effective control of coronavirus outbreaks[48], and this may cost much amount, which some low economic countries cannot afford[49]. Although it has a higher cost, the outcome is also very high if implemented properly. With the onset of air travel and the consequent arrival of passengers before the end of the incubation period, quarantine became much less effective, because the differentiation between those exposed and not exposed is difficult.

Another type of quarantine is the quarantine of persons with no known exposure or making them avoid all places that make them in contact with other persons such as public gathering places and stay at home as far as possible, or in other words social distancing. Social distancing is effective in mitigating disease epidemics[50], but usually multiple such policies, including more restrictive measures such as isolation and quarantine—are implemented in combination to boost effectiveness[51]. The level of development in e-commerce can fully overcome logistical obstacles[52]. Economic protection measures and social consequences need to be considered. Social distancing interventions may be important to public health but must be used judiciously. On the other hand, if interventions are established too late, they may be ineffective. Social distancing may cost invisibly by the opportunity cost that some economic countries cannot afford[53]; instead, low economic countries can use strict policies for travel controlling and monitoring and isolation of the individuals[54]. Therefore, using social distancing measures judiciously without delay may be efficient, and other restrictive measures such as isolation and quarantine would boost its efficiency. But it may be inefficient for low-economic countries, instead, they can use strict policies for travel control and monitoring and isolation of individuals.

A lifestyle change to reduce the incidence and prevalence of the infection, like not sharing clothes, sittings or eating dishes, and cleaning dishes with soap or detergent after eating, and covering the mouth and nose during coughing or sneezing using medical masks, cloth masks, tissues or a flexed elbow, followed by hand hygiene should be practiced by all, especially ill persons, at all time[55], but may be difficult to comply, such as not to handshake[56]; health

47 OW and JF, Medical virology, pp. 303; A. Lombardi et al, Duration of quarantine in hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection: a question needing an answer, Journal of Hospital Infection, 2020. pp. 3.

48 Tang et al, An updated estimation, pp. 253.

49 Khan S et al, Novel coronavirus, pp. 1.

50 Heymann et al, Global health security, 1897; Simiao Chen et al, COVID-19 control in China during mass population movements at New Year, Lancet 395, 2020. pp. 1.

51 Ibid

52 Pan et al, Lessons learned, 89.

53 Khan S. et al, Novel coronavirus, 2; Clements and Casani. Disasters and Public Health, pp. 405.

54 Ibid

55 Dawson et al, Coronavirus SARS-CoV-2 outbreak, pp. 13.

56 OW and JF, Medical virology,303; Yang et al, The deadly coronaviruses, pp. 13.

education may help compliance[57]. Lifestyle or behavioral change not costly, unfortunately, some changes in lifestyle for contact and droplet precautions have some risks like elbow using instead of handshake. However, maintaining a distance between people whenever is possible would be more efficient for this measure than other lifestyle change practices if well complied.

Hand hygiene with alcohol-based hand rub is globally recommended as one of the most effective and low-cost procedures against SARS-CoV-2 cross-contamination. Good hand hygiene programs are dependent on systemic strategies, including access to supplies and the education of people[58]. It should be performed by applying the correct technique recommended by the WHO and using either soap and running water or an alcohol-based hand sanitizer[59]. Hand hygiene does not cost much. Thus, hand hygiene would be the most efficient single measure when used correctly. Wearing gloves may improve hand wash practices by reducing the touching of transmission route parts of the body, thus the hand wash frequency.

Wearing a medical mask is one of the prevention measures to limit the spread of certain respiratory diseases, including SARS-CoV-2 from an infected person to someone else and potential contamination of the environment by droplets. Wearing medical masks by healthy people who are not in contact with symptomatic patients to protect them from droplet particles is not required, as no evidence for disease transmission from healthy people, it may take masks away from symptomatic patient contacts and healthcare workers in short supply times, may cause unnecessary cost and a false sense of security. However, minimizing the transmission of respiratory disease through protective mask use leads to better outcomes for healthcare workers, caregivers or those sharing living space with persons suspected of COVID-19. Cotton cloth masks are not considered appropriate for healthcare workers[60], and respirator masks are specifically required for aerosol-generating procedures[61]. The potential advantages of using masks by healthy people in the general public include: reduced potential exposure risk from asymptomatic persons, so healthy people should use non-medical masks in areas with the known or suspected widespread transmission or no capacity to implement other containment measures for potential source control. This will reduce stigmatization, remind people to be compliant with other measures, encourage the availability of masks and create a source of income for manufacturers. Vulnerable populations must use medical masks for protection62. In these sentences, we can say that mask use is not efficient for healthy people in community settings. However, if medical masks are used by patient contacts combined with other measures in a perfect way, the result will be better. For example, if they are used with adequate hand washing, it helps to keep hands away from mouth

57 Smith, Responding to global infectious disease outbreaks, pp. 3116.

58 Peteres et al, The economics of infection prevention, pp. 1.

59 Dawson et al, Coronavirus SARS-CoV-2 outbreak, pp. 12.

60 World Health Organization. Advice on the use of maks: Interim guidance 6 April 2020, pp. 1-3.

61 Ibid; World Health Organization. Coronavirus disease 2019 (COVID-19), pp. 1.

62 World Health Organization. Advice on the use of masks: Interim guidance 5 June 2020, pp. 7.

and nose until washing hands. But using it incorrectly when wearing, removing, and disposing of hampers its effectiveness. Specifically, respirator masks may give good efficiency results for healthcare workers in aerosol-generating procedures. Anyways, using medical masks is simple and cheap and their use by symptomatic patients and their contacts or healthcare workers may be efficient in preventing the spread of COVID-19.

Health education motivates people to protect themselves from infections as well as to protect others if they are infectious[63]. Health education needs a lot of work to empower people to adopt preventive behavior and improve their understanding of the infection and how to prevent and control its spread[64]. Studies have shown that the dissemination of timely and clear health information through various channels has worked well in some epidemics[65]. Without health education, almost preventive measures will be meaningless, dissemination of timely and clear health information through various channels, such as using media technologies, like social media, may show efficiency as people have part of social responsibilities.

Vector Control: is not very useful to prevent this epidemic effectively, as there is no valid information about primary and intermediate hosts, although some studies have tried to give information without any reliable evidence66. Thus, disease control with this measure would be difficult, and extensive research is needed to be done to identify the vector in order to prevent the disease from the source with greater efficiency[67]. However, most patients worked at or lived around the local Huanan seafood wholesale market, where live animals were also on sale[68]. Therefore, now all possible preventive measures should be taken when dealing with animals and their products. WHO's standard recommendations for the general public to reduce exposure to and transmission of COVID-19 and other respiratory illnesses include: when visiting live markets in areas currently experiencing cases of the novel coronavirus, direct unprotected contact with live animals and surfaces in contact with animals and the consumption of raw or undercooked animal products should be avoided. Raw meat, milk or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices[69].

Lastly, Chinese doctors have efficiently controlled the outbreak of COVID-19 in China, and limited the mortality rate to less than 3% only[70]. So other countries must learn from them and ask them for help, and countries must apply "One Health" teams and

63 Barratt, Shaban and Gilbert; clinician perceptions of respiratory infection risk, pp. 173.

64 Heymann et al, Global health security, pp. 1896.

65 Pan et al, Lessons learned, pp. 89; Smith, Responding to global infectious disease outbreaks, pp. 3120.

66 Trilla, one world, one health, pp. 175

67 Zhang et al, Emergence of SARS-like Coronavirus, pp. 7.

68 Nanshan Chen et al, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395, 2020. pp. 507.

69 Dawson et al, Coronavirus SARS-CoV-2 outbreak, pp. 7-8.

70 M. Adnan Shereen et al, COVID-19 infection: origin, transmission, and characteristics of human coronaviruses, Journal of Advanced Research, 2020. pp. 14.

international cooperation for the prevention and control of COVID-19. "One Health" is an approach that can improve the effectiveness of public health response and interventions, which offers unique diversity in expertise[71], and international cooperation is a key element in preventing, detecting, and extinguishing epidemics early[72].

V. Conclusion

No single measure can show efficiency alone, but the incorporation of all preventive and control measures in a balanced way can efficiently limit the epidemic with the lower expense. Early recognition of the problem, early identification of infected patients, and early mobilization of healthcare resources are critical in limiting morbidity and mortality. Thus, there is an urgent need for the development of novel diagnostic assays that enable the early detection of the virus, help screen a large number of people and animals, and testing of travelers from at-risk regions. Then, proper treatment and control should be in place as early as possible. In addition, the preparation of vaccines and antiviral drugs should be done to ensure high-efficiency rates. Additional efforts should also be made to find the animal source, including the natural reservoir and any intermediate amplification host, to prevent any new epidemic foci or resurgence of similar epidemics. "One Health" teams must be developed and collaboration must be implemented. "One Health" teams can work to identify sources of emerging pathogens and ways to reduce the threat of outbreaks. The implementation and development of "One Health" collaborations on a global scale are critical in reducing the threats of emerging viruses.

Acknowledgments

The author is grateful to all healthcare operators involved in the care of patients with COVID-19 and prevention of the infection who made incredible sacrifices.

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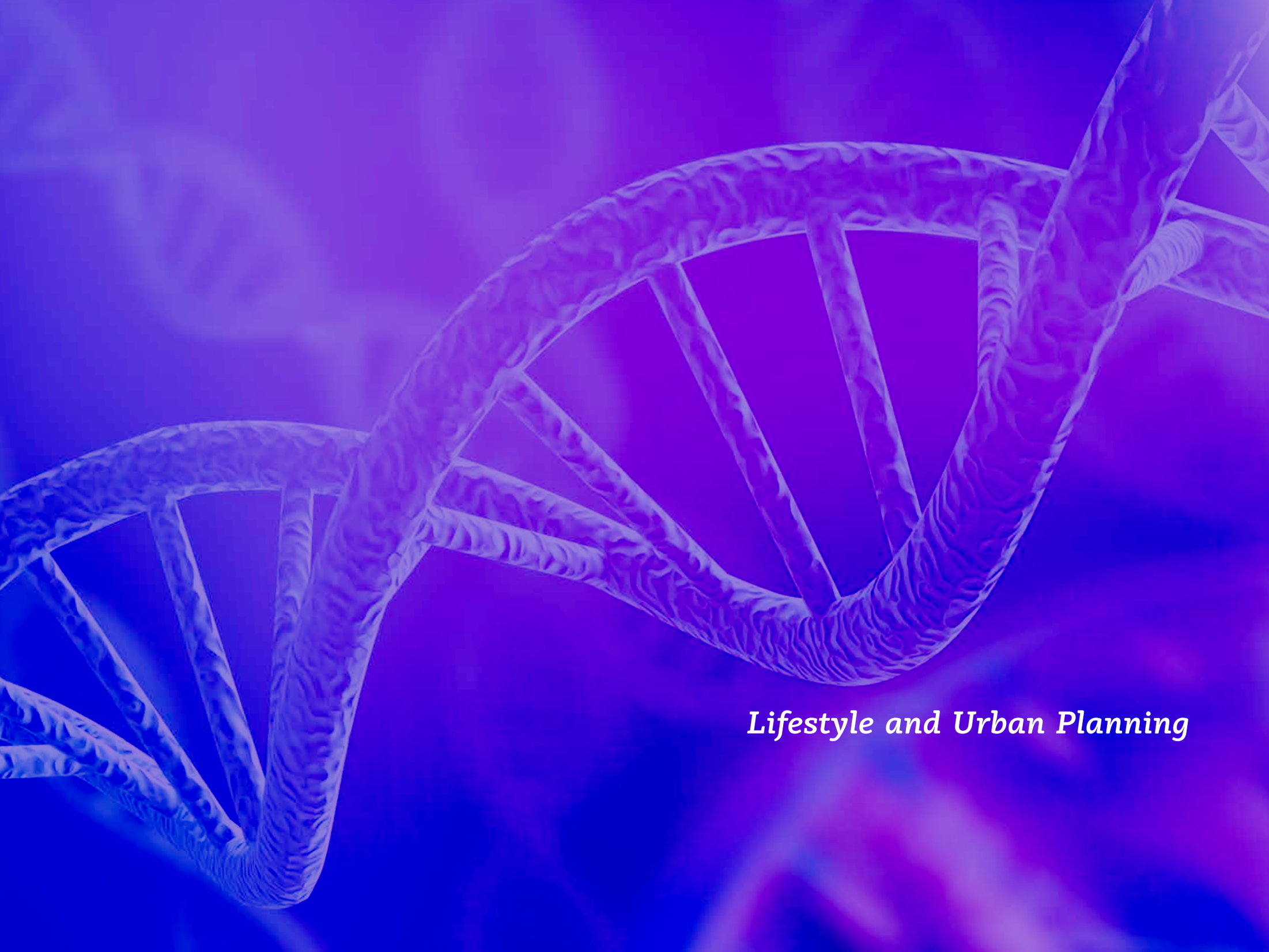
Lifestyle and Urban Planning

An Outlook of Post COVID-19 Urban Planning & Design

Haji Kidui Suleiman*

Abstract

Pandemics have been prevalent throughout human development history. They turned out to be major factors that shaped societies and how people live through their everyday life. Among the factors contributing to pandemics include global travel, urbanization, climate change, increased human–animal contact, and antibiotic resistance along with others. Some of the notable pandemic occurrences in the past include the 1918 global flu pandemic that claimed the lives of approximately 50 million people and the Plague pandemic in the 14th century, which killed between 75 – 200 million people. The most recent pandemics being HIV/AIDS and COVID-19. Responses to pandemics in most cases result in a paradigm shift in the status quo hence usually considered as turning points in civilization. They include shifts

Özet

İnsanlık, tarih boyunca sık sık pandemilere şahit olmuştur. Pandemiler, toplumları ve insanların günlük hayatlarını şekillendiren önemli olaylardandır. Pandemiye katkıda bulunan faktörler arasında küresel seyahat, şehirleşme, iklim değişikliği, insan-hayvan ilişkisinin artması ve antibiyotik direnci sayılabilir. Yaklaşık 50 milyon insanın hayatına mal olan 1918 küresel grip salgını ve 14. yüzyılda 75-200 milyon insanın ölümüne neden olan Veba salgını geçmişte görülmüş kayda değer pandemilerden bazılarıdır. HIV/AIDS ve COVID-19 salgını en yakın salgınlardır. Çoğu vakalarda salgınlara verilen yanıtlar, mevcut durumda bir paradigma değişikliğine neden olur bundan dolayı genellikle medeniyette dönüm noktaları olarak kabul edilir. Bunlar, ideolojilerdeki değişimleri, yeni teknolojik buluşları, politika çerçe-

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in ideologies, new technological inventions, change in policy frameworks, the establishment of new institutions, and change in societal norms. This paper focuses on the responses to the coronavirus pandemic in cities and how they will impact future planning, design, administration, and the governance of cities. As a preliminary response to the pandemic, most cities implemented social distancing measures supplemented with digital intervention to curb its spread. Digital tools such as surveillance and technologies, real-time dashboards, and remote service delivery systems were among the key technological facets adopted. This was augmented by restrictions in movements, control of human interactions, modifications of public transport systems, and regulation of the general social relations in public realms. The moves significantly affected social life, an essential component of a healthy city. Will this be the new norm? Urban areas are complex sociotechnical systems consisting of both physical and social fabrics. Understanding this complex relationship is a daunting task, however, this paper attempts to highlight the possible adjustments of the general townscape after the COVID-19 pandemic.

Keywords: *Pandemic, COVID-19, Cities, Transformations, Public Realm*

vesindeki değişiklikleri, yeni kurumların kurulmasını ve toplumsal normlardaki değişimi içerir. Bu makale, şehirlerdeki COVID-19 pandemisine verilen yanıtlara ve bunların gelecekteki şehir planlamasını, tasarımını, yönetimini ve yönetişimini nasıl etkileyeceğine odaklanmaktadır. Pandemiye bir ön yanıt olarak, çoğu şehir salgının yayılmasını engellemek için dijital müdahale ile desteklenen sosyal mesafe önlemleri uyguladı. Gözetim ve teknolojiler, gerçek zamanlı kontrol panelleri ve uzaktan hizmet sunum sistemleri gibi dijital araçlar, benimsenen temel teknolojik unsurlar arasındaydı. Bu, hareketlerdeki kısıtlamalar, insan etkileşimlerinin kontrolü, toplu taşıma sistemlerinde yapılan değişiklikler ve kamusal alanlarda genel sosyal ilişkilerin düzenlenmesi ile artırıldı. Hareketler, sağlıklı bir şehrin önemli bir bileşeni olan sosyal hayatı önemli ölçüde etkiledi. Peki, bu yeni norm olacak mı? Kentsel alanlar, hem fiziksel hem de sosyal dokulardan oluşan karmaşık sosyoteknik sistemlerdir. Bu karmaşık ilişkiyi anlamak göz korkutucu bir iştir, ancak bu makale COVID-19 salgını sonrasında genel şehir manzarasının olası ayarlamalarını vurgulamaya çalışmaktadır.

Anahtar kelimeler: *Pandemi, COVID-19, Şehir Planlama, Kamusal Alan*

*

I. Introduction

COVID-19 outbreak, a global pandemic that was declared by the World Health Organization (WHO) as of March 2020 has been spreading rampantly across the globe resulting in lockdowns, remote working, banning of gatherings, curfews, and restricted movements within cities between countries. Major cities such as Paris, Madrid, Milan, New York, Istanbul, and London among others have equally been grappling in what manner to contain the pandemic. The situation has driven nations and their respective cities to a standstill. The impacts of the COVID-19 pandemic have severely been felt in urban areas, where the majority of the people reside. According to the world bank, 55.7% of the world population reside in the cities as of 2019 and the percentage is projected to

increase to 68% by 2050 (World Bank, 2019). This shows that the population in cities will keep on rising at least for the next three decades. Cities are equally considered the global engines of development, this is due to the several advantages predominantly offered by cities, including economies of scale, agglomerations & localizations, efficient infrastructure, services, communications, governance, human interactions, and basic infrastructural services. This makes cities very instrumental in propagating human civilization and key drivers towards global economic prosperity. Hence the need to make them adaptable, liveable, sustainable, smart, and resilient to adverse conditions such as pandemics, climate change, disasters, and calamities.

The onset of COVID-19 has greatly affected the level, kind, and quality of services offered in cities. Urban areas are affected in terms of physical elements, social interactions, local economy, infrastructure and service delivery, and the general public life, among other facets. These changes have a long-term repercussion and likely to influence the future planning, designing, management, and general administration of cities. Matthew Gevers 2020 explains the current state of urban planning and design as being influenced by previous interventions to curb diseases and pandemics. Moritz Maria, 2020 correspondingly mentions that health concerns have always steered urban planning and designs of cities throughout the history of human civilization. In essence, urban planning as a professional field emerged in the 19th century as a means to address health concerns arising from the rampant environmental pollution brought about by the industrial revolution (Jachnow A, 2020). It was used as a means to bring order, harmony, and coordination to cities. However, due to the recurrent nature of pandemic, disasters, and calamities striking both urban areas and regions, the profession should rather take a proactive role such that cities are planned and designed to enable the prevention of diseases as opposed to fighting them after the occurrence. To achieve this, there is a need for an adaptive, flexible, and integrated approaches to urban planning and design. This is very essential in the wake of pandemics such as COVID-19 whereby in most cases, cities bear the brunt.

II. Methodology

This research is guided by the general research question of "what are the effects of COVID-19 in the future planning and design of Cities?" In order to respond to the main question, the following sub-questions were pondered upon:

- What is the history of global pandemics?
- How have the pandemics impacted urban planning and design?
- How will COVID-19 shape the future planning and design of cities?

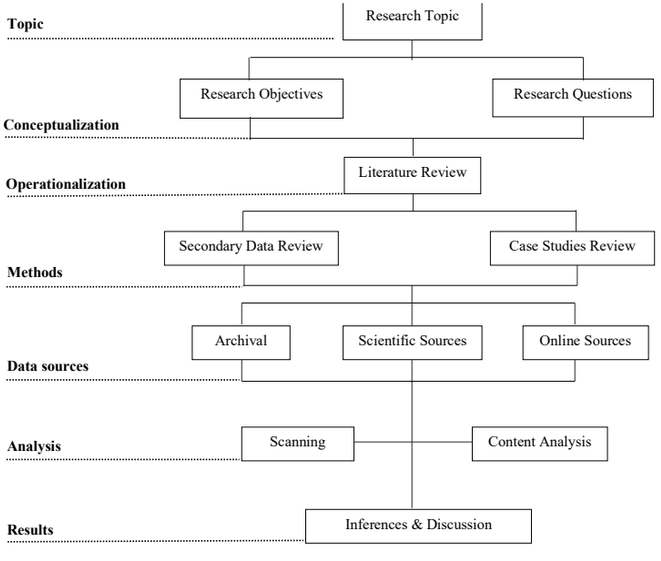
The goal of this paper is to understand the history of global pandemics in relation to COVID-19 and how it will shape the future direction of the planning and design of cities.

The specific objectives of this paper entail:

- To understand what are the previous pandemics which have stricken the world
- To evaluate how the different pandemics impacted the planning and design of cities
- To evaluate how COVID-19 will influence the future planning and design of cities.

The paper adopts pure exploratory research. It entails reviews of secondary data both published articles, papers, and online sources relating to pandemics, their history and impacts in the urban arena, and futuristic ideologies regarding shifts in policies, public space interactions, zoning guidelines, urban planning and design strategies and sustainable urban development.

Figure 1: Research Methodologyt



Source: Author, 2020

III. Literature Review

History of global pandemics

The world health organization (WHO) defines the pandemic as "an epidemic occurring worldwide or over a very wide area, crossing international boundaries and usually affecting a large number of people." The centers for disease control and prevention(CDC) on the other hand explains it as an epidemic that has spread over several countries or continents usually affecting a large number of people. The two definitions give us two key characteristics that distinguish a pandemic. These are, 'covering a large geographical extent while affecting more than one country' and 'involving a significant number of people'.

Several pandemics have afflicted the world over human development history. These range from plague, smallpox, flu, cholera, tuberculosis, typhoid, polio, and yellow fever outbreak. The earlier pandemics were primarily caused by people's movement mainly soldiers during wars. Pandemics like the plague were famous between the period 430 – 750 AD. They were prevalent in several parts of the world including Athens, Italy, Egypt, and Constantinople among others. As a sequence, the plague wiped at least a third of Europe's population. The other common pandemic was the black death of 1331 – 1353. The pandemic claimed almost 200 million lives around the world. It started in Asia and ravaged Europe. Another notorious pandemic is the 1918 flu which infected 5oo million people. The death reports from this pandemic are approximated to be 100 million. Other common pandemics include the cholera outbreak which occurred in the period between 1817 – 1975. It occurred in areas like India, China, Japan, Indonesia, Russia, Europe, South & Central America, and Africa. Another stubborn pandemic was the Spanish flu of 1918 – 1929 which claimed almost 50 million lives, Asian flu of 1957 – 1958, Hongkong flu of 1968 – 1969, and the swine flu of 2009 – 2010. The flu pandemic claimed a million fatalities globally. Sagar Aryal, 2020 attributes the contemporary global challenges such as climate change, rapid urbanization, antibiotic resistance, increased human-animal contact contributing significantly to pandemic prevalence. Hence, following the current global trends, pandemics are anticipated to be even more common in the future.

COVID-19 Pandemic

COVID-19 (Coronavirus disease 2019) is the most recent pandemic declared by WHO in March 2020, famously known as the Coronavirus pandemic. It started in Wuhan city, China, and has been spreading all over the globe with more than 25.6 million confirmed cases as of September 2020. The total number of deaths during the same period amounted to 852, 758 whereas the extent of its geographical coverage included 188 countries and territories out of the global total of 195 (WHO September 2020). The virus is mainly transmitted via saliva droplets or discharge produced from an infected person through coughing, sneezing, or speaking. Studies have confirmed that the virus can survive in the air for up to three hours and can stay on hard surfaces for a period of up to three days. When a healthy person inhales or gets into contact with the droplets they get infected. Among the symptoms of COVID-19 include aches and pains, sore throat, diarrhea, fever, tiredness, dry cough, and loss of taste and smell, among others. Older people and those with underlying medical conditions like heart diseases, diabetes, and respiratory illnesses tend to face a higher risk of developing serious complications. However, the majority of the people experience mild illness without the need to seek special medical attention. Among the measures taken to curb the spread of the

disease include as suggested by CDC, WHO, and health experts include; washing hands often using soap and water of sanitizer containing at least 60% alcohol, avoiding close contact by keeping at least 1.5 m, covering mouth and nose with a mask when in public places, covering coughs and sneezes, cleaning and disinfecting frequently touched surfaces, monitoring daily health through temperature and COVID symptoms check-ups. The measures adopted to curb the disease greatly influence the level of human interactions in cities and more so public spaces since these places were planned and designed to allow social interactions amongst the users, a core principle for a socially cohesive city.

Urban planning responses to pandemics

Megahed and Ghoneim 2020 explain epidemics to have transformed the built environment from its architecture to urbanism. The views are shared by Freestone 2001 who explains urban planning's role to have undergone remarkable changes constantly adapting to place, culture, and circumstances as a result of external factors such as pandemics, disasters, and calamities, among others. Urban planning and design have experienced tremendous insights and innovation during crises such as pandemics, natural disasters, and economic depressions. This is because planners and designers are forced to think of solutions that would prevent cities from collapsing. According to historical records, responses to pandemics in urban areas differ from one to another depending on their nature. Jachnow, 2020 explains that pandemics caused by water-borne diseases tend to spur responses involving physical interventions in urban space such as improvement of infrastructure network or redesigning of street layouts and the urban form as it was done in cities such as London, Hamburg and Marseille after the water-borne pandemics of the 1850s.

The recurring cholera outbreaks in the 19th century resulted in massive infrastructural development in cities like London, Paris, and New York (Sara Jensen, 2019). This included the installation of underground wastewater systems, improved housing conditions, design of long and straight boulevards, and large open spaces in cities that act as urban breathers allowing ample air circulation and access to sunlight in the cities. New York city's central park was created after the cholera pandemic in 1853 to improve general public health. The event marked the onset of the urban park movement, which Wyne Stormann 2009, explains as a social movement that advocated for the creation of urban parks within America. The practice was equally adopted in other parts of the globe including Europe and was embraced in mainstream urban planning as a principle of designing healthy cities. This promoted citizen's well-being by introducing adequate green spaces and parks while at the same time creating recreation opportunities in cities.

Airborne pandemics such as flu and tuberculosis in the 20th century called for social distancing measures and the need to reduce human-human contact as evidenced in the Spanish flu of 1918 – 1920 in the city of Philadelphia. In order to reduce human contact, there was a need to address densities in urban areas. And areas with a very high density of people such as slums and other informal settlements were cleared.

Other measured adopted included proper waste management, increased provision of ventilated spaces, and also the development of single zoning codes. This enabled separation of land uses, whereby incompatible land uses such as industrial and residential uses were alienated to minimize pollution and contaminations. The zoning codes were equally instrumental in controlling population densities. Residential densities were introduced, whereby neighborhoods were identified as low density, medium density, and high density. This controlled the human population in the respective cities, movements, and traffic congestions (Catherine Brinkley, 2020).

IV. Discussion

In the wake of globalization, rapid population increase, and industrialization, pandemics have been very common in the urban arena. Urban planners, designers, and municipalities' managers all over the globe have constantly faced the challenge of how to effectively respond to pandemics to minimize casualties and provide sustainable solutions. As a result, planning regulations all over the globe have been in constant change and adaptation to maximize health, wellbeing, resilience, liveability, and sustainability in the urban areas.

The coronavirus pandemic has arguably resulted in several shifts in normalcy in the urban realm. These include digitalization of the urbanscape, social interactions in public spaces, housing design & construction, commercial & office space provision, public transport, sustainable transport options, and construction technology, among others. These are further discussed in detail below.

Digital transformation

The general urbanscape has been significantly shifting in the awake of COVID-19. Many functionalities in municipalities have gone digital in an attempt to minimize physical human interactions to curb the spread of the pandemic. Among the technological tools applied include the use of drones to enforce COVID-19 rules such as social distancing, spraying disinfectants, and supply of medicines in cities like Madrid. The City of Vilnius in Lithuania has been using drones to pass flyers to their older citizens. Surveillance tools and sensors such as remote temperature sensing have equally been widely applied to address the pandemic. Realtime dashboards and data sharing technologies have greatly been applied to crowdsource data from the public including location information and also disseminating useful information to the public. The dashboards equally show real-time heat maps of crowding in public spaces hence crucial in crowd management. Mobile applications have correspondingly been used to enhance communication between city administrators and the public. Cities such as London and Berlin have been using mobile applications to send precautions to their citizens, monitor the progress of those in quarantine, and pass the information on how citizens could take care of themselves and their loved ones during this pandemic. Other cities that heavily invested in digital tools and showed significant success in curbing the pandemic include Hongkong, Taiwan, and South Korea. This kind of technological intervention is anticipated to continue even after the pandemic. Cities will continue applying these tools to

enhance service delivery; provide information to the public; gather useful information from the public and support the daily administration of the urban areas.

Public spaces

Public spaces are among the key facets of the urban realm considerably impacted by the pandemic. Areas such as squares, plazas, streets, parks have been left vacant devoid of their vibrant social life. By virtue of their nature, these places are open to the public and designed to encourage social interactions. However, the aspect of keeping social distance has had a detrimental effect on these spaces. This has resulted into closure, removal, or barricading of shared facilities and services on these places to curtail virus spread. Empty public squares have been prevalent in cities Famous urban squares in London, Barcelona, Berlin, Istanbul, and Milan among other famous public spaces. Among the prominent changes expected in public spaces include reduction in shared facilities, physical barriers that would guarantee social distance between strangers, the introduction of surveillance, and crowd management technologies. This will regulate the number of users within public spaces and reduce overcrowding. The physical location of public spaces on the other hand will equally change. Authorities are focusing on bringing public spaces within walking distances from residential neighborhoods to eliminate longer commuting distances.

Housing

With regard to the housing sector, questions arise concerning housing layouts, densities, and indoor air quality. During the COVID-19 pandemic, people have been spending significant time indoors due to lockdowns. They gave rise to the popular phrase 'working from home', online learning, online conferences, and meetings, among others. As a result, there is an increasing demand for better home offices that would offer privacy and safety devoid of disturbance from family, pets, and other domestic things. This, therefore, calls for a shift in housing designs and real estate development to offer homes that can as well function as offices. Since people are spending a substantial amount of time indoors, there is a need to design homes that would maximize outdoor benefits such as allowing maximizing air circulation, access to natural sunlight, and incorporating plants and green elements within the indoor environments. This would promote the mental, physical health of communities residing within. Real estate development will also need to focus on providing commercial spaces 'corner shops' within residential premises. This will reduce the need to visit malls and also minimize commuting distance for domestic shopping.

Commercial and office spaces

According to digital commerce statistics 2020, online sales have risen from $ 266.84 to $ 347.26 billion in the first half of 2020, just in the US alone, representing an increase of 30.1% A similar situation is observed all over the globe including Turkey. This presents a negative shift in the need for commercial space provisions in urban centers. Since most commercial needs are accomplished online. Remote working has equally been very popular during this period and has been proving to be cost-effective and convenient to companies since they do not need to pay rents and employees could

work from the comfort of their homes. Global companies such as Google and Facebook which occupy a huge chunk of office spaces in Central Business Districts (CBD) are considering remote working up to mid-2021, a move which has been adopted by several multinational corporations too. As a consequence, offices are left vacant, their future demand is equally anticipated to decrease. This raises questions on the future of office space provision in the CBD and whether they will continue to function as commercial hubs or rather largely function as entertainment and cultural centers.

Public transport

Public transport is very key in the daily movement of people, goods, and services within an urban setting. In the wake of the COVID pandemic, this sector has been adversely affected and is considered among the risky places in spreading the virus. Systems such as trains, busses, trams, and BRTs tend to collect people together thereby increasing the exposure. As a strategy to minimize this, most municipalities have opted to decrease the fleets and also capacities of public transport facilities thereby reducing congestion. Some went a notch further by promoting pedestrianization and micro-mobility transportation options like bicycles, electric scooters, and other single-user transport options that enable observing social distancing guidelines. The future of public transport is thus linked to less crowded mass transit fleets and increased use of micro-mobility transport options which occupy less space on road, environmentally friendly, less crowded, and flexible.

Compact development – 15 min city concept

COVID-19 has strengthened the concept of 15 minutes city, an urban planning paradigm that encourages compact development by ensuring all the basic human activities such as shopping, working, entertainment & recreation, healthcare, education, and administrative services are within 15 minutes-walk. It is geared towards decentralization of cities' services to the lowest possible level, where people could just walk or ride to their destinations. Paris and New York have piloted this paradigm and looking forward to adopting this as a strategy to rejuvenate the cities amidst the pandemic. This paradigm will likely gain popularity in many urban areas since it reduces commuting distances, brings closer services to communities, and equally curtails urban sprawl.

Sustainable transport

Sustainable transport options such as walking, cycling have greatly been emphasized among key strategies to battle the COVID-19 crisis. The modes separate people physically, encourage physical exercise, and alleviates pressure on public transport. This drive encouraged cities to improve on walking infrastructure by allocating street space to pedestrians and cyclists. Cities such as Bogota and Berlin introduced temporary bike lanes to promote cycling. Seattle and Francisco have encouraged the 'open street' and 'slow streets' concepts. The former allows opening streets to pedestrians and closing them for vehicles. Whereas the latter blocks through traffic and allow streets to be used by a pedestrian, cyclists, and local traffic only. In the short run, these practices are seen as measures to mitigate the spread of the virus, however in the long run they are

prone to be permanently adopted in the cities since they are equitable and zero-carbon transport options.

Green practices

Among the strategies sought after by city leaders to revive cities is the incorporation of green practices to battle climate change and promote eco-friendly development practices. The International Coalition of Inclusive and Sustainable Cities (ICCAR) deliberated on funding green stimulus plans as the most promising post-COVID-19 recovery strategy for cities. This will see increased investment in renewable energy sources, promoting energy-efficient buildings and transportation options, creating more parks & green corridors within the city, and promoting micro-mobility transport among other alternatives.

V. Summary

Metropolises, cities, towns, and all urban areas in their entirety are anticipated to experience significant shifts in planning design, administration, and governance after the COVID-19 pandemic. Section 4 above discusses the key sectors currently transforming which include digital transformation, public spaces, housing, commercial & office spaces, public transport, compact development, sustainable transport, and green practices. Table 1 below gives a breakdown of the anticipated changes in the respective sector in an attempt to highlight the primary intervention likely to be upheld long after the pandemic is gone.

Table 1: Summary of key interventions per sector

Sector	Key areas of Interventions
Digital transformation	▪ Increased use of drones: - Communication; Service delivery; Monitoring people and activities. ▪ Sensors: - Monitoring environmental quality; health check-ups, public health safety. ▪ Surveillance technologies: - Traffic & Crowd management; urban security. ▪ Dashboards: - Communications; Entertainment; city information
Public spaces	▪ Reduced shared facilities, ▪ Located in close proximity to the users – mostly within neighborhoods to eliminate long commuting distances ▪ Adaptable public spaces for individual and small group activities ▪ Installation of monitoring and surveillance technologies to manage crowds
Housing	▪ Change in housing design layout to incorporate functional home offices – Ideal space for learning, working, and businesses. ▪ More Exposure to natural light; natural air circulation; and greenery – enhanced local microclimate. ▪ Locating corner-shops, local shopping centers, and social places within close proximity
Commercial & Office spaces (Central Business District - CBD)	▪ Increased availability of local commercial stalls within neighborhoods and walking distances. ▪ Change in CBD land uses from strong commercial centers to entertainment and cultural centers ▪ Adaptable office spaces, which can be reorganized to suit different needs
Public transport	▪ Use of low capacity public transport fleets ▪ Conversion of more streets to 'open streets' or 'slow streets' ▪ Encouraging micro-mobility such as bicycles, electric scooters, walking.
Compact development	▪ Provision of all essential services within 15 min walking or cycling distance
Sustainable transport	▪ Increased provision of pedestrian and cycling lanes, encouraging micro-mobility such as scooters, electric mobility ▪ Wide use of zero carbon-emitting transportation options.
Green practices	▪ Increased investment in renewable energy sources ▪ More energy-efficient buildings. ▪ Increased provision of neighborhood parks and green spaces within walking distance

VI. Conclusion

COVID-19 can be viewed as a blessing in disguise when it comes to the general planning, design and management of cities. During this period, cities have witnessed increased harmony between human activities and nature, sustainable environmental practices, rapid digital transformation, increased remote working and service delivery across many sectors such as education, health, commerce, and finance, among others. A transformation that was long overdue and likely to be the new normalcy. These intermittent changes have further exposed the huge inequalities and disparities existing between cities in terms of the level of infrastructure development, emergency response capacity, effective service delivery, crisis management, and the general management

of urban areas. Correspondingly, disparities have equally manifested amongst the general public whereby low-income communities and minorities were adversely affected compared to the middle and high-income groups. This was exacerbated by their lack of adequate access to health services hence further aggravating their situation. In the order to realize sustainable development cities need to address the inequalities within and ensure equitable access to services for all. Concurrently, there is a need to fast-track investment in infrastructure, enact a supportive policy framework to enhance citizen's data privacy in the wake of the digitalized urban realm.

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Rethinking Urban Planning:

A Perspective for Post-COVID-19 Urbanism

Tendai Sylvester Mhlanga *

Abstract

The global outbreak of the COVID-19 virus, which exponentially swept across the globe has caused detrimental ramifications to the global health, economy, and paralyzed urban metabolism. The impact of the COVID-19 pandemic on urban planning has provided urban planners with a broad insight on rethinking the role of urban designs and planning to strengthen urban resilience to future pandemics and diseases. Since the evolution of urban planning from the 19th century, diseases have played a significant role in shaping cities. The global outbreak of the COVID-19 pandemic has affected billions of urbanites globally particularly on the aspect of urban economy and society, infrastructure and environment, health and wellbeing in the scope of the City Resilience Concept. Although it's too early to conclude

Özet

Katlanarak tüm dünyayı kasıp kavuran COVID-19 virüsü salgını, küresel sağlık, ekonomi ve kentsel metabolizmada zararlı sonuçlara neden oldu. COVID-19 salgınının şehir planlaması üzerindeki etkisi, şehir planlamacılarına kentsel tasarımların rolünü yeniden düşünme ve gelecekteki salgınlara ve hastalıklara karşı kentsel dayanıklılığı güçlendirmek için planlama konusunda geniş bir iç görü sağlamıştır. 19. yüzyıldan itibaren kentsel planlamanın evriminden bu yana, hastalıklar şehirlerin şekillenmesinde önemli bir rol oynadı. Koronavirüs salgını, küresel olarak milyarlarca şehirli nüfusu özellikle Kentsel Dayanıklılık Kavramı kapsamında kentsel ekonomi ve toplum, altyapı ve çevre, sağlık ve refah açısından etkiledi. Kentsel planlama bağlamında tipik planlama kavramları üzerine bir sonuca varmak için

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on the typical planning concepts in the context of urban planning, the contemporary findings point to pragmatic approaches required to improve the planning and designing of our cities. The study examines the relationship between urban planning, designs, and urban public health. It further explains the pathways and mechanisms by which urban planning affects the different domains of urban resilience to pandemics. The study used a desktop review of books and academic articles to study the urban planning transformations induced by the past major pandemics, epidemics, and diseases as case studies to base the discussion on how coronavirus would likely affect post-COVID-19 urbanism. Interviews with academics, government officials, resilience specialists, health officials, town planners, architects, and landscape architects were also conducted to have a better understanding of the current impacts of COVID-19 and urban planning.

Keywords: *COVID-19, Urban resilience, Urbanism, Urban design, Urban public health, Regional disparities*

henüz çok erken olmasına rağmen, çağdaş bulgular şehirlerimizin planlama ve tasarımını iyileştirmek için gerekli olan pragmatik yaklaşımlara işaret ediyor. Çalışma, kentsel planlama, tasarımlar ve kentsel halk sağlığı arasındaki ilişkiyi incelemektedir. Ayrıca, kentsel planlamanın pandemilere karşı kentsel dayanıklılığın farklı alanlarını etkilediği yolları ve mekanizmaları açıklamaktadır. Çalışma, koronavirüsün salgın sonrası şehirciliği nasıl etkileyeceğine dair tartışmayı ele almak için geçmiş büyük pandemiler, salgınlar ve hastalıkların neden olduğu şehir planlama dönüşümlerini incelemek için kitapların ve akademik makalelerin bir masaüstü incelemesini kullandı. Ayrıca COVID-19 ve şehir planlamasının mevcut etkilerini daha iyi anlamak için akademisyenler, hükümet yetkilileri, dayanıklılık uzmanları, sağlık yetkilileri, şehir planlamacıları, mimarlar ve peyzaj mimarları ile görüşmeler yapıldı.

Anahtar Kelime: *COVID-19, Kentsel dayanıklılık, Şehircilik, Kentsel tasarım, Kentsel halk sağlığı, Bölgesel farklılıklar*

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I. Introduction

The global rapid urbanization is posing a large population at risk during COVID-19 as cities are mainly the hotspots. Most global cities are disproportionally affected but they constitute areas of high infections and deaths making the pandemic an urban crisis that requires a solution based on a multidisciplinary approach. However, urban planners have a significant role to play in re-examining post-COVID-19 urbanism. Cities are both social and economic hubs whose functionality is being greatly affected due to COVID-19. Although the pandemic has resulted in high human and economic losses, it has brought an opportunity to evaluate urban resilience to pandemics and or contagious diseases along with an opportunity to rethink the role of urban planning, designing, and management to strengthen urban resilience. Urban form, morphology (shape, size, density, structure), and the critical infrastructure, (water, electricity, telecommunication infrastructure, buildings environment, or public spaces) are critical in strengthening urban resilience. Although ancient cities recovered from several past health crises, COVID-19 response strategies must be reflective, built, and remodeled upon the strengths of previous strategies to strengthen urban resilience to the future health crises. Planning for resilient cities in the 21st century is planning in unchartered territories full of knowns

and unknows solvable and unsolvable both planned and spontaneously uncertainties which must be comprehensively incorporated in all urban planning domains. Future uncertainties and predictability are best explained by the mathematician Edward Lorenz commonly known as the 'Butterfly Effect'. "Does the flap of a butterfly's wings in Brazil set off a tornado in Texas? [1]"

The extent of the impact of the health crisis in the built environments is influenced by other underlying factors such as chronic stress which requires substantive planning procedures and practice. In the 'new normal', social distance has become the current dominant mitigatory measure, until a vaccine could be discovered. Therefore, new substantial urban planning approaches have to be put in place to accommodate the flexible practice of social distancing in public space and spheres to mitigate the outspread as a short-term measure, and to be adopted in planning practice in the future long-term measures. Urban planning discipline was predominately instituted from the perception that cities were disorderly organized, filthy causing numerous health crisis and a harmonized development was essential to rectify these urban challenges. Coronavirus has left many urban planners puzzled and wondering how post-pandemic urban planning would be. Not only those in the planning profession are perplexed, but all professional disciplines are also contemplative on how best they can withstand future pandemics. Nonetheless, unlike some other professions, the planning discipline particularly spatial planning is not based on 'trial and error' procedures but rather on substantive planning approaches which have to prove their worth for a considerable time in the future.

II. Global Perspective of Pandemics and Urban Planning

Diseases play a significant role in urban planning and design. Previous studies on pandemics show that pandemics and diseases influence urban planning and design. Numerous pandemics that precede COVID-19 such as the Black Death, Spanish Flu, SARS, MERS, Ebola only to name a few. The Black Death which happened during the 13th century has shaped European cityscapes through 'additive' and 'argumentative' processes[2]. It resulted in the establishment of zoning laws and the creation of more public spaces which were used as quarantine zones and to improve the wellbeing of neighborhoods[3]. Geographers such as Slater and Conzen played a vital role in the conceptualization of the urbanscape following the Black Death through the application of morphological concepts[4]. The third plague was used as an instrument of crafting urban policies that fostering racial residential segregation between the colonizers in

1 Lorenz, E., "Predictability: Does the Flap of a Butterfly's Wings in Brazil Set Off a Tornado in Texas?" 2012 L&R Uddannelse A/S, 2012, pp. 11–13. static.gymportalen.dk/sites/lru.dk/files/lru/132_kap6_lorenz_artikel_the_butterfly_effect.pdf.16, August, 2020.

2 Lilley, K. D., "Urban Planning after the Black Death: Townscape Transformation in Later Medieval England (1350-1530)." Urban History 42, no. 1, 2015. pp. 22–42.

3 Ibid.

4 Ibid.

the Anglophone and Francophone countries[5]. Public urban health has led to the wide application of Geographic Information Systems (GIS) in urban planning, spatial data presentation, and analysis. In 1832, a French Geographer, Charles Picquet mapped cholera epidemiology in the 48 districts of Paris using GIS. Two decades later, in 1854 in a similar health crisis, John Snow depicted cholera deaths in London. This shows how real-time geospatial technologies are crucial in urban planning and public health. In some African countries like Nigeria and Kenya, urban planning was institutionalized as an urban health crisis response strategy to fight cholera and bubonic plague epidemic[6].

The third plague has led to decentralized operations, the enacting of urban sanitary building codes and standards resulting in clearance of urban slums, urban renewal, and the upgrading of the dilapidated infrastructure[7]. Subsequently, this improved urban planning in a broader perspective including safety and security, public health and hygiene as well as the establishment of property rights. During the 19th century, the world was struck by a series of cholera epidemics. The industrial revolution created deprived living standards and shanty crowded housing developments in industrial and manufacturing cities. The industrialization has caused haphazard city development and consequently, a wide outbreak of diseases initiated the redevelopment of cities to improve their sanitary conditions. In English and Welsh cities, the deteriorated urban water quality resulting from sewage contamination was the key driver to the outspread of cholera[8]. Cholera influenced the improved water and wastewater planning and management (the municipalization of water, treatment & catchment management), improvement in housing designs and standards[9]. The substandard housing developments were infested by insects, bats, and rats. These houses were regarded as disease incubators. Housing Acts and policies were established to guide an orderly development of standard housing. Strikingly, the outbreak of the coronavirus is linked to a meat market in Wuhan where the virus is perceived to have been transmitted from bats[10].

The Spanish flu pandemic which occurred toward the end of World War 1 in 1918 had similarities with coronavirus in terms of transmission and mitigatory measures. Wearing masks, quarantine after exposure, the practice of social distancing, hygiene, and sanitary measures were mandatory. Its spread was accelerated by the mass movement of soldiers across Europe. At the end of the Spanish flu pandemic, cities focused on further

5 Bigon, L., "Bubonic Plague, Colonial Ideologies, and Urban Planning Policies: Dakar, Lagos, and Kumasi." Planning Perspectives 31, no. 2, 2016. pp. 205–26.

6 Cobbinah, P. B., Erdiaw-Kwasie, M, and Adams, E. A., "COVID-19: Can It Transform Urban Planning in Africa?" Cities & Health. 2020. pp. 1–4.

7 Bigon, L., "Bubonic Plague, Colonial Ideologies, and Urban Planning Policies: Dakar, Lagos, and Kumasi." Planning Perspectives 31, no. 2, 2016. pp. 205–26.

8 Davenport, R. J., Satchell, M., and Sahw-Taylor, L, M. W., "Cholera as a 'Sanitary Test' of British Cities, 1831–1866." History of the Family 24, no. 2, 2019. pp. 404–38.

9 Ibid.

10 Hu, B., Ge, X., Wang, L., and Shi, Z., "Bat Origin of Human Coronaviruses Coronaviruses: Emerging and Re-Emerging Pathogens in Humans and Animals Susanna Lau Positive-Strand RNA Viruses." Virology Journal 12, no. 1, 2015. pp. 1–11.

improvements of housing standards, provision of public spaces, parks, playing grounds, decongesting of streets, zoning regulations, and the establishment of spatial justice.

In the aftermath of the SARS epidemic, Hong Kong introduced wastewater regulations to enhance the reticulation and management of wastewater after realizing that SARS was spread through connected drainage systems[11]. Following the Black Death, Los Angeles adopted urban renewal programs and approximately 2,500 Mexican houses were destroyed to pave way for slum upgrading purposes although the program was also criticized as a weapon of segregation[12].

Ebenezer Howard propounded the garden city movement in 1898 as a strategy to control urban density, the spread of diseases, pollution as well as the provision of open spaces and public parks which were converted to quarantine zones during health crises. His concept is one of the most influential urban planning concepts during the 20th century. Though the model faces some critics, even in the 21st century planning realm it's still being revitalized to suit the prevailing urban challenges. In 1998 Peter hall revised the concept and more recently in the "Sociable Cities: The 21st Century Reinvention of the Garden City" a second edition he co-authored with Colin Ward that was published in 2014[13]. Another prominent architect was Le Corbusier who has greatly influenced urban planning, "his works epitomize the megalomania of high modernism[14]."

Undoubtedly, the risk mitigatory changes in urban planning policy and practice that were adopted in the aftermath of every past pandemic enabled the study and urban planners to evaluate the significance of these approaches to curb coronavirus and might influence post-COVID-19 urbanism. In the backdrop of these major developments that triggered the evolution, social and structural changes of urbanism and urban designs, the study hypothesizes that the COVID-19 pandemic will trigger transformation in urban planning and urban public health.

III. Methodology

The study adopted a qualitative research method based on a desktop review of secondary data sources. These include academic articles, textbooks, and newspapers. The desktop review provided a background on how previous pandemics, epidemics, and diseases have impacted urban planning and designs. This helps in examining the prevailing trends of COVID-19 and projecting possible pragmatic pathways and domains to adopt in order to strengthen urban resilience to future pandemics. Furthermore, the study draws some data from 35 online interviews conducted between 10 August

11 Lau, J.T.F., Yang, X., Pang, E., Tsui, H. Y., Wong, E., and Wing, Y.K., "SARS-Related Perceptions in Hong Kong." Emerging Infectious Diseases 11, no. 3, 2005. pp. 417–24.

12 Deverell, W., Whitewashed Adobe: The Rise of Los Angeles and the Remaking of Its Mexican Past. University of California Press. Berkeley: University of California Press, 2004.

13 Hall, P., and Ward, C., Sociable Cities: The 21st Century Reinvention of the Garden City 2nd Edition. New York: Routledge, 2014.

14 Hemenway, T., "The Permaculture City: Regenerative Design for Urban, Suburban, and Town Resilience." Library Journal, 2015.

and 15 September 2020 with academics, government officials, resilience specialists, academia, health officials, town planners, architects, and landscape architects from Zimbabwe, South Africa, Zambia, Ghana, Kenya, and Turkey.

IV. Urban Planning in Post-COVID-19

As has been discussed earlier, previous pandemics have shaped cities since the 19th century. The novel coronavirus outbreak was first recorded in Wuhan, China, and rapidly spread to other countries[15]. Coronavirus pandemic which occurred in this 21st century, like the past pandemics, will also transform modern urban planning policies and designs. Currently, cities are implementing short-term mitigatory measures to minimizes the widespread of the virus. long-term measures are still been designed and widely contested as some approaches are seemingly contradictory to the current approaches that were being advocated for building urban resilience. Planning for urban resilience during pandemics like coronavirus is still in the initial phase, systematic evaluation of urban policies and planning strategies is vital to avoid overlooking other critical aspects as evidenced by the overwhelmed scenario of the current urban resilience strategies. Generally, cities were planning towards climate change resilience and ignored planning for global pandemics.

Digitalization of Cities (Smart Cities)

There is a great need for a global transition in the digitalization of our cities, the adoption of the smart city concept particularly in the Global South where Information and Technology (ITC) services are still lagging. Although before COVID-19, the application of digital services was largely used by the private sectors, it is a prerequisite for public services to be digitalized to ensure undisrupted service delivery during future pandemics. In countries such as Turkey, America, Singapore where better internet network is provided, experienced a smooth transition on the adoption of online services. For instance, most schools in Turkey adopted online classes whilst most schools in the Global South, in countries like Zimbabwe, Malawi, and Mozambique failed to adopt such services because of the inaccessibility of the services by the majority of the students. This was mainly because of the affordability, availability, and reliability of the services.

Geographical Information System (GIS) is essential in urban planning during COVID-19. It can be used for spatially monitoring and implementation of social distance measures and the spatial distribution of different urban activities using proximity analysis. GIS can be used to calculate the maximum capacity of the population that can utilize different public spaces such as parks and recreational facilities like beaches whilst maintaining social distances. For instance, Esri conducted a beach capacity analysis on Bournemouth beach in southern England and found out that the beach can accommodate approximately a population of 78,000 people which would make it easy in regulating people within a stipulated figure.

15 Zhu, H., Wei, L., and Niu, P., "The Novel Coronavirus Outbreak in Wuhan, China." Global Health Research and Policy 5, no. 1, 2020. pp. 2019–21.

COVID-19 has proved the essentiality of Big Data in local authorities. The necessity of virtual real-time, geo-referenced spatial data in monitoring and analyzing data. For example, real-time surveillance can be used in public places. This would assist policymakers, resilience strategists, landscape architects, architects, and urban planners to better understand urban population flow and enables them to forecast, assess and identify locations and times of potential widespread diseases. The adoption of the smart city concept and other modern technology into urban planning is paramount. The use of the urban twinning system which can integrate a wide range of urban data and present a visual 3D analysis and graphs on spatial analysis in real-time has been usefully applied to monitor urban traffic flow, building safety, disaster management, air quality, implementation of economic plans among others. However, there must be a balance in the adoption of technology in urban planning, strengthening cyber securing is also important.

Polycentric Vs Monocentric Urban Designs

The monocentric approach in urban spatial planning creates huge population movements basically to city centers which are economic and administrative hubs of the entire city. This intrinsically increases population density flow on a single city node. Subsequentially this compromises social distancing and causes a rapid upsurge in the spread of contagious diseases and quickly spreads the disease to all neighborhoods that depended on a particular monocenter for various activities. This also calls for cities to decentralize essential services. Generally, most of the essential public services are highly centralized both in management and operations. Previous diseases such as the Spanish Flu, the SARS epidemic, Ebola epidemic have proved the frangibility of the centralization of economic hubs and public services. Singapore closed three hospitals during the SARS outbreak to contain the outspread of the diseases. On the same note, during this COVID-19 pandemic, supply linkages of health care, food supplies are being disrupted which exposed the fragility of cities. Regional disparities in many cities particularly the urban and peri-urban development expose higher vulnerability during health crises. When towns and cities are poorly planned and managed, it creates regions of inequalities that problematizes health crisis management across the urban-rural spectrum[16]. Although decentralization is credited for enhancing resilience, however, precautions must be done to avoid increasing fragility by the same concept[17]. During disasters, decentration and polycentric spatial designs enhance urban resilience through their multiple nodality which reduces single nodality failure as in a centralized system. Therefore, decentralization and the adoption of polycentric urban designs are paramount in contemporary city planning.

Transport Planning

The globalized travel and market chains have consolidated the connectedness of cities which peddled the spread of coronavirus. Indisputably, the transport sector can be at-

16 Cobbinah, P. B., Erdiaw-Kwasie, M, and Adams, E. A., "COVID-19: Can It Transform Urban Planning in Africa?" Cities & Health 00, no. 00, 2020. pp. 1–4.

17 Batty, M., "The Coronavirus Crisis: What Will the Post-Pandemic City Look Like?" Environment and Planning B: Urban Analytics and City Science 47, no. 4, 2020. pp. 547–52.

tributed as a key driver for the global spread of the COVID-19 virus from Wuhan, China where it emerged. Therefore, travel restrictions, social distance, and proper hygiene were implemented worldwide as measures to mitigate the outspread of the virus. A city can be referred to as a complex system with interconnected nodes linking its functionality. During a system failure, it is somehow cognizant to disconnects or removes some of the links to other nodes to ensure continual functionality with minimal vulnerability. Globally most cities experienced changes in modes of transport and travel restrictions. Discussion with urban planners indicated that most people preferred cycling or walking while some preferred private transport to public transport. COVID-19 has proved that roads can be a risk reduction tool in mitigating new infections by stopping mobility. If transport is the virus transmission avenue, then a transport-based solution needs to be put in place to ensure urban mobility and resource flow. Road designs and networks need to be improved to minimize traveling distances. Therefore, urban planners must adopt compact and mixed planning city designs. Urban layout designs influence traveling distances[18]. Road and street design networks vary considerably across countries. Experiences from COVID-19 indicate that there is also a need for wider sidewalks to provide enough space for social distancing. Spatial designs need to promote walkability and cycling, particularly for short routes. This means that cities ought to provide basic essential services within walkable distances.

Green Spaces Designs

Public space is a public good that must be provided in both good and bad times. Public spaces reduce stress and improve physical, psychological, and mental health[19]. According to the World Economic Forum (2020), children in the Netherlands have 90% of physical and psychological well-being which is attributed to the provisions of neighborhood parks and playing grounds for children. Recent urban studies have identified the relationship between humans and nature for improved wellbeing. Pavements and trails in public parks need to be widened to enable people to move freely while practicing social distance. Public water points and toilets need to be installed with touchless flushing systems. This system can be applied to all public places and institutions. Public parks might also be supported by the provision of parks at a building level by retrofitting the existing buildings to provide room for greener balconies or through the top-up method by adding green roofs as building parks. This would help in decongesting public parks and enables easy contact tracing. Public open spaces and parks are essential for installing makeshift hospitals and clinics during disasters.[20]

Urban Density

In the light of the previous urban health crisis, such as cholera outbreaks has led to decongestion of crowded neighborhoods and improvement of sanitary measures. History has proven that past epidemics (SARS, MERS, Ebola, etc.) and globalization have influenced the transmission of infectious diseases.[21] The relationship between density and public health is largely contested in the context of urban planning and epidemiology. There are two schools of thought, one which supports that urban density influences the spread of contagious diseases and the other which criticizes the notion. Studies on the spatial pattern and the spread of the 1918-199 influenza in England and Wales indicated that there was "no association between transmissibility, death rates and indicators of population density and residential crowding."[22] In contrast, some studies concluded that socioeconomic demographic characteristics such as income and apartment size had a strong effect on the transferability and mortality rate of the same 1918-1919 influenza pandemic.[23]

Metropolitan areas with higher populations have higher COVID-19 infection and mortality rates.[24] "Country density is not significantly related to COVID-19 infection rate possibly due to more adherence to social distancing guidelines."[25] A comparison study on country density and COVID-19 mortality rate indicated that countries with higher densities have lower virus-related mortality rates as compared to countries with lower densities, possibly due to superior health care systems.[26] Connectivity matters more than density, regions, countries, or cities, with higher socioeconomic and commuting linkages are the most vulnerable during pandemics.[27] Contrary to a similar study done in Algeria on the relationship of the spatial distribution of COVID-19 infections and mortality, and population density shows that the two variables are significantly correlated.[28] Population density might be a catalyst for the spread of COVID-19 if social distancing and other measures for mitigation purposes are taken lightly. A recent study of COVID-19 and population density in England shows that higher infections were recorded in locations with higher population densities probably because these areas are located near major transport hubs like airports.[29] There was a significant drop in infections in these densely populated areas after the implementation of social distancing measures.[30]

18 Ercoskun, O., and Mhlanga, T. S., "Mapping, Modeling and Measuring Photovoltaic Potential in Urban Environments Using Google Project Sunroof." Gazi University Journal of Science Part B: Art Humanities Design and Planning 8, no. 2, 2020. pp. 593–606.

19 Jacobs, J., The Death and Life of Great American Cities. Random House, 1961.

20 Cobbinah, P. B., Erdiaw-Kwasie, M, and Adams, E. A., "COVID-19: Can It Transform Urban Planning in Africa?" Cities & Health 00, no. 00, 2020. pp. 1–4.

21 Haverland, M., "Rethinking Urban Planning in a Post COVID World," 2020. https://www.wsp.com/en-GL/insights/rethinking-urban-planning-in-a-post-covid-world. accessed 16, August, 2020.

22 Chowell, G., Bettencourt, L. M. A., Johnson, N., Alonso, W. J., and Viboud, C., "The 1918-1919 Influenza Pandemic in England and Wales: Spatial Patterns in Transmissibility and Mortality Impact." Proceedings of the Royal Society B: Biological Sciences 275, no. 1634, 2008. pp. 501–9.

23 Murray, C. J.L., Lopez, A. D., Chin, B., Feehan, D., and Hill, K. H., "Estimation of Potential Global Pandemic Influenza Mortality on the Basis of Vital Registry Data from the 1918-20 Pandemic: A Quantitative Analysis." Lancet 368, no. 9554, 2006. pp. 2211–18.

24 Hamidi, S., Sabouri, S., and Ewing, R., "Does Density Aggravate the COVID-19 Pandemic? Early Findings and Lessons for Planners." Journal of the American Planning Association 86, no. 4, 2020. pp. 495–509.

25 Ibid.

26 Ibid.

27 Ibid.

28 Kadi, N., and Khelfaoui, M., "Population Density, a Factor in the Spread of COVID-19 in Algeria: Statistic Study." Bulletin of the National Research Centre 44, no. 1, 2020.

29 Tammes, P., "Social Distancing, Population Density, and Spread of COVID-19 in England: A Longitudinal Study." BJGP Open 4, no. 3, 2020. pp. 1–5.

30 Ibid.

Therefore, population density might be a major variable to consider in urban planning though it might not be directly related to the spread of pandemics, however, the maintenance of proximity measures to minimize transferability might be difficult to observe in cities with high informality and high density. This brings a new question that, should we promote sparsely horizontal urban expansion or vertical expansion, upzoning with compactness? These become two extreme ends that need to be examined as climate change resilience policies are championing for optimum land-use efficiency and compactness over sprawling.

Urban Design

History had already proved that pandemic, epidemic, and diseases enlighten urban planning, architectural and neighborhood layout designs. It also influences changes in the administrative structures of local authorities and disaster management. Coronavirus has raised debates in terms of the spatial distribution of different urban activities, land use, and neighborhood layout designs. During this COVID-19 there is an upsurge in the use of 'virtual mobility' through the use of online interviews, classes, and political meetings.[31] Virtual mobility was also noticed as remote working increased which might contribute to urban decay because of the shift of offices from the Central Business Districts to the suburban. Mixed layout patterns with offices and residential places might be widely adopted to minimize mobility. Urban land-use patterns influence urban mobility,[32] therefore urban economic zones need to be strategically and spatially distributed to minimize traffic on one zone.

Regularization or Upgrading of Informal Settlements

Historically, we have learned how diseases, pandemics, plagues, and epidemics transformed urban planning. In most cases, there was the clearance of the informal sector as some of these urban health crises were ascribed as 'lack of sanitary syndrome'. The lack of critical infrastructure especially water and wastewater reticulation system in slums settlements aggravates the spread of diseases.

In countries like Zimbabwe where the unemployment rate is approximately above 70% according to some studies[33] of which most of this percentage are informally employed. This proportionally shows the scale of the socioeconomic impact of total lockdown measures initially adopted. The urban informal economy was greatly affected because informal traders do not have savings to depend on during the closure of their operations. Local authorities in Zimbabwe destroyed some of the informal market stalls in major cities. Therefore, planning and provision of formalized market stalls that enable

31 Haverland, M., "Rethinking Urban Planning in a Post COVID World," 2020. https://www.wsp.com/en-GL/insights/rethinking-urban-planning-in-a-post-covid-world. accessed 16, August, 2020.

32 Ercoskun, O., and Mhlanga, T. S., "Mapping, Modeling and Measuring Photovoltaic Potential in Urban Environments Using Google Project Sunroof." Gazi University Journal of Science Part B: Art Humanities Design and Planning 8, no. 2, 2020. pp. 593–606.

33 Bhebhe, T. B., Sulochana, N., Zororo, M., Obert, S., and Desderio, C.M., "Effects of the Educated Youth Unemployment Nexus in Zimbabwe." IOSR Journal of Humanities and Social Science Ver. II 20, no. 10, 2015. pp. 1–11.

informal traders to operate while maintaining WHO COVID-19 regulations is essential. The neoliberal policies that were implemented by many countries are immensely affecting urban planning and management particularly on the provision of housing for the poor. In Zimbabwe, the decentralization and the privatization of land development to housing cooperatives coupled with the socio-economic challenges have caused urban land speculations, increased informal settlements. Housing policies need to be revised in order to ensure standard housing for all, sanity, and order in human settlements. The socio-economic and political quagmire which have hit Zimbabwe for the past two decades has brought challenges in urban planning, land administration, and service delivery. The need for ownership of urban housing land upsurged causing urban sprawl, created unsustainable housing settlements and overcrowding as household occupancy rate increased posing much threat to urban resilience.

V. Conclusion

It can be concluded that there is a relationship between urban planning, design, and public health. The study argues that urbanism, urban planning, and designs are essential instruments that have compound implications on urban public health. Although the impacts of urban health crisis are predefined, the response strategies follow a nonlinear system though with high embeddedness of path dependency that needs to be retrofitted to strengthen urban resilience. Resilient livable cities can be explained by the magnetic poles, 'like poles repel' 'unlike poles attract'. Thus, in the urban planning domain, resilience needs diversity. The study discussed various substantive urban planning issues being faced during the COVID-19 pandemic ranging from, policy, designs, and management. Lessons learned from coronavirus and other earlier pandemic on how urban planning impacts urban health, mobility, cubing health crises need to be taken into account in planning for future cities. Coronavirus is a signal of how devastating future pandemic might be, this should be an eyeopener to urban planners, local and central governance to reschedule their investment priorities and priorities in investing in resilient human settlements with the aspect of pandemic in consideration. COVID-19 has proved that global cities were unprepared for such a huge catastrophe of respiratory virus. Most cities were planning and focusing on other acute and chronic disasters such as climate change, floods, landslides, fire, droughts, and earthquakes. Planning for a pandemic is still in that infancy stage. However, simultaneously planning for a pandemic like COVID-19 and other global challenges such as climate change placed planners in a dilemma of two extreme ends that are contradictory. There is a need to further develop universal comprehensive strategies and tools to assess urban resilience as most approaches and tools are focusing on a single urban challenge, 'resilience of what' while overlooking the resilience of other aspects. This would inform common planning principles and practices that consider a wider range of resilience challenges that would inform new policies and city resilience framework. History repeats itself, hence another pandemic will emerge. The question is, when? Let that one come when cities are prepared.

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Architecture as a Part of Cure: Will Living Spaces Turn Into Hospitals After the COVID-19 Pandemic?

Dania Abdel-Aziz*

Abstract

Architecture is not only inspired by imagination. It is also a response to human needs. Architecture and urban planning have always played a fundamental role during pandemics and post-pandemic times. Pandemics, whether synthetic or natural, have long been a catastrophe for cities. Meanwhile, they had an enormous influence in shaping environments, buildings, and cities. Human responses to this pandemic are what helped in shaping architecture, not the pandemic itself. Health pandemics such as; Cholera in the nineteenth century helped develop the city's infrastructure, building

Özet

Mimarlık insan ihtiyaçlarına cevap olma niteliği taşır ve sadece hayal gücünden ilham almaz. Mimari ve kentsel planlama, pandemi sırasında ve pandemi sonrası dönemde her zaman temel bir rol oynamıştır. Sentetik veya doğal salgınlar her zaman şehirler için bir felaket olmuştur ve bunlar, çevrenin, binaların ve şehirlerin oluşumunda muazzam bir etkiye sahiptir. Bu pandemiye insan tepkileri, pandeminin kendisine değil, mimarinin şekillenmesine yardımcı oldu. On dokuzuncu yüzyıldaki kolera salgını, şehrin altyapısının gelişmesine, geniş bulvarların ve parkların inşasına katkıda bu-

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wide boulevards and parks. Likewise, in the twentieth century, Tuberculosis led to modern urban planning and architecture. Currently, COVID-19 is the most pressing health problem as a cause of death worldwide. Will this recent pandemic have a similar effect on the built environment in the near future? Will a new architectural movement evolve in response to this pandemic? In an attempt to visualize the post-pandemic architecture, a historical review has been carried out studying the impact of the previous pandemics on the built environment. The consequences COVID-19 had on human interactions within the built environment were discussed by tracking this pandemic's current architectural response. This review found that this epidemic has affected public perceptions and future behaviour to become more immune, responsible, and caring for nature. The awareness of sustainability and energy use among people and governments has arisen. Throughout the post-pandemic, it can be seen that the architecture will be more dynamic and intelligent, meaning that the city will be safe for all groups. Meanwhile, the interest in employing technology in designs will continue due to the leading role in providing solutions to this epidemic.

Keywords: *Post-pandemic Architecture, Sustainable Architecture, Built Environment, Human Interaction*

lundu. Aynı şekilde, yirminci yüzyılda tüberküloz, modern şehir planlaması ve mimarisine yol açtı. Şu anda, COVID-19, dünya çapında ölüm nedeni olarak en acil sağlık sorunudur. Bu son salgın yakın gelecekte yapılı çevre üzerinde benzer bir etkiye sahip olacak mı? Bu salgına yanıt olarak yeni bir mimari hareket gelişecek mi? Pandemi sonrası mimariyi görselleştirmek amacıyla, önceki pandemilerin yapılı çevre üzerindeki etkisini inceleyen tarihsel bir inceleme yapıldı. COVID-19'un yerleşik ortamlarda insan etkileşimi üzerindeki etkileri, bu salgına verilen mevcut mimari yanıtı takip ederek tartışıldı. Bu inceleme, bu salgının halkın algılarını ve gelecekteki davranışları etkilediğini ve böylece daha korunaklı, sorumlu ve doğaya özen gösterdiklerini gösterdi. İnsanlar ve hükümetler arasında sürdürülebilirlik ve enerji kullanımı bilinci ortaya çıktı. Pandemi sonrası dönemde mimarinin daha dinamik ve akıllı olacağı, yani şehrin tüm gruplar için güvenli olacağı görülebilmektedir. Bu arada, bu salgına çözüm sağlamada oynadığı öncü rol nedeniyle tasarımda teknolojiyi kullanmaya olan ilgi devam edecek.

Anahtar kelimeler: *Salgın Sonrası Mimari, Sürdürülebilir Mimari, Yapılı Çevre, İnsan etkileşimi*

*

I. Introduction

The shift in our daily lives

Architecture is an intertwining of sociology, psychology, economics, environmental sciences, beauty values, history, and geography, all of which fuse to achieve an architectural philosophy and new urban visions[1]. In the global crisis, architecture alongside urban planning played a significant role in preventing health pandemics[2]. With the

1 Jencks, Charles, and Karl Kropf, Theories and, Vol. 312. Chichester: Academy Editions, 1997.

2 Guenther, Robin, and Gail Vittori. Sustainable healthcare architecture. John Wiley & Sons, 2008.

spread of the COVID-19 virus around the world, city by city was closed. Transportation - including public transit, commercial, and civil aviation - has stopped, see Figure (1).

The COVID-19 pandemic changed the rhythm of the entire world in a few days. Due to its rapid spread, it resulted in millions of patients and hundreds of thousands of victims. People all over the world overwhelm the concern for social distancing and wear masks. It is changing the way we live and work in dramatic ways. Again architects and urban planners face an unprecedented challenge to gradually reconfigure the city and suppress this global crisis just as they succeed in former times.

Figure (1): Traffic before and after pandemic's lockdown in Yangon, India.[3]

A study conducted by Sung & Monschauer (2020) investigated the changes in transport behaviour during the COVID-19 crisis. The investigation indicates that by the end of March 2020, the global road transport activity was 50% less than the average in 2019. The commercial travel activity also had decreased by 75% by mid-April 2020. The study also found that there has been a global decline in demand for passenger transportation and remarkable growth in bicycle use.

This change also affected human interactions with the built environments. All over the world, things have shifted a lot from working remotely to virtual events, which provoked less noise, traffic, and pollution in different cities, check Figure (2). These tangible effects of this crisis on the environmental and health levels prompted governments to take critical sustainable decisions towards energy use policies, climate change issues, and transportation.

3 Soutik Biswas, India coronavirus, accessed June 20, 2020

Figure (2): New Delhi's air quality improved drastically between November 2019 and April 2020 because of lockdown measures to curb COVID-19.[4]

This crisis prompted us to notice how the built environment affected the speed of disease spread among the world's countries on the one hand, and how it limited human interaction in which affected the global economy negatively. It can be inferred that this is not just a health crisis; It's a design issue, too. During this crisis, architects and planners must rethink how cities are planned, built, and used the space and land available in this crisis. Urban resilience in according to Meerow et al. (2016),[5] is *"the ability of an urban system … to rapidly maintain or return to desirable functions in the face of disruption, adapt to change, and rapidly transform systems that limit current or future adaptive capacity."* This suggests that built environment designing methods should be resilient and must depend on human interaction with nature and with each other.

From this point, many questions have pondered on; how can cities survive a global pandemic? Can architecture, by adopting new concepts and theories related to building design and urban planning, help us adapt to the pandemic? Since Tuberculosis has shaped modernity, will our quarantine experience in the COVID-19 period affect the future of architecture?

To evaluate how COVID-19 will influence the built environment's design and planning, one must understand how previous pandemics shaped the built environment. Various articles, published papers, and online resources were reviewed relating to pandemics' history and their impacts on the built environment and the current situation of COVID-19.

Explaining the relationship between the built environment and human interaction, Architects and planners should identify and articulate the opportunities that cities can seize to make a strong comeback after the end of an era of unprecedented social and economic unrest caused by the pandemic.

4 Thomas Wintle, COVID-19 and the city, accessed July 25, 2020.

5 Meerow, Joshua and Melissa. Defining urban, Landscape and urban planning 147, 2016. pp. 38-49

II. Previous Scenarios

A group of economists, academics, and policymakers in the world, believe that the COVID-19 epidemic is an opportunity to reform the economy, the environment, and lifestyle in the long term, creating opportunities for a dynamic push in the current situation and raising serious questions about the future and in all sectors of life.

Today the whole world is fighting the COVID-19 pandemic and carefully awaiting the profound changes that will affect us. Rarely does an epidemic pass without leaving deep imprints on our societies. Epidemics also helped inform a new kind of architecture that continues to inspire architects today - have influenced the design of our houses, buildings, and cities- such as; Cholera and Tuberculosis.

Design in the time of cholera: the rise of the modern city

In the summer of 1832, cholera claimed the lives of 3,500 residents in New York City in weeks.[6] Muddy streets filled with garbage, human waste, and animal excrement, unsanitary and overcrowded conditions contributed to the spread of cholera, causing several pandemics. This had a lasting impact on the built environment. This spurred the need for better ventilation (French authorities tore down 12,000 buildings), new drainage and sanitary systems, as well as new zoning laws to curb congested living.[7] In the twentieth century, Haussmann in 1850 remodelled Paris by demolishing crowded neighbourhoods favouring broad avenues, parks, and public squares, see Figure (3).

Figure (3): Paris before and after Haussmann's renovation.[8]

6 Lee Flannery, Design in the Time of Cholera, accessed June 8, 2020.

7 Christopher Klein, How Pandemics Spurred Cities to Make, accessed April 30, 2020.

8 Stefan Andrews, Paris upside down: the city under, accessed May 20, 2020.

Response to the disease ended up spurring urban design elements such as wide tree-lined boulevards and parks (such as Central Park in New York), erected fountains; streets were paved, aqueduct system designed to carry potable drinking water. These responses resulted in discoveries in public sanitation and urban design interventions with a lasting impact on the built environment in some of the world's most famous cities, for example, New York and London.[9]

Tuberculosis pandemic and shaping modernist architecture: form followed fear of infection, just as much as function

In the early twentieth century, Tuberculosis was one of the most pressing health problems, as was the leading cause of death. At that time, people usually lived in residences and apartment buildings dating back to the Victorian era. These homes contained heavy wood, upholstered furniture, carpets, long curtains, and lots of accessories. All this helped accumulate dust, in addition to their use of small windows that limited access to natural light and ventilation.[10]

What distinguishes this disease is that; it is so contagious that isolation was the key to prevention. Doctors prescribed sunlight, fresh air, healthy eating, and outdoor walks for Tuberculosis patients, impacting a new architecture style and a healthier lifestyle.

Sanatoriums began as huts in mountainous regions where patients could be cared for in an open, green, and rural environment rather than in the city's dense urban conditions. Later, the need arose to design facilities that merged modernity and healthcare, for example, Paimio Sanatorium, which Alvar Aalto designed in Finland (1932-1933). The building has balconies and large windows for views, ample daylight, and air. Aalto also paid attention to the interior design; to aid patients' healing.[11]

Le Corbusier was so obsessed with this disease and hygiene that he placed a free-standing sink in Villa Savoy's entryway (1929) in France. He also lifted the villa off the humid ground to avoid contamination.[12] Adolf Luce's Villa Muller (1930) in Prague included a separate quarantine space for sick children.[13]

Early Modernist architecture is distinguished by clean lines, empty white surfaces, bare floors, large expanses of glass, and indoor and outdoor living. It wanted to get rid of dark rooms. This interior helped promote a lighter, more airy, open, and healthy environment.[14]

9 Lee, Design in the; Christopher Klein, How Pandemics; Guenther and Gail, Sustainable healthcare

10 Campbell, Margaret. What tuberculosis did for modernism Medical history 49, no. 4, 2005. pp. 463-488.

11 Kyle Chayka, How the Coronavirus Will Reshape; Rebecca Gross, How a Tuberculosis Pandemic

12 Rebecca Gross, How a Tuberculosis Pandemic; Campbell; What tuberculosis

13 Kyle Chayka, How the Coronavirus Will Reshape Architecture, accessed June 27, 2020.

14 Campbell, Margaret. What tuberculosis did for modernism Medical history 49, no. 4, 2005. pp. 463-488.

The modern furniture design also contributed to this. The furniture has raised legs demonstrate their cleanliness; eradicate dusty corners where bacteria lurk, and materials like stainless steel and leather. The reclining chair also frequently appeared and is inspired by the reclining chairs of sanatoriums, see Figure (4). Much of modernist architecture can be understood as a consequence of the fear of disease; that's why this disease helped make modern architecture "modern".

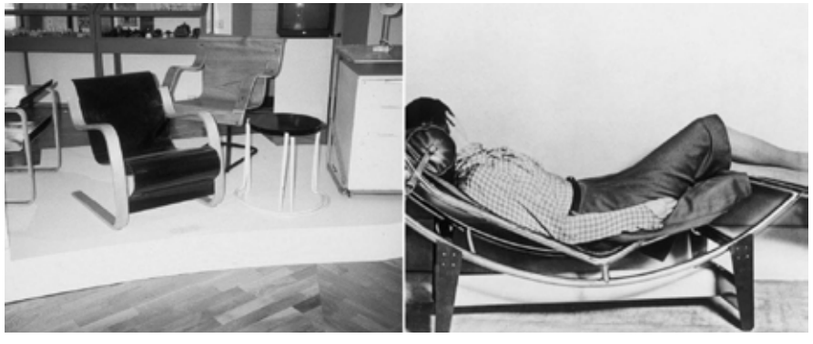

Figure (4): Left, Alvar Aalto, 'Cure' chair, 1933. Right, Le Corbusier, chaise longue, 1928.[15]

III. The Effect of COVID-19 Pandemic on Domestic Space

During the quarantine, users were struggling with a critical transformation in their homes. The home has changed in terms of space function and occupancy time. The home in which was about eating, resting, and family time, is now a workspace, a classroom, a meeting room, a store, and is a public square for political discussions.

In this period, users paid attention to forgotten elements in their homes, such as; balconies, courtyards, roofs, and gardens. In many countries, people started to communicate through balconies; residents in Turkey gave a collective salute to doctors through balconies. During the quarantine period, the balcony is an outlet towards the outside world and the street that made people feel reassured and that they are not alone. This period has brought us back to the value of local life and the importance of belonging to the neighbourhood.

Quarantine made all users more intimately acquainted with their homes' confines; the lack of daylight in one room, the need for an extra bathroom, the small windows, the lack of balconies or outdoor area, etc. The quarantine has exhausted people with the things they keep in space, even though they are relatively few. If they had little things, they would feel freer. While the existence minimum suggests the least you need to feel comfortable in a space; existence maximum could be; as much as possible in as small a space as possible. Neither a minimum of existence nor a maximum of existence is

15 Ibid., pp. 463-488.

perfectly functional at the moment. Personal spaces have to be physically connected and enriching even amid social distancing; users have to adapt.

Users are suffering from isolation while sheltering at home. Spending a long time in one space may require an environment that can change more freely so that users don't feel bored or hate the space; for example, post-pandemic designs can rely on using walls on wheels instead of static ones.

Post-pandemic houses can have open-plan communal spaces while preserving closed private spaces that ensure acoustic divisions if more than one family member has an online meeting or class. Bedrooms should be spaced apart for the same reason, and it should include more office footage space. The kitchen, dining room, and living room are all recommended to be detachable rather than flush together. Architects should dedicate more square meters for exterior space, with varied outdoor options. The future design should have bright walls, big windows to disinfect surfaces with sunlight.

Space is what to have in mind. At the time the person is physically distant, he is more socially engaged. Designing to promote social distancing could make spaces more universally hospitable. The difficulties which people have faced in the quarantine time will be taken into account in the future.

In COVID-19 Pandemic, the essential issue is distancing and quarantine spaces. The space needed for quarantine is primarily defensive, and barriers are essential in dividing the outside world into socially distant safe zones. Large open spaces are best avoided, unlike modern ones.

IV. Shifts From Open Plan Office Space

Offices were very crowded before the COVID-19 pandemic, but with the onset of this pandemic, they began to reduce crowding. As office spaces begin to reopen, architects are putting out pieces of advice on how to adapt to this pandemic. On May 6, the American Institute of Architects issued guidelines to provide a set of general mitigation measures to consider, such as moving activities outside and reconfiguring furniture to keep people away from each other indoors.[16]

As an urgent solution for the pandemic, office spaces have a lower density with more square meters per person, which does not mean expanding the office's space because many employers are working remotely. For home-based employers, the separation of work and personal life may be very blurry. That's why; it is essential to recreate an office workspace at home to get the proper physical and mental state to work efficiently.

Many offices now are using planters as a barrier to separate one-way entry-exit. Each side of this vestibule has a hand sanitizer station along the wall, precisely like Le Corbusier sink. Besides this, they reduced the number of chairs in conference rooms.

16 Kim Tingley, How Architecture Could Help Us Adapt, accessed July 9, 2020.

Spaces will not flow into each other anymore; there will be virtual walls, if not physical ones, installed between departments. Offices will have wider corridors and doorways. New designs should include grand open staircases in lobbies as a healthy option for taking the elevator. Office doors and elevators will all be opening automatically using facial recognition or any mobile software.

New designs should ensure that all spaces are well lighted and different air circulation that encourages people not to feel overstimulated. Social distancing should be achieved at least 1.5 meter spacing between desks.[17] There's always the temptation to seek a stable solution in architecture, the perfect design that will solve a problem forever. The better designs- healthier spaces - might be those that evolve from the bottom up as users all Figure out their post-pandemic routines.

V. Emergency Healthcare Spaces During the Early Stages of COVID-19

As many hospitals have reached their capacities, architects worked to find fast and efficient design solutions that can be implemented anywhere. For example, they (1) converted hospital spaces to serve infectious patients, (2) repurposed existing structures such as; conference venues, stadiums, and parks to the virus's demands into temporary hospitals. In Sao Paulo, Brazil, a Football stadium has been turned into a temporary hospital to accommodate 200 patients[18], and (3) other countries started building field hospitals as temporary modular space design that can treat thousands of patients, see Figure (5).

Figure (5): Construction of a field hospital in Rafah, Gaza Strip.[19]

Architects have adapted modular architecture during the pandemic because expanding without disrupting healthcare facilities' activities is very important. Modular construc-

17 David Shukman, Coronavirus: Could social distancing of less than two metres, accessed June 30, 2020.

18 BBC news, Coronavirus: Field hospitals treating patients, accessed May 24, 2020.

19 Ibid.,

tion involves the use of prefabricated units made in factories ready to be assembled on desired sites. This method allows for fast assembly, cheaper cost, flexible, and more efficient design solutions. It needs a low number of workers. These units can be shipped and moved to any location or stored as necessary.[20] Architects succeed in building two new hospitals (Huoshenshan facility and Leishenshan Hospital) within two weeks In Wuhan, China.[21]

VI. Impact of COVID-19 on Cities and Mobility

Quarantine turns city users into explorers of the familiar; it feels like discovering a new place. People have discovered that they don't know their neighbourhood very well. When users do not notice the built environment, they often do not belong to this environment.

During the COVID-19 pandemic, the city has played a different role for its inhabitants. Cities are empty from cars while lanes are full of cyclers and sidewalks are full of pedestrians. The pandemic's impact on urbanism has shown up in minor fast changes; gathering in public spaces and streets comes with added risk. In Diyarbakır, a south-eastern Turkey province, the prayers kept two meters apart; check Figure (6) below. It was a grid of people evenly dispersed perfection into the mosque's courtyard. People had to wear masks during the prayer.[22]

Figure (6): Muslims collectively performed Friday prayer, which was banned to stem the spread of COVID-19. Diyarbakır, Turkey.[23]

COVID-19 pandemic has opened a window for urban cycling to gain prominence. In Paris, the street was re-designed. One of the existing lanes was designated and restricted to bicycle use, resulting in more than 640 km of bike lanes throughout Paris that did not exist before the pandemic. Milan's new plan targets more than 30 km of the city's high-traffic roads. Re-designing the four-lane street to accommodate cycling and pedestrian movement,[24]as shown in figure (7).

Figure (7): Transformation of city streets in Milan.25

COVID-19 imposes another challenge on architects and urbanites related to re-consideration of the neighbourhood with its old concept. The pandemic suggests we should strengthen local centres by making our cities more walkable and make facilities more accessible to a different spectrum of users. Thinking seriously about activating public spaces allows interaction between neighbourhood residents while maintaining safe distances between people.

Instead of constructing huge facilities and locate them far, such as health facilities, education facilities, and so on, smaller units should be distributed within the urban tissue so there will be no need to travel long distances across the city to get to them. The future of cities will be a fundamental issue of density. Urbanization has focused on and cultivating density through affordable housing, small-sized studio apartments, and mixed-use zoning. Now, again repeating Haussmann's model, high density is something to be avoided as a response to disease.

People's contribution to making safe spaces

Resulting from COVID-19, a curfew has been imposed at a national scale in Turkey on people aged 65 years old and above, and those with chronic illnesses. A group of 120 Cyclist volunteers started the "BisiDestek" initiative to meet these people's needs by transporting their daily shopping needs and medicines in Izmir at an urban scale, see Figure (8). The bicycle transport plan initiative has trained volunteers for adherence to the rules, safe and appropriate methods of local precautions for COVID-19. Due to their mission, they want to contribute to the carbon emissions reduction to cope with

20 Thomas Wintle, COVID-19 and the city, accessed July 18, 2020.

21 Lubell, S. Commentary: Past pandemics changed the design of cities, Los Angeles Times April 22 (2020).

22 ilkha, Muslims collectively performs Friday prayer, accessed May 30, 2020.

23 Ibid.,

24 Joshua Robinson, Coronavirus Accelerates Plans, accessed August 30, 2020.

25 Joshua Robinson, Coronavirus Accelerates Plans, accessed August 30, 2020.

climate change and support policies and actions for sustainable cities by providing this service with bicycles and supporting each other in such epidemics. These interventions fell under the label of tactical urbanism; that is not master-planned but comes from the bottom up.[26]

Figure (8): Cyclist volunteers support the fight with COVID-19 in Izmir.[27]

VII. Life After COVID-19 Pandemic

Today, more than half of the world's population lives in cities, and this number is assumed to rise in the coming decades. The reliance on remote work has increased during the COVID-19 pandemic that will have implications for urban and architectural design. There will be a great chance to attract residents to the suburbs where there is no need to go to offices, decreasing cities' density. Cities may have a good chance to undergo a process of rebuilding, as some large companies will move with their employees outside the city, leaving a new opportunity for urban renewal across the city.

Isolation, then and now, helps prevent the spread of infectious diseases such as COVID-19, and it could well influence the design of our future homes and buildings. Digital platforms have played a prominent role as a communication tool in the pandemic period. This role appears to continue as it achieves safety. Urban architects and planners should be aware of such new forces that affect people's behaviour around the world, especially the new era of remote working.

In the post-pandemic period, Architects must innovate in designing public buildings such as libraries. New designs must attract people and maintains their safety at the same time. Architects and planners have already started the first steps in forming a new architecture that will be more sustainable and dynamic. But it is still hard to claim total exposure to the future and our cities' state in the post-pandemic period.

VIII. Conclusion

COVID-19 has affected local authorities, policymakers, planners, and people's perceptions; it increased their awareness about climate change and their future behaviour to become more immune, intelligent and controlled. The post-pandemic architecture will require a shift in ideology; it is not like something you can handle by changing some aspect of a single space in some city. Architecture should be more sustainable and embrace our co-dependence. Design strategies that reduce the spread of COVID-19 in buildings will keep buildings alive, whether or not a vaccine becomes available.

26 Gunhaber, Cycling enthusiasts carry goodness, accessed Nisan 11, 2020.

27 Ibid.,

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Thomas Wintle (b), "COVID-19 and the city: The future of pandemic-proofed buildings", accessed July 18, 2020. https://newseu.cgtn.com/news/2020-07-12/COVID-19-and-the-city-The-future-of-pandemic-proofed-buildings-RCqRHMSn72/index.html

Resilience in the Traditional Commercial Centers Before and During the COVID-19 Pandemic: Case of the Historical Bazaar of Bursa

Havva Tlemsani Bozdağ*

Abstract

Bazaar area was maintained for centuries and was characterized by its strong spatial structure which allowed it to be successfully recognized as the breathing heart of traditional city centers, possessing the ability to resist over time and space whilst maintaining its own identity thanks to many past-coming factors that ensured its resilience. Today, the Bazaar area is still standing, keeping its viability in most Islamic cities, besides its ability to face the intense and speed transformations required by modern life, now it is in the face to a new challenge: to feat the COVID-19 crisis without losing its values, soul, attractiveness, and

Özet

Yüzyıllar boyunca, çarşı alanları, kendi dayanma kapasitesinin ve güçlü mekânsal yapısının sayesinde, geleneksel kent merkezlerinin kalbi olarak başarıyla karakterize edilmiştir. Geçmişten gelen birçok faktör, çarşıların zamana ve mekâna karşı ayakta kalabilmelerini aynı zamanda kendi dayanıklılığını ve kimliğini korumasını sağlamıştır. Günümüzde çarşı alanları çoğu İslam kentinde yaşayabilirliğini koruyarak, modern yaşam tarzının gerektirdiği yoğun ve hızlı dönüşümlerle baş edebilme yeteneğinin yanı sıra, şimdi yeni bir meydan okumayla karşı karşıyadır: değerlerini, ruhunu, çekiciliğini ve aktif bir ticari alan olarak rolünü

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its role as a vital commercial area. This paper investigates the resilient features of a specific case study: the bazaar of Bursa as a living model World Heritage in the Islamic world. It is worth noting that the chosen bazaar showed a repetitive success to feat significant number of disasters that threatened it in the past; it has been changed in different period of history, while the historical commercial axes, fortunately, are the most important urban spaces preserved until the present. For this reason, the idea of investigating the resilient aspects of this bazaar before and during the crisis of COVID-19 pandemic comes from the desire to understand deeply the resilience awareness transmitted from the past by exploring the hidden abilities behind the success in term of risk management, adaptability, and re-organization.

Keywords: *COVID-19, Pandemic, Adaptive Capacity, Historical Bursa*

kaybetmeden COVID-19 krizini aşmak. Bu makale, belirli bir çalışma alanının dayanma özelliklerini incelemektedir: Bursa çarşısı, İslam Dünyasında Yaşayan bir Dünya Mirası Modelidir. Seçilen Bursa çarşısı, yaşadığı önemli sayıdaki tehditleri başarıyla atlatması ile dikkat çekicidir, tarihsel süreç içerisinde sürekli bir değişim halinde olmasına rağmen tarihi ticari akslar günümüze kadar korunmuş olan en önemli kentsel mekânlardır. Bu nedenle, COVID-19 pandemi krizinin öncesi ve sonrasında bu çarşının dayanım yönlerini inceleme fikri, geçmişten gelen dayanıklılık farkındalığının ardındaki gizli kapasiteleri, risk yönetimi, uyarlanabilirlik ve re-organizasyon açısından bu başarıyı yakından keşfetmek arzusundan kaynaklanmaktadır.

Anahtar kelimeler: *COVID-19, Pandemi, Adaptif Kapasite, Tarihi Bursa*

*

I. Introduction

Islamic city has been able to develop gradually and to resist over time and space whilst maintaining its own identity. In the same way, bazaar areas have been gaining much attention due to their vital role as the most significant socio-economic structure and one of the most significant socio-spatial systems in the urban traditional centers of Islamic cities. Nowadays, most of the bazaars are fortunately still alive and keep their unique identity and their viability despite different disturbances (disasters, epidemics, war, changing economic balances, globalization, and industrialization). This makes us think about the nature of resilience and sustainability mechanisms that bazaar areas possess.

This paper attempts to show the importance of analyzing the resilience indicators behind the sustainability of traditional bazaars, we will discuss the issue related to the hidden abilities ensuring the resilience of bazaars during long centuries and factors which made bazaar areas able to stay alive and resist until today, despite different intern and extern disturbances as well as the intense and speed transformations of modern life. The paucity of research on the concept of resilience in the bazaar historical area's level -in term of adaptability and self-protection in response to natural and biological hazards especially the current COVID-19 crisis and how the bazaar area clung to its architectural identity, economic and cultural values as symbols of a resilient adaptive system, the continuity and viability despite repetitive different disasters- distinguished this research from the rest. The purpose of the study is to develop a practical guide to make bazaars more vital and more vibrant by understanding the lessons coming from the past in matters of self–protection, self-organization, and adaptability. This understanding will be illustrated by the case study of the Bursa bazaar historical area. Therefore, without the analysis and the evaluation of the traditional mechanisms and the resilience indicators, and the particular characteristics behind the sustainability of these traditional organisms until today, we could never understand how well they have worked in the past and how well they might function in the future.

II. Literature Review:

The General Experience of Resilience in Face to the COVID-19 Pandemic

The 'Resilience' term often refers to the notion of returning to the initial state and resistance to any disturbances. Resilience has been used first by Holling in 1970 and has emerged as a conceptual framework to refer to a description of models of change in the structure and function of ecological systems[1]. The unexpected impact of the disturbance induced by the COVID-19 fits a basic realization of Holling and ecologists who followed him: 'the nature of Nature is change'.It has been considered later that resilience and stability refertothe tendency of a system returns to a state of equilibrium after a disturbance[2];The theory of Holling was based on considering resilience as a tool to measure the capacity of systems to resist change and to absorb disturbances without losing the original relationships between components of society or state variables. The ability of a system to cope with change refers also tothe capacity to absorb disturbances and still retain its identity[3].If we compare the COVID-19 with other hazards and if we examine its various impacts on people and economic activity, we can easily note that the pandemic's scale is very large compared to other disasters, also, the pandemic is the only disaster that's has a very long duration of the disturbance[4].

At the urban level, resilience is influenced by a risk and danger management paradigm. It indicates the capacity to change in order to maintain the same identity3. Some scholars applied the concept of resilience to communities in relation to urban scale or cities which are considered as continuously changingcomplex adaptive systems. Urban resilience is mainly concerned with analyzing the way in which cities absorb and then adapt to change. Here, the term "resilience" is often used to describe the capacity of a system to absorb various sudden shocks (economic, social, or environmental) including

1 Holling, C. S. 1973. "Resilience and stability of ecological systems". Annual review of ecology and systematics, 4(1), pp.1-23.

2 Gunderson, L. H. 2001. "Panarchy: understanding transformations in human and natural systems". Island press., pp.16.

3 Cumming, G. S., & Collier, J., 2005. "Change and identity in complex systems". Ecology and society, 10(1), pp. 2-3.

4 Litman, T., 2020. Pandemic-Resilient Community Planning: Practical Ways to Help Communities Prepare for, Respond to, and Recover from Pandemics and Other Economic, Social and Environmental Shocks.,pp. 6.

disasters and epidemics. The capacity of cities to persist has been widely studied and many important concepts seem to be behind this ability to persistduring periods of turbulence.According to (Litman, T., 2020), the basic principle of good planning is that individual, short-term decisions should be consistent with strategic, long-term community goals. In order to reduce contagion risk factors depending on shared vehicles,one of the important solutions proposed by (Litman,T., 2020) was the idea to improve active transport by encouraging walking and bicycling, micro-mobility (electric scooters and bicycles) through improved sidewalks, crosswalks, bike lanes, and to pedestrianize streets which increase sustainability. Persisting while preserving their own soul, identity and basic morphological structure is a sign of success in the most memorable places[5]. Talking about urban resilience is not limited to the capacity of cities to cope with hazards, it also includes the capacity of the community to respond well to crises by strengthening and maintaining social capital and place attachment.[6]

On the human scale, stress researchers have developed a "3 Cs" model to account for resilience in disaster situations: control, coherence, and connectedness[7]. Control is reflected in the belief that personal resources can be accessed to achieve valued goals. Goals can be short or long-term. Coherence is founded in acceptance-based coping. The third "C," Connectedness refers to the need for human contact and support, which is consistent with empirical evidence documenting social support as one of the most impactful and consistent resilience factors following natural disasters[8]. In relation to Public Health and Disasters, the framework adopted by the WHO in 2019 refers to the systematic analysis and management of health risks, posed by emergencies and disasters, through a combination of (1) hazard and vulnerability reduction to prevent and mitigate risks, (2) preparedness, (3) response and (4) recovery measures. In the same vein, the analysis of key factors in China's efforts to combat COVID-19 has shown that these factors include strict regulation, strong governance, strong citizen participation, and community vigilance[9]. While researchers in social complex adaptive systems have gathered resilience enhancing factors in the notions of adaptability, transformability, innovative learning, and the acceptance of change[10], with the need to maintain the focus on anticipating and preparing for potential change[11].

5 Carmona, M., Heath, T., Tiesdell, S., & Oc, T. 2010. Public places, urban spaces: the dimensions of urban design. Routledge.

6 Cohen, O., Leykin, D., Lahad, M., Goldberg, A., & Aharonson-Daniel, L. 2013. "The conjoint community resiliency assessment measure as a baseline for profiling and predicting community resilience for emergencies". Technological Forecasting and Social Change, 80(9)., pp. 1734-1734.

7 Polizzi, C., Lynn, S. J., & Perry, A. 2020. "Stress And Coping in the Time Of COVID-19: Pathways To Resılience And Recovery". Clinical Neuropsychiatry, 17(2),pp. 60.

8 Rodriguez-Llanes, J. M., Vos, F., & Guha-Sapir, D. 2013. "Measuring psychological resilience to disasters: are evidence-based indicators an achievable goal?". Environmental Health, 12(1),pp. 115.

9 Djalante, R., Shaw, R., & DeWit, A. 2020. "Building resilience against biological hazards and pandemics: COVID-19 and its implications for the Sendai Framework". Progress in Disaster Science, 100080,pp 4.

10 Folke, C., Carpenter, S. R., Walker, B., Scheffer, M., Chapin, T., & Rockström, J. 2010. "Resilience thinking: integrating resilience, adaptability and transformability". Ecology and society, 15(4), pp. 1-4.

11 Newman, L., & Dale, A. 2005. "The role of agency in sustainable local community development". Local environment, 10(5).,pp 483-484.

Many other authors have investigated resilience and adaptive capacity enhancing factors in communities which is considered as a function of the ability of individuals and groups to 1) accumulate and keep in memory the lived experiences; 2) transform this memory into a way of learning, innovating and reorganizing resources to be able to adapt to environmental changes as required; and 3) make a connection inside and outside the community to share experiences and lessons learned, self-organize or reorganize in the absence of leadership[12],[13],[14].

Disaster Risk Management for Cultural Heritage

As s symbol of resilience, monuments are the main target of heritage conservationactions. The 1972 World Heritage Convention is a reflection of the attempt to identify and apply universal principles and policies. UNESCO is one of the international conservation movement characterising the second half of the 20th century and participates within several agencies in disaster managementactivities for cultural heritage. In the same vein, disaster risk management (DRM) is a systematic approach to avoiding, transferring, and reducing the adverse impacts of hazard events. Its objective is to help people in terms of anticipating disasters and take action to protect life and property. While disaster events remain difficult to predict, activities that will reduce disaster impact can be categorized by Pre-disaster preventive actions or "peacetime", Emergency response preparedness actions, and Post-disaster recovery and preventive reconstruction actions[15].

With these arguments in mind, we frame the challenge of exploring the resilience of the historical bazaar of Bursa before and during the risk of the COVID-19 pandemic, through the analysis of two important capacities characterizing a resilient adaptive system: learning from the past and adaptability, including the application of disaster cyclecorresponding to our case study. Exploring the precautionary measures against the current crisis and the factors reinforcing the attempts of the bazaar to defy the present hazard can help to reflect on the state of the bazaar in the post-epidemic phase.

III. Methodology

There is a vast amount of literature on the concept of 'Resilience', although there has been considerable interest in resilience indicators behind the sustainability of historical centers in western cities. However, unfortunately, it is worth noting the great lack of research on bazaar historical areas as the most resilient structure of Islamic cities. The

12 Mileti, D. S., & Sorensen, J. H. 1987. "Determinants of organizational-effectiveness in responding to low probability catastrophic events". Columbia journal of world business, 22(1)., pp. 13-21.

13 Gunderson and L.H. and Holling, C.S. (eds) 2002. "Panarchy: Understanding Transformation in Human and Natural Systems". Island Press, Washington, DC.

14 Longstaff, P. H., Armstrong, N. J., Perrin, K., Parker, W. M., & Hidek, M. A. 2010. "Building resilient communities: A preliminary framework for assessment". Homeland security affairs, 6(3).,pp. 1-23.

15 Lattig, J. W. 2012. "Calamities, catastrophes, and cataclysms: Current trends in international disaster risk management practices for cultural heritage sites"., pp.23-26.

same lack is considered about researches on the COVID-19 pandemic risks and solutions since it is a new challenge for the whole world and a great mystery to be solved.

In the light of recent events, there are now some specific efforts in order to maintain the healthy viability of the bazaar areas and economic centers. In this paper, we intend to evaluate and compare the resilience of the bazaars in the face to lived disasters in the past as well as the current state of COVID-19, the comparison includes the differences between precautions made in the past and those taken today, and what can we recommend as planners and designers, to make bazaars more safe and resilient by understanding the lessons given by the Islamic cities in matters of self-protection, risk management, and adaptability. In this context, we tried to explore factors enhancing resilience in the face of hazards by taking in consideration the present crisis of the COVID-19 pandemic. The aim is to provide lessons and specific framework able to guide the future practice, interventions, and measuresthat will be taken in such cultural heritage areasin face to suddenly risks; without neglecting the main abilities to consider which facilitate acting in such historical areas and guarantee theirresilience, and this, distinguished our research from the rest.

IV. Case Study: The Historical Bazaar of Bursa

The historical city of Bursa representsthe first departure of the great Ottomans dynasty as the first capital of the Ottoman Empire. Since the 13th century, Bursa within its bazaar has become an interesting commercial crossroads linking East and West, taking place on the most important trade routes of Anatolia, especially: the Silk Road. In 2014, Bursa within the bazaar area was considered by UNESCO as a living heritage model in the Islamic World. The bazaar of Bursa has a great historical heritage: it survived and overcame different constraints in the past without losing its identity and viability. The main reason for studying the resilience of thisbazaar comes from the fact that most elements of this city have changed in different periods of history, while the bazaar areafortunately still hasits own characteristics. Despite the damage that some parts of the bazaar area have been suffered because of several geological, biological and human-induced disasters (earthquake, epidemics, fire, war, drought, etc.) the conversion of damaged parts has been successfully completed and are currently alive and still serving different functions. It means that the bazaar of Bursa must have its own resilience and sustainability mechanisms. For these reasons, the bazaar of Bursais a good example to understand deeply the resilience awareness transmitted from the past.

To define the different mechanisms of 'Resilience' in the bazaar of Bursa, especially during the current stressful period of the pandemic, it is necessary to study near the features and indicators enhancing resilience over time and their influences on the spatial and socio-economic scales. One of the most important factors behind the resilience of this bazaar as a living cultural heritage is the capacity to adapt to change and the ability to learn from experiences and to transform this learning into a way to anticipate or manage future and unexpectable events ensuring that the unchangeable identity of the bazaar area as a whole.

The Capacity to Learn From the Past

Pre-Disaster Phase: Risk Assessment

The historical process of Bursa has undergone significant structural changes at different periods since the creation of the city until today. In parallel with this transformation process which crossed the city, changes have taken place in the historical trade center or the 'Covered Bazaar'.Changes that took place in the 19th century can be summarized in disturbances due to disasters and epidemics namely the Bursa earthquake in 1855, the Cholera epidemic between 1890-1895 and later in the 20th century, the fire in the bazaar in 1958. Besides,many important changes took place after in the historical center due to the first interventions and zoning works established in this period and have affected the spatial structure and physical integrity of the historical city center[16].

Peri-Disaster Phase: Emergency Response

The careful precautions and emergency responses havetaken today against the COVID-19 pandemic are not foreign to those taken in the past against the Cholera epidemic. Both have acted fastly to prevent the disease from spreading, these measures have been taken by health commissions throughout the country. In an official document of the 19th century (figure4), the measures to be implemented by the governorshipincluded first of all that the entrance and exit of the city of Bursa should be strictly controlled and the quarantine application should be applied. The taken measures insisted strongly on the issue of hygiene namely: paying more attention to the cleaning of the city streets, buildings, and Hans in the bazaar area, wrapping meat and food products for sale in the bazaar. It was stated that legal proceedings would be initiated against officials or local populations who do not respect the implementation of the taken decisions. In order to prevent the disease from spreading to other parts of the city, police checkpoints were established in many different areas[17].

Today, measures taken face to the COVID-19 are not far from those taken in the past. Past experiences have been an important factor in making and implementing and sharing decisions as fast as possible thanks to Media and social networking (figure 5).It is noteworthy to act quickly and to take many measures to prevent disease. The question of hygiene especially the use of masks has received a big interest and interaction from both merchants and customers. The advantage to having many open spaces and alleys in the bazaar of Bursa provides open-air walkability, where people can safely interact with minimal contagion risks. However, the bazaar as a dense public space makes social distancing measures difficult to be implemented. As part of solutions to the COVID-19 pandemic problems, the emergency measures implemented in Bursa caused traders and people to fall into financial difficulties. Therefore, any planning strategies should be comprehensive and support economic development, social equity, and envi-

16 Tekeli, İ., 1999, "Bursa'nın Tarihinde Üç Ayrı Dönüşüm Dönemi",Osmanlı Devletinin Kuruluşunun 700. Yıldönümünde Bursa ve Yöresi, 06-08 Mayıs 1999, Uludağ Üniversitesi.

17 Kumaş, N. 2011. "Bursa'da kolera salgını ve alınan karantina önlemleri (1890-1895)". Uludağ Üniversitesi Fen-Edebiyat Fakültesi Sosyal Bilimler Dergisi,12(21)., pp. 216-218.

ronmental protection in such historical areasthrough the use of local knowledge, skills, and resources.

Post-Disaster Phase: Recovery and Reconstruction

Pandemics differ from most other disasters because they threaten people but not infrastructure; also, they have long durations and huge economic impacts. So their mitigation is primarily concerned with protecting people and providing economic security, with little need for infrastructure protection and repair. In the case of Bursa, the idea of self-protection especially in the bazaar area emanates in large part from the contribution of two traditional mechanisms (Waqf, Guilds,) and their socio-economic role on the bazaar development. These two systems have been considered as the basis of maintaining the bazaar through the reinforcement of Human values namely solidarity and equity. Nowadays, the rapid changes have imposed new systems of governance in the bazaar area of Bursa. Although, this change seems useful and necessary since changing kinds and styles of governance can shape resilience over time[18].Today, the decrease or disappearance of the role of the Wakf and Guild systems did not prevent resilience in the bazaar area. The recovery guaranteed by traditional institutions has been transmitted to new local government institutions (craftsmen's room, union of tradesmen in Bursa, local authorities) and international organisations (UNESCO) which have the same goal of safeguarding this historical area through long-term planning strategies. In light of the current COVID-19 pandemic, and by considering health as critical infrastructure, the recovery in Bursa consisted of decisions to apply a gradual normalization taken by the local authorities in order to stimulate shops and trade as well as artisans and merchantsin financial difficulties due to quarantine and emergency measures, with taking in consideration the need to reduce the contagion risk factors. The success of the recovery process in the bazaar of Bursa is a good example of the rapid adaptability to change and the high degree of community vigilance and citizen participation which distinguished this bazaar for centuries.

Adaptive Spatial Reuse Over Time

The adaptability of the bazaar area to absorb unexpected disturbances is one of the most resilience-enhancing characteristics that the bazaar of Bursa fortunately possesses. This bazaar as an important resilient socio-economic and urban space in the city has the spatial adaptive capacity to adapt itself continually over time to novelty and changes in order to meet the user's new needs as required. Therefore, the bazaar of Bursa has evolved into a physical and architectural resilient system in which spatial structures, professions, and specialized functions were integrated into a unique living place thanks to rich flexibility represented by the 'Adaptive Spatial Reuse' capacity.

18 Davis, J., & Uffer, S. 2013. "Evolving Cities: exploring the relations between urban form 'resilience'and the governance of urban form".

The dominant position of the bazaar of Bursa besides the great mosque (Ulu Cami) in the city center has guaranteed spatial and functional flexibility in the bazaar and has allowed remarkable compactness and flexible design of shops and places used for various purposes. Thus, a high degree of interaction between its spaces has been allowed thanks to the lack of rigidity in the design of the bazaar. Favorable exchanges between merchants were promoted thanks to the spatial proximity of shops, it allowed an evolution of ideas concerning the ways to adapting, producing, selling, and innovating. One of the good examples of this ability was seen in the cautious and functional reuse of the courtyard during the COVID-19 pandemic crisis. The first Friday prayer performed in the courtyard of the Bursa grand mosque (Ulu Cami) in the center of the bazaar area took place after the end of the quarantine process. During the prayer, the use of personal prayer rugs, social distancing, and self-protection precautions by using masks was respected and noteworthy.

V. Discussion and Conclusion

In history, the bazaar area of Bursa has suffered from different disasters and has successfully survived thanks to its capacity of self-protection using traditional mechanisms (Waqf, Guild systems). Today, the district become an important example of human-scale urban form thanks to other local governance institutions and international organizations; Accessibility -transportation as well as the emergency and disaster management are ones of different objectives and action plans of the Management Plan prepared during the (UNESCO) nomination process in 2014. Today, this cultural heritage is facing a big challenge: to defeat the risks of the COVID-19 pandemic which represents a good learning experience. During this stressful period, the bazaar of Bursa has shown again its capacity to deal with a sudden disturbance with success thanks to the careful emergency response taken by the decision-makers in the city. It was a great benefit to act quickly and take serious measures to prevent the disease from spreading. The bigger benefit was the remarkable understanding and participation of citizens which sped up the emergency response phase. During the current biological hazard of the COVID-19, the exposure and vulnerability of the bazaar area including health, social, physical, economic, and environmental dimensions showed that both cities we live and bazaar areas are so fragile, however, at the same time, they are full of hidden potentials and undiscovered abilities which make them resilient over time and boost this resilience by managing functionally the socio-economic complications resulting from such a crisis. One of the most important potentials behind the resilience of the bazaar of Bursa is the capacity to adapt to change, the ability to learn from experiences and to transform this learning into a way to anticipate or manage future and unexpectable events ensuring that the unchangeable identity of the bazaar area as a whole. The second hidden potential is represented by the spatial adaptive capacity to adapt itself continually over time to novelty and changes thanks to its rich flexibility which allows adaptive spatial reuse of its urban and architectural components as required. The management of the current crisis emanates largely from the ancestral culture of learning from local and neighboring experiences, the transformation of this learning facilitates greater knowledge to innovative ways for re-adaptation and recovery. The COVID-19 is a good opportunity to find a more resilient framework that addresses both global risks

and explores the relevant abilities in the bazaar area (Figure 9). Now we are still in the recovery phase, however, we are invited right now to re-think the ways of enhancing resilience in the bazaar historical area of Bursa while preparing for future potential change and unknown risks.

We are all invited (urban planners and decision-makers) to re-think the business and planning models used in the historical bazaar of Bursa as well as the urban and economic models that could be adopted in the Post-COVID-19 phase, appropriate to the new changes in our lifestyle that gives priority to health and puts in foreground hygienic precautions and social distancing. The speed propagation of disease due to the high level of interconnectivity between people requires the implementation of new procedures to meet social distancing standards and eliminate transmission of the COVID-19 by seeking more creative preventions, mitigations of risks solution, and interventions in social, economic and urban levels. The proposed framework may help decision-makers and problem solvers to take the right decision at the right time during such a stressful period like the one that we live in now, it shows the key abilities which should be taken into consideration during each phase to feat the current crisis as well as the future disasters. This study is limited in the case of the historical bazaar of Bursa as a living World Heritage in combat with a murderous pandemic, at the current moment, it explores just two among several other hidden capacities behind the resilience and the stability of this historical district as a whole. However, this research opens lots of paths for future research that are needed to fill the huge gap in the literature about conserving cultural heritage areas while dealing with crises of similar nature and complexity as the COVID-19.

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Technology

Post COVID-19: Impact on Modern Technological Innovations

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Abstract

The uncertain nature of the pandemic had resulted in the generation of unwarranted fear and hysteria upon the populace. This has blurred the future of humankind; whether the possibility of returning to the old ways of doing things still lingers, or the chance of such opportunity is lost and would now have to adeptly adapt with what is left in the hands to create a way of life that seems to resemble that which was used to. As such a relation was established by closely examining the measures that were put in place, by various countries right from the onset, to control the spread of the outbreak: social distancing, wearing

Özet

Pandeminin belirsiz doğası, halk üzerinde yersiz korku ve histerinin doğmasına neden olmuştur. Bu, insanoğlunun geleceğini bulanıklaştırdı; eski iş yapma yöntemlerine geri dönme olasılığı hala var mı, yoksa böyle bir ihtimalin kayboldu ve şimdi eskiye benzeyen bir yaşam biçimi yaratmak için, ellerinde kalanlarla, ustaca uyum sağlaması gerekecekti. Böyle bir ilişki, salgının yayılmasını kontrol etmek için çeşitli ülkeler tarafından salgının başından itibaren alınan önlemler yakından incelenerek kuruldu: sosyal mesafe, maske takma, evden çalışma, teslimat hizmetleri ve polis devriyesinin 'reforme edilmiş'

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masks, work from home, delivery services, and the 'reformed' method of police patrol. From the established relation, a positive gradient could be deduced in the usage of technology and the compliance of the populace to the measures to reduce the spread. Given the dread incited by the pandemic coupled with the urge to completely do away with the virus, despite the novelty of some ideas in the Sciences, there is most likely to be massive development, research, unprecedented general acceptance, and incorporation of technology and novel concepts to curtail the situation adapt to this new life and if possible to completely wipe every trace of the virus. In view of this, this piece seeks to evince the aftermath of that which resounds in every conversation held between individuals and headlines news; how the world is likely to be after the pandemic.

Keywords: *COVID-19, Technology, Pandemic, Virus, Innovation*

yöntemi. Kurulan ilişkiden, teknolojinin kullanımı ve virüsün yayılmasını azaltacak önlemlere uyum arasında pozitif bir gradyan çıkarılabilir. Pandeminin teşvik ettiği korku ve virüsü tamamen ortadan kaldırma dürtüsü göz önüne alındığında, Bilimlerdeki bazı fikirlerin yeniliğine rağmen, durumu kısıtlamak, bu yeni hayata uyum sağlamak ve mümkünse virüsün izlerini tamamen silmek için teknolojide ve yeni konseptlerde büyük bir gelişme, araştırma ve bunları şimdiye dek benzeri görülmemiş bir şekilde kabullenme ve dahil etme muhtemeldir. Bunu göz önünde bulundurarak, bu çalışma, insanlar arasında çokça konuşulan ve haberleri yapılan sorunun cevabını açığa çıkarmayı amaçlamaktadır: pandemiden sonra dünya nasıl olacak?

Anahtar kelimeler: *COVID-19, Teknoloji, Pandemi, Virüs, Yenilik*

*

I. Introduction

Since the dawn of time, humanity has always struggled to survive and to adapt to the environment. With the experienced difficulties came forth evolution and innovation as such could persevere through the harsh realities of the world to this very moment in time where a man can bend the natural laws of nature to his own will as a tool to propagate its species and ensure the continuation of life for the generations yet to come. This is not the first pandemic experienced in humanity's history. Not to be cynical, however, yet most likely would not be the last. Among the over ten significant pandemics throughout humanity's history with the severest being Bubonic Plague (1347-1351)[1], humankind has consistently found, mostly either a versatile instrument or extemporised measures to overcome such experiences[2]. To consider it, why had there been such a lopsided display of fear and hysteria over the pandemic?[3]. Considering the mortality rate, COVID-19 does not come close to any major historical pandemic, yet even tissue paper and masks were in short supply at the onset out of fear and anxiety.

1 Nicholas Lepan, "Visualizing the History of Pandemics," 2020, https://www.visualcapitalist.com/history-of-pandemics-deadliest/.

2 Dave Roos, "How 5 of History's Worst Pandemics Finally Ended - HISTORY," 2020, https://www.history.com/news/pandemics-end-plague-cholera-black-death-smallpox.

3 Tzur D et al., "Fear of COVID-19 Scale: Psychometric Characteristics, Reliability and Validity in the Israeli Population. Psychiatry Research [Revista En Internet] 2020 [Acceso 17 de Noviembre de 2020]; 289(2020): 1-5.," no. January (2020), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7227556/pdf/main.pdf.

A careful stroll through the order of events since the first case would better help understand the nature and reasons for the resultant hysteria and uncertainty. Its origin, mode of transmission, and treatment approach were vaguely known if not speculative. The fear of uncertainty surrounding the pandemic at the beginning of its detection, the portrayal in news media, and the potential doom of humanity could explain the resultant exaggerated fear upon the populace[4]. Although the mortality rate of COVID-19 was relatively low, the public was enveloped in fear, uncertainty, and persnickety[5,6]. With the pangs of such fear still reverberating, it is likely the masses would not like to return to such an ordeal.

Consequently, measures and conditions that would be put in place to check the potential emergence of a second wave are likely to be readily complied with. This concerns, most especially innovation in science and technology, which has, until recently, been slowly embraced and integrated into our lives[7]. The dread ascribed to the pandemic is bound to influence humankind as far as tolerating advances in bio-electronic augmentations, the attitude towards global warming to detect possible future pandemics and viral infections, and the need for humanity to stay alert for all that is yet obscure. Given these, this piece seeks to outline the possible ways by which COVID-19 would impact the development of new scientifically revolutionary ideas and the advancement of our cutting-edge innovations with its effects on major engineering disciplines to prepare humankind a step ahead of future occurrences.

II. Pandemics and Technological Development

Technology has always been the tool with which great civilisations were built and which shaped the history of mankind. Like the great civilisations of old, the same can be said about the shaping of the future still to come with today's technological advances. Over the last two decades, innovation has rapidly expanded to an unfathomable degree that the human race ends up in amazement with the manifestations, portrayal of the ability and capacity to attain considerably more remarkable heights than those that exist. With every new technological advancement, the need to solve the daunting societal problems has always been the key force driving new ground-breaking scientific ideas from researches that are brought forth, technological revolutions become a reality and the acquisition of a new understanding and perspective with which future problems would be solved. With this stated, COVID-19 with its related problems imposed on society, mankind is left but to find solutions to such problems for the continuation of daily life activities and to ensure the production of essential services required for normal or

4 Bryan Musolino, "PERSPECTIVE: Media Coverage of COVID-19 and Outcomes of Fear Generation – Homeland Security Today," 2020, https://www.hstoday.us/subject-matter-areas/pandemic-biohazard/perspective-media-coverage-of-COVID-19-and-outcomes-of-fear-generation/.

5 Anon.(WHO), "World Health Organization. (2020). Coronavirus Disease 2019 (COVID-19): Situation Report, 46. World Health Organization. Https://Apps.Who.Int/Iris/Handle/10665/331443" 2019, no. March (2020), https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

6 Tony Cartalucci, "Stanford Study Proves COVID-19 Was Overhyped. 'Death Rate Is Likely Under 0.2%' - Global ResearchGlobal Research - Centre for Research on Globalization," 2020, https://www.globalresearch.ca/mit-tech-review-smears-study-proving-COVID-19-overhyped/5710088.

7 James Gallagher, "Coronavirus: What Is a Second Wave and Is One Coming? - BBC News," accessed April 17, 2021, https://www.bbc.com/news/health-53113785.

an adaptable way of life till society finds a cure or fully understands the nature of the virus. Consequently, technology needs to be advanced such that sectors of very high importance can keep up with the needs of society to ensure the continuity of life.

Outcome of the COVID-19 Pandemic on Innovation

The COVID-19 pandemic has been detrimental to the major sectors of society which are essential to the existence and the continuity of life. To adapt to the current situation and to prepare for a future occurrence, the need to grow profoundly trend-setting innovations to give solutions for current and future issues is not a choice but an unquestionable requirement. Among the fields that will probably be affected include:

- Robotics and Artificial Intelligence
- Nanotechnology and bioengineering
- Global Warming Mitigation Techniques
- IoT and Smart Cities
- Energy and data
- Drones
- Gene Editing
- 3D Printing

Robotics and Artificial Intelligence (AI)

The utilisation of robots during the pandemic has incredibly alleviated medical service personnel of ordinary undertakings. In this way, preserving their limited vitality and time for more specialised tasks. Robots had been programmed to execute fundamental errands like UV cleansing, temperature check-ups, food distribution, waste removal, and testing agents. Some additionally connected people in seclusion with their family members through video conferencing. The AI industry has also been utilised to advance the easy sharing of data through open-source technologies[8], follow the spread of the pathogen, and monitor a patient's continuous temperature through wearable gadgets. Altogether not to intensify the developing panic noticeable all around, some AI applications have been programmed to detect and screen the spread of false news on the web[9].

High censorship of information and data mining by machine learning programs are required to keep a close eye on the public. By using AI, a person's movements can be tracked, and his/her identity (even while wearing a mask)[10] can be determined in minutes while walking on the street. Using AI is likely to result in the form of 'restriction' and 'invasion' of privacy.

8 Anon., "GHDDI Launches A Scientific Research Data and Information Sharing Platform to Support Collective Research on 2019-NCoV I," 2020, http://ghddi.org/en/node/236.

9 S Tong, "Coronavirus: Can Artificial Intelligence Be Smart Enough to Detect Fake News?," 2020, ?", https://www.marketplace.org/2020/02/12/coronavirus-can-artificial-intelligence -be-smart-enough-to-detect-fake-news/.

10 Jane Li and Jane Li, "China's Facial-Recognition Tech Can Crack Masked Faces amid Coronavirus — Quartz," 2020, https://qz.com/1803737/chinas-facial-recognition-tech-can-crack-masked-faces-amid-coronavirus/.

Concerning the post-pandemic world, the robotics industry is likely to experience a boost in terms of quality and the amount of research being done to solve societal problems. Hence it would be more developed and robust despite the fear of robots replacing human labour in many sectors of work. The consequence of the COVID-19 pandemic on the robotics industry will be attributable to the need to preserve a pseudo-normal life, regardless of the difficulties that could be faced, while maintaining an equal footing, irrespective of the conditions and standards of living. In view of the uncertain nature of the pandemic, in particular, the unavailability of the approved vaccine, measures such as social distancing are likely to remain in place to reduce human-to-human interactions to minimise the spread of the virus; hence the need to integrate the employment of medical aid robots in the medical sector as they are highly efficient in executing such tasks, immune to infection and are less likely to transmit infections. Among the major concerns raised is the inability of robots to show human-like emotions while providing services, particularly to people in quarantine. As a result of this, the need to augment robots with Artificial Intelligence-based software programs to enable them to learn and show a degree of human emotion, and thus, the psychological dimension of treatment would seem to be catered for appreciably.

Due to the pandemic, many companies have suffered unprecedented losses, and some have unavoidably collapsed. The rate of joblessness continues to increase as employees are laid off due to the feared infection among staff and the lack of adequate resources to continue production[11].Notwithstanding, some businesses are as well emerging while incorporating new technologies to bridge the gap in the old procedure of managing systems[12]. Looking at the world after the pandemic, it is possible robots would be much more incorporated into the various sectors of production, most notably in tasks that are consistently manual, cognitive, and repetitive. Given the margin of error of human workers and the comparatively tagged inefficiency, the need for businesses to spring to their feet amidst these inadequacies would drive this era of robotic incorporation. Along these lines, with the limited assets in question, yields can be significantly increased with higher productivity and increased rate of production. Contrary to the general perception that robots push humans out of employment is in a way false. In juxtaposition to the former industrial revolutions, the trend of employment rates moved contrary to expectations, thus new jobs were created in a more efficient system. With a close look at incidents, the medical sector has witnessed a significant need for the specialised services of more staff (doctors and nurses) due to the escalating number of cases reported worldwide. As a result, automatable tasks were assigned to robots. Moreover, the current 'unemotional' nature of robots makes it unsuitable as 'fully autonomous consultants' to replace human health personnel. Robots should be seen as an augmentation of the human efforts, more or less like an aid, to fill up and to reduce the work intensity on a limited labour force.

Nanotechnology and Bioengineering

11 Rakesh Kochhar, "Unemployment Rose Higher in Three Months of COVID-19 than It Did in Two Years of the Great Recession," 2020, https://www.pewresearch.org/fact-tank/2020/06/11/unemployment-rose-higher-in-three-months-of-COVID-19-than-it-did-in-two-years-of-the-great-recession/.

12 Sean Ludwig, "Coronavirus: Businesses That Are Succeeding During the Pandemic," 2020, https://www.uschamber.com/co/start/strategy/coronavirus-successful-businesses.

Among the promising fields of engineering that would be positively affected by the emergence of the COVID-19 pandemic includes the development of nanotechnology and bioengineering. This field has gained rapid recognition and research interest over the last few decades. Due to numerous setbacks in the field, little has been accomplished in the practical application of discoveries in real life because of people's nonacceptance of external or acclaimed foreign particles into the body. However, considering the world after the pandemic, vaccinations and, if possible, other forms of treatment for different diseases in the form of nanoparticles will be embraced due to the fear generated by the pandemic. Since the risk of a second wave remains, that would sensitise people to be more accepting of various technologies and hence pave the way for on-subject tests, assessments, and subsequent further developments in the field. As a result, there would be a drive to address the pressing needs to be met.

With the augmentation of nanotechnology and bioengineering, devices can be nano-scaled and then introduced and or implanted into a living organism to serve as artificial white blood with specific genetic coding to differentiate between the natural cells and foreign disease causative agent that might be difficult for white blood cells to nullify. This technology will aim to eliminate all types of 'alien' cells in the human body. Unlike vaccines and other medications, bio-engineered nano-devices can serve the general purpose of curing and preventing diseases regardless of the origin of the disease-causing organism or the mode of infection. Such bio-engineered nano-devices can be programmed to initiate a particular sequence of biological and chemical reactions related to the nullification of the target disease-causing organism with minimal effects on the surrounding cells and organs.

Global Warming Mitigation Techniques

According to experts in climate change research and related fields, glaciers host some ancient viruses that are yet to come into contact with modern-day humans. Further study and development into glacial ecosystems are required to discover new viruses, their biological nature, and to develop treatment procedures for them before they encounter the population. Thus, arming ourselves against possible future pandemics.

For instance, in the summer of 2016, the resulting high heat wave thawed a layer of permafrost that overlaid the anthrax-infected carcass of a reindeer for 75 years. This outbreak in the Yamal Peninsula infected 2000 reindeers and witnessed the death of a 12-year-old boy and the hospitalisation of at least 20 others[13]. Given this probability (solely due to global warming caused by the activities of humans) and the fear of another lock-down from viral infection from the glaciers would contribute to this awakening. Now, in the post-pandemic world, humanity's awareness of environmental issues is likely to spike. Much more focus is likely to be paid to environmental protection and conservation practices. Most people are not ignorant of the battle that is waged against global warming, but mostly turn a deaf ear to the voices of environmental conservation

13 Jasmin Fox-Skelly, "BBC - Earth - There Are Diseases Hidden in Ice, and They Are Waking Up," 2017, http://www.bbc.com/earth/story/20170504-there-are-diseases-hidden-in-ice-and-they-are-waking-up.

activists and have abandoned environmental protection practices in theoretical stages without implementation.

The cause of global warming is quite clear and efforts to mitigate the use of greenhouse gas-producing chemicals and fuel for energy are being considered. This will lead to comprehensive research into high-efficiency renewable energy production methodologies as a substitute for fossil fuel-based energy generation methods. Solar energy and tidal power generation methods are among the technological innovations that have the potential to improve efficiency. Considering the current inefficiency of solar panels, extensive research work into their production methods and procedures to achieve the highest performance and efficiency possible will enable a smooth transition from fossil fuels to more environmentally friendly means. Thus, curbing global warming, therefore reducing the melting of glaciers and thereby, reducing the risk of exposure to new viruses.

IoT and Smart Cities.

Advancements in the Internet of Things (IoT) and the interconnectivity of different devices to create an interconnected smart city where data is continuously collected and processed in real-time by supercomputers and AI-based cloud storage analysis tools. This can provide an overview of developing conditions in society, thus allows the early detection of potential future pandemics.

With existing accumulated data and studies on COVID-19 and the associated uncertain nature of the pandemic, even further steps will have to be taken to avoid a second wave from erupting, just as the Spanish Flu. As vaccinations are yet to be developed, there is a risk of a second wave of transmission. Due to this, drastic steps are likely to be put in place to minimise human-to-human interaction and to quickly pick up signs of potential infections within any community.

To enhance the efficiency of outbreak prevention, several countries had released mobile phone monitoring applications to boost the effectiveness of contact tracing and to identify carriers quickly[14]. In like manner, as the pandemic becomes prevalent, a more sophisticated approach is required in handling massive data acquisition and processing capabilities to ensure accurate results are obtained and valid conclusions drawn from the acquired data.

Within a smart city environment where each device interface is directly connected to data collection and information management networks, data from wearable sensors, such as real-time location and vital signs, can be channelled and integrated with a 'Public Health and Safety Data Acquisition Program' system. This allows forecasts to be conveniently made based on the data type, patterns, trends, and frequency. This will go a long way towards tracking outbreaks of potential pandemics (not just COVID-19)

14 Paul Schwartz, "Illusions of Consent and COVID-19-Tracking Apps," 2020, https://iapp.org/news/a/illusions-of-consent-and-covid-tracking-apps/.

and facilitating easy localisation of new outbreaks based on the frequency of similar symptoms reported by people in a particular locality. One big drawback to this phase is people's reluctance to give personal data to government agencies with the fear that it may be sold to or even used against them by third-party entities in court prosecutions. However, intending to find a solution to the global pandemic, people are more likely to be accepting in giving out personal data if that would provide hope for survival.

Energy and Data

This pandemic has resulted in an unprecedented mass global lockdown. As the number of vehicles on the road, aircraft in the air, and ships on the waters reduced, carbon emissions had consequently reduced. This resulted in improved quality of air, cleaner beaches, reduced environmental noise, and seismic vibrations. Negatively, there was an increase in waste production and reduced levels of recycling. As the lockdown measures eased across the globe allowing people out, the old ways resumed. It is likely world leaders would give priority to the development, adoption, usage, and incorporation of renewable energy sources as exemplified by Germany. As the world moved 'indoors' and had to work from home, the intensity of internet usage surged. But the current state of the internet needs to be upgraded to conveniently accommodate such massive usage. As a result, the focus is likely to be shifted from sectors such as road expansion to bandwidth expansion to contain this surge.

Drones

Using drone technologies in agriculture for aerial inspections, monitoring, and application of herbicides and pesticides may not be a novel concept, but envisioning a city where drones fly above the locality will undoubtedly be seen as science fiction. However, this pandemic has turned the tables. At its peak, China witnessed the use of drones to facilitate aerial disinfection and transport medical samples. For certain nations, drones have been used by the police to implement quarantine regulations, relay lock-down measures, and carry out aerial thermal check-ups to quickly detect outbreak hotspots. However tragic as it is, given the possibility of a second wave, the application of drones might witness the addition of complex functions to perform more precise tasks like the measurement of heart rates and sneezing persons within a crowd. As such, a way is paved for the justification of the use of surveillance technologies on the public which would gradually be accepted as a 'new normal', and the initial concerns over its effects on the right to privacy and anonymity pushed to oblivion.

Gene Editing

The collective efforts of the international medical community to shorten the timeline for the development of a vaccine are commendable. The time required for developing a vaccine averages (5-10) years[15], but having to live with this pandemic for such a stretch is mind-boggling. The more reason an even faster approach is much needed, given the situation at hand.

15 Douglas Broom, "5 Charts That Tell the Story of Vaccines Today," 2020, https://www.weforum.org/agenda/2020/06/vaccine-development-barriers-coronavirus/.

Even though mainly still experimental, the potency of gene editing as a faster and less expensive method than vaccines could be a chance given the current situation of the scientific community in coming up with a credible vaccine in a fearfully short time frame. After having successfully used CRISPR to fight drug-resistant bacteria and to treat Alzheimer's in mice, tests are underway to validate an even faster approach to test for the virus.[16] There are concerns over how possible it is for a product without clear clinical human trials to get approval for usage and over the potential risks in usage as biological weaponry and the alteration of the human genome which could be passed on to other generations. Given these concerns which need strong evidence from human trials and strongly established standards for its application on one hand, the potency and urge of gene editing as the next virus killer over a vaccine would accelerate the work in this field to clear the hurdles and to gain support in research and funding.

3D-Printing

Three-dimensional printing (3D-printing), unlike conventional methods of manufacturing, is a process in which the layers of the product -according to a computerised model- are gradually and sequentially applied (additive manufacturing) to create the last piece. The key benefit provided by 3D-printing is that it is a comparatively cheaper process, as components that are required in limited quantities can easily be manufactured at a reasonably low cost in a relatively short period[17]. As the number of cases rose exponentially, putting a strain on medical supplies (ventilators, face masks, and ventilation filters), there needed to be a quick but efficient method to meet these demands. Governments around the world as well implemented drastic measures to curb the tide of this acute shortage. Medical supplies were needed urgently to manage the explosive number of infections, and doctors needed protective equipment. Companies that had the blueprints for manufacturing these supplies only had to send a soft copy and the recipient health institution could manufacture the same product locally with the available materials.

However, important questions have been posed about the distribution, development, and quality of products before usage. That is whether the manufacturers are conversant with the complexities of medical practice, whether locally produced products undergo adequate testing and certification for clinical use, and whether they conform to safety standards for medical use. Given the novelty of this technique and its usefulness in emergencies, there is a likely increase in investment and research by government bodies to improve quality and ensure compliance with production standards. By extrapolation, given the assumption that a second wave is likely to arise, this field is expected to attract even more research attention than ever, given its potential to deliver support in emergencies.

16 Daniel Markus, "CRISPR Developer Jennifer Doudna on Reset Podcast: How the Gene-Editing Technology Works - Vox," 2020, https://www.vox.com/2020/2/28/21154930/jennifer-doudna-crispr-gene-editing-babies.

17 Jay Peters, "Volunteers Produce 3D-Printed Valves for Life-Saving Coronavirus Treatments - The Verge," 2020, https://www.theverge.com/2020/3/17/21184308/coronavirus-italy-medical-3d-print-valves-treatments.

III. Conclusion

For any major technological development, the key factor pushing modern, ground-breaking scientific innovations is the desire to solve daunting societal problems. With this said, COVID-19 with its associated problems placed on society is left to man to find solutions to those problems. As a result, technology needs to be developed in such a way that highly essential industries will meet the needs of society to ensure the improved quality of life and to provide the driving force for significant technological growth. Technology may be the salvation or the doom of humanity, and it all depends on the outlook and purpose for which people find it necessary to invest resources in. It is not the occurrence (however unpalatable) that matters, but how the situation is handled, and the lessons learned. The situation does not make, but rather reveals the real self. That is why it is better if the pandemic is understood as a corrector and not as a destroyer. It is disconcerting to realise that this very occurrence of a pandemic could be simulated with technologies of today[18], to give a forecast of the potential nature of a viral infection and the possible measures to control such an occurrence yet the needed attention was not allotted. On the contrary, the world continued to wage war against itself with investments in highly dangerous innovations rather than engaging in world-saving technologies. Funds allocated to the manufacture of large quantities of weapons and military spending by governing bodies could, as well, have been channelled to research major global threats to humanity.

Now the enemy is here, yet humankind seems unarmed. This leaves the question, 'where are all these weapons?' calling for an answer. It is certainly not ignorance: who or what would be the most significant enemy within the next decade was accurately predicted. The lingering question now is why nothing was done. In as much as it is undesired, the possibility of a more severe second wave break-out is nakedly staring humanity in the eye. The COVID-19 pandemic is an eye-opener, a real case study with data for forecasting and planning for possible future pandemics whilst putting in place measures to curb and prevent a similar situation as this. Granting humanity, the opportunity to re-evaluate and reflect on the choices made as governments, institutions, people in power, and more importantly personally. Subsequently, armed with such insight, a better strategy is likely to be employed in preparing for what awaits should the threshold be exceeded.

Following the subject of this article, it is therefore likely and expedient that there would be a massive investment and general incorporation of technology into the daily life of mankind, much more investment into the research of yet unknown viruses, and a general awakening toward the need to address the pressing issues of global warming. Also, from the collected data, the most important requirements for human survival and life-facilitating technology are to be given even greater production priority.

18 Manuel A. Zambrano-Monserrate, María Alejandra Ruano, and Luis Sanchez-Alcalde, "Indirect Effects of COVID-19 on the Environment," Science of the Total Environment 728 (2020), https://doi.org/10.1016/j.scitotenv.2020.138813.

So, when asked, 'how would COVID-19 affect humanity's future?', the response need not be far-fetched. Not to automatically assume the position of an optimist but to take a stance and draw a conclusion from the carefully outlined determinants; sometimes a fall, a push, or a challenge is needed to validate complacence and the belief in inherent capabilities. Therefore, humanity needs to sit back, think through things, and then re-strategize for a stronger comeback.

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Detection of COVID-19 From Chest X-Ray Images Using Feature Descriptors and Machine Learning

Huda M.S. Algharib*

Abstract

Early detection of novel coronavirus disease (COVID-19) is necessary for disease cure and control. Different medical imaging modalities like Computed Tomography (CT) and X-ray images have played an important role in providing useful information for the purpose of diagnosing COVID-19. However, there is an urgent need to produce meaningful texture and a good representation of the image since they offer great information for correct classification. In X-ray images, the texture of the diseased tissue is more rough or chaotic than the healthy ones and thus can be characterized for an automated diagnostic system

Özet

Yeni koronavirüs hastalığının (COVID-19) erken tespiti, hastalığın tedavisi ve kontrolü için gereklidir. Bilgisayarlı Tomografi (CT) ve X-ışını görüntüleri gibi farklı tıbbi görüntüleme modaliteleri, COVID-19 teşhisi için yararlı bilgiler sağlamada önemli bir rol oynamaktadır. Bununla birlikte, doğru bir sınıflandırma için harika bilgiler sundukları için, anlamlı bir doku ve görüntünün iyi bir temsilini üretmeye ihtiyaç vardır. X-ışını görüntülerinde, hastalıklı doku sağlıklı olanlardan daha pürüzlü veya kaotiktir ve bu nedenle, çalışmamızda ele alındığı gibi otomatik bir teşhis sistemi için karakterize edilebilir. Bu makalede, X-ışını

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as addressed in our work. In this article, several techniques of feature descriptors and machine learning were employed to detect COVID-19 in X-ray images. First, invariant texture Features are extracted using different techniques named Local Binary Pattern (LBP), Histogram of Gradients (HOG), and Discrete Wavelet Transform (DWT). More information is obtained by fusing multiple features. The resulted features are reduced by Principal Component Analysis (PCA) and then classified using three benchmarked classifiers named Multilayer Perceptron (MLP), Random Forest, and Multinomial Logistic Regression.

Keywords: *COVID-19, Pneumonia, Feature Descriptors, Wavelet Transform, Random Forest, Logistic Regression*

görüntülerinde COVID-19'u tespit etmek için çeşitli özellik tanımlayıcıları ve makine öğrenimi teknikleri kullanılmıştır. İlk olarak, değişmez doku Unsurları, Yerel İkili Örüntü (YİÖ), Yönlendirilmiş Degradelerin Histogramı (YDH) ve Ayrık Dalgacık Dönüşümü (ADD) adlı farklı teknikler kullanılarak çıkarılır. Birden çok özelliği birleştirerek daha fazla bilgi elde edilir. Ortaya çıkan özellikler, Ana Bileşenler Analizi (ABA) ile azaltılır ve ardından Çok Katmanlı Algılayıcı (ÇKA), Rastgele Orman ve Çok Terimli Lojistik Regresyon adlı üç karşılaştırmalı sınıflandırıcı kullanılarak sınıflandırılır.

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I. Introduction

The wide and rapid spread of the novel coronavirus disease (COVID-19) in many countries around the world has forced a lot of researchers in several areas, including the field of Artificial Intelligence (AI), to work hard to confront this disease. COVID-19 is a class of coronavirus family that causes critical problems of the respiratory system and a severe respiratory symptom and in the worst cases leads to the whole destruction of the respiratory system and death[1]. With increasing numbers of deaths from coronavirus around the world, the World Health Organization (WHO) on 11 March 2020 declared that the emerging coronavirus (COVID-19) is a "Global Pandemic"[2]. There is a necessary need to diagnose the COVID-19 at an early stage and instantly quarantine the infected persons to prevent transmission of infection to others. The gold standard to discover the presence or absence of COVID-19 was by the clinicians using the real-time reverse transcription-polymerase chain reaction (RT-PCR) technique[3]. unfortunately, this technique gives a low positive rate in the early stage of this disease. Consequently, medical imaging modalities especially the computed Tomography (CT) and X-ray chest images were relied upon by clinicians to help in the early diagnosis of COVID- 19 instead of (RT-PCR) technique. At this point, the medical imaging modalities have been targeted by researchers in the field of AI for an early detection of COVID-19.

1 Elisabeth Mahase. Coronavirus: COVID-19 has killed more people than SARS and MERS combined, despite lower case fatality rate. The BMJ, 368: m641, 2020.

2 https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-COVID-19 accessed11-march-2020.

3 Kasotakis, George. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases, 2020.

A Literature Review

Li et al developed a three-dimensional deep learning model for detecting COVID-19 from chest CT images [4]. They suggest extracting the visual features of the CT images using the proposed model, and then the extracted features are used to distinguish between COVID-19, community-acquired pneumonia, and other lung diseases. Gozes et al. designed AI-based automated CT image analysis tools for detection and quantification of COVID-19 [5]. The system outputs the abnormality localization map of the infected lung and measures the "Corona score" progression of patients over time. Shan et al. developed a deep learning-based system that automatically segments all the lung and infection sites from chest CT images [6]. Xu et al. used deep learning techniques to develop a prediction model that discriminates COVID-19 pneumonia and influenza-A viral pneumonia on pulmonary CT images [7]. Wang et al. developed a deep learning method to extract the graphical features of COVID-19 based on the radiographic changes in CT images of the infected lung [8]. Narin et al. proposed three different convolutional neural network-based models for the detection of COVID-19 infected patients using chest X-ray images [9]. These models were analyzed using 5-fold cross-validation. Sethy et al. designed a deep learning-based methodology for detecting COVID-19 from X-ray images [10]. They used the support vector machine to classify the COVID-19 affected X-ray images from others using the extracted deep feature. Singh et al. used a convolutional neural network (CNN) to classify the COVID-19-infected patients as infected or not [11]. They utilized multi-objective differential evolution (MODE) to tune the initial parameters of CNN. To avoid overfitting, they also utilized 20-fold cross-validation. Alqudah et al. employed different Artificial Intelligence (AI) techniques for the detection of COVID-19 using chest X-ray images [12]. They used a CNN in two different scenarios, the first one to classify the X-ray images using a softmax classifier, and the second one to extract automated features from the images and classify these features using other classifiers

4 Li L et al, Artificial intelligence distinguishes COVID-19 from community acquired pneumonia on chest CT. Radiology. 2020

5 Gozes O et al (2020) Rapid AI development cycle for the coronavirus (COVID-19) pandemic: initial results for automated Detection & patient monitoring using deep learning CT image analysis. arXiv preprint arXiv:2003.05037

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12 Alqudah AM, Qazan S, Alqudah A "Automated Systems for Detection of COVID-19 Using Chest X-ray Images and Lightweight Convolutional Neural Networks", Europe PubMed Central, 2020.

named support vector machine (SVM), Random Forest, and K nearest neighbor (KNN). The SVM is commonly used in the medical field for classification problems and has been used to determine the abnormality degree of abnormal classes in medical imaging [13]. In another study, a deep CNN model called Darknet-19 has been employed for binary classification (COVID vs. No-Findings) and multi-class classification (COVID vs. No-Findings vs. Pneumonia). Using 5-fold cross-validation, they achieved an accuracy of 98.08% and 87.02% for binary and multi-class classification problems, respectively[14]. Most of the previous works do not consider the different types of features that are used to describe the texture of the chest. Therefore, this paper suggests extracting various types of texture features (LBP, HOG, and Wavelet features) from chest X-ray images, and then applying those features in different classifier algorithms to diagnose COVID-19, normal and pneumonia classes.

Organization

The rest of the paper is organized as follows. Section 2 presents the dataset description, texture feature extraction techniques, feature fusion and dimension reduction, different classifiers, and performance evaluation. Section 3 elaborates the results and discussion followed by the conclusion in Section 4.

II. Materials & Methods

Dataset Description

In this research, chest X-ray images of 310 normal, 310 pneumonia, and 310 COVID-19 patients were collected from different publicly available sources [15],[16],[17], Hence the total number of the images is 930. In our experiments, all images were resized to 64 x128 pixel size. Figure 1 shows sample chest X-ray images of normal, pneumonia, and COVID-19 patients, respectively. The Chest X-ray images of COVID-19 infected patients exhibit different texture patterns (see Figure 2). [18]

Feature Extraction with LBP

The Local Binary Pattern (LBP) introduced originally by Ojala et al. is defined as a grey scale invariant texture measure, it was proposed for texture analysis first, then it has

13 A. M. Alqudah, H. M. S. Algharib, A. M. S. Algharib, and H. M. S. Algharib, "Computer aided diagnosis system for automatic two stages classification of breast mass in digital mammogram images," Biomedical Engineering: Applications, Basis and Communications, vol. 31, no. 1, Article ID 1950007, 2019.

14 T. Ozturk, M. Talo, E. A. Yildirim, U. B. Baloglu, O. Yildirim, and U. Rajendra Acharya, "Automated detection of COVID-19 cases using deep neural networks with X-ray images," Comput. Biol. Med., vol. 121, Jun. 2020, Art. no. 103792.

15 Joseph Paul Cohen, Open database of COVID-19 cases with chest X-ray or CT images https://github.com/ieee8023/covid-chestxray-dataset

16 https://www.kaggle.com/paultimothymooney/chest-xray-pneumonia.

17 Alqudah, Ali Mohammad; Qazan, Shoroq,"Augmented COVID-19 X-ray Images 21 Dataset", Mendeley Data, v4 2020.

18 M. Hosseiny, S. Kooraki, A. Gholamrezanezhad, S. Reddy, and L. Myers, "Radiology perspective of coronavirus disease 2019 (COVID-19): lessons from severe acute respiratory syndrome and Middle East respiratory syndrome," American Journal of Roentgenology, vol. 214(5), pp.1078-1082, 2020.

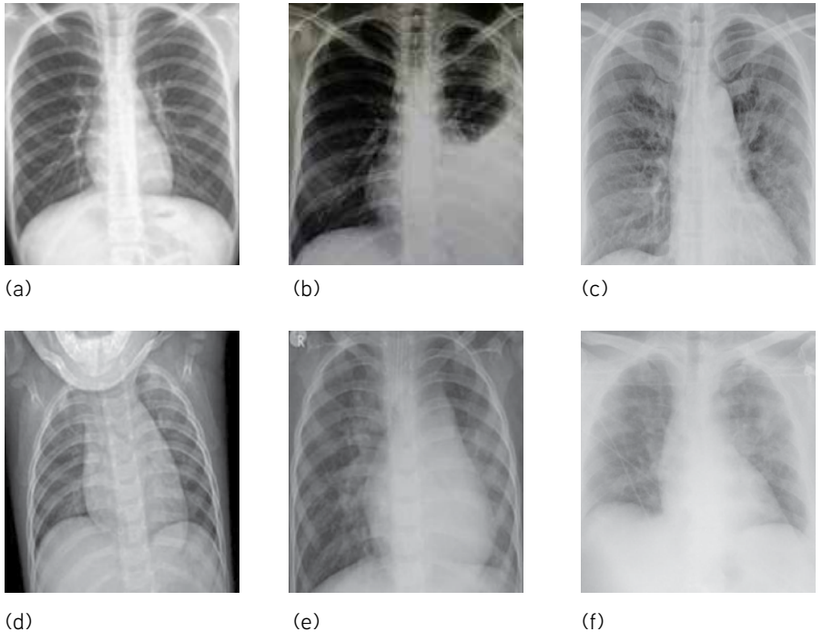


Figure 1. Sample chest X-ray images: (a-d) Normal, (b-e) Pneumonia (c-f) COVID-19.

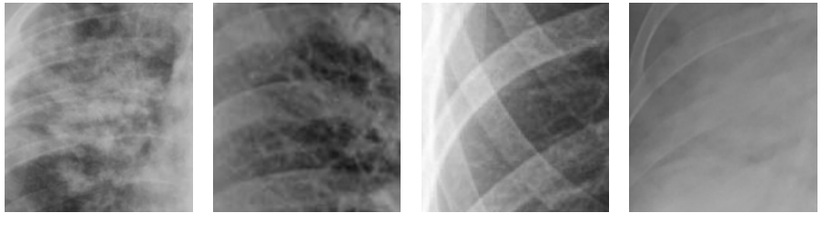


Figure 2. Chest X-ray images of COVID-19: (a) Ground-glass opacity (b) Reticular opacity (c) Mild opacity (d) Pulmonary consolidation.

proved a simple yet powerful approach to describe local structures [19],[20]. Let us consider a grayscale image, $\boldsymbol{\rho}$, with an arbitrary resolution. The LBP computation for a given pix-

19 T. Ojala, M. Pietikainen, and D. Harwood, "A comparative study of texture measures with classification based on feature distributions," Pattern Recognition, vol. 29, no. 1, pp. 51–59, 1996.

20 T. Ojala, M. Pietikäinen, and T. Mäenpää, "Multiresolution gray-scale and rotation invariant texture classification with local binary patterns," IEEE Trans. Pattern Anal. Mach. Intell., vol. 24, no. 7, pp. 971–987, Jul. 2002.

el at with surrounding pixels evenly spaced on a circle of radius of R can be expressed in decimal form as follows:

$$\mathrm{LBP}_{P,R}(x_c, y_c) = \sum_{P=0}^{P-1} s\big(I(x_p, y_p) - I(x_c, y_c)\big)2^P \qquad (1)$$

is a LBP value at the center pixel . and are the values of surrounding pixel and center pixel respectively. is the weight of a surrounding pixel with index . The radius determines the circular surrounding pixels of the center pixel . The function s(x) is defined as follows:

$$S(x) = \begin{cases} 1, & if\ x \geq 0 \\ 0, & if\ x < 0 \end{cases} \qquad 2)$$

The LBP can be computed using different number of surrounding pixels of different sizes as shown in Figure 3. for an example of circular surrounding pixels. Figure 4. shows an example of the calculation of the LBP for a single pixel with (P=8, R=1.0). A Sample application of LBP to a Chest X-ray image is shown in Figure 5.

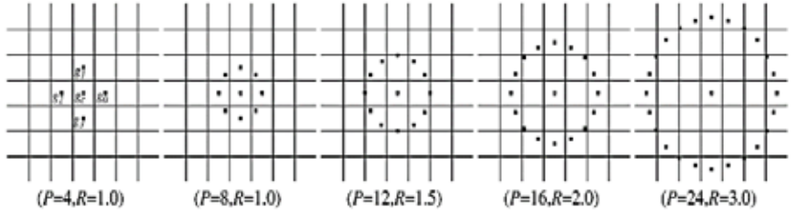


Figure 3. The circular surrounding pixels for different (P, R).

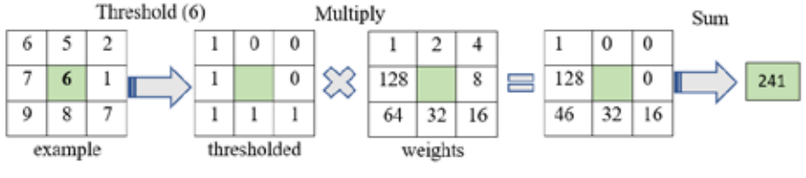
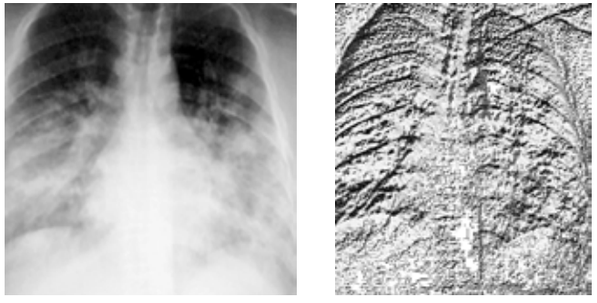


Figure 4. The LBP calculation for a single pixel.



(a) (b)

Figure 5. Applying LBP to a chest X-Ray image: (a) original image. (b) LBP image.

To determine the frequency values of binary patterns, the corresponding histogram should be computed. The number of histogram bins depends on the number of involved pixels in the LBP calculation. If LBP uses 8 pixels, the number of histogram bin will be 2^8 or equal to 256. The computed histogram can be used as a descriptor.

Feature Extraction with HOG

The HOG feature descriptor counts the occurrences of gradient orientation in localized portions of an image [21]. Thus, the structure or the shape of an object in the image can be defined by the HOG features. The following steps explain how to compute the HOG features:

Step1. Computing the x, y derivatives of the pixels

The x, y derivatives are defined as the small change in the x and y directions. Thus, the derivatives of pixel in x and y directions can be computed as follows:

$$I_x(r,c) = I(r,c+1) - I(r,c-1) \qquad (3)$$

$$I_y(r,c) = I(r-1,c) - I(r+1,c) \qquad (4)$$

Step2. Computing the Magnitude and Orientation of the gradient

The obtained x, y derivatives (and) in the above step were used to compute the magnitude and orientation of the gradient for each pixel value.

$$G = \sqrt{I_x^2 + I_y^2} \qquad (5)$$

$$\theta = \arctan\frac{I_y}{I_x} \in [-\pi, \pi] \qquad (6)$$

21 N. Dalal and B. Triggs. Histograms of oriented gradients for human detection. In CVPR, 2005.

Step3. Computing the Histogram of cell orientations

To compute the cell orientation histograms, the image firstly is divided into adjacent, non-overlapping cells of size C x C pixels (here C = 8). Then, the histogram of gradient orientations is generated for each cell with 9 orientation bins. The bins are numbered from 0 to 9 over the interval [0˚,180˚], thus, the width of each bin is 20. Bin has boundaries and center . The bin number of a pixel with magnitude and orientation is determined by the bilinear interpolation voting as follows:

$$v_j = G\frac{c_{j+1}-\theta}{w} \text{ to bin number } j = \left[\frac{\theta}{w}-\frac{1}{2}\right] \bmod 9 \quad (7)$$

$$v_{j+1} = G\frac{\theta-c_j}{w} \text{ to bin number } (j+1) \bmod 9 \quad (8)$$

The computed histogram for each cell is a vector with dimensions 9 x1.

Step4. Block Normalization

The aim of this process is to reduce the effect of variations in contrast between the portions of the image. The blocks can be built by grouping 4 neighbored cells into a larger overlapped block with size 2C × 2C pixels. As previously mentioned, each cell has a 9x1 histogram vector. Thus, we will get a block feature vector with dimensions 36x1. The block features vector can be normalized as follows:

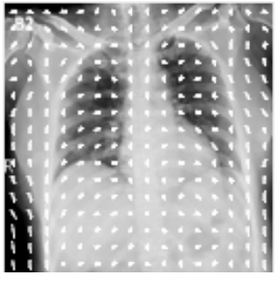
$$f \leftarrow \frac{f}{\sqrt{\|f\|^2+\epsilon}}$$

Where is the Euclidean norm, and is a small positive constant.

Step5. HOG Features for the complete image

In this step, the normalized block feature vectors are concatenated into a single HOG feature vector. In our experiments, the image size is 64 x 128 pixels and this result in 8x16 cells and 7x15 overlapped blocks. Each block has 36 x1 histogram vector. Hence, the total features for the image is 7x15x36x1=3780 features. A Sample application of HOG to a Chest X-ray image is shown in Figure 6.

(a)



(b)

Figure 6. A Sample application of HOG to a Chest X-ray image: (a) original image. (b) HOG features over the original image.

Feature Extraction with Wavelets

The Wavelet transform is a powerful tool used to extract the texture features for diagnostic purposes in many biomedical imaging applications [22]. This is due to the discriminating power of wavelet features and the availability of rapid techniques for implementing discrete wavelet transform (DWT). In Two-dimensional DWT, the image is decomposed into four sub-bands by passing it through Two-dimensional filter banks composing of low-pass and high-pass filters as shown in Figure 7. The outputs of the filter banks after decomposition level is

$$[A_K, \{H_i, V_i, D_i\}_{i=1,\ldots,K}] \quad (10)$$

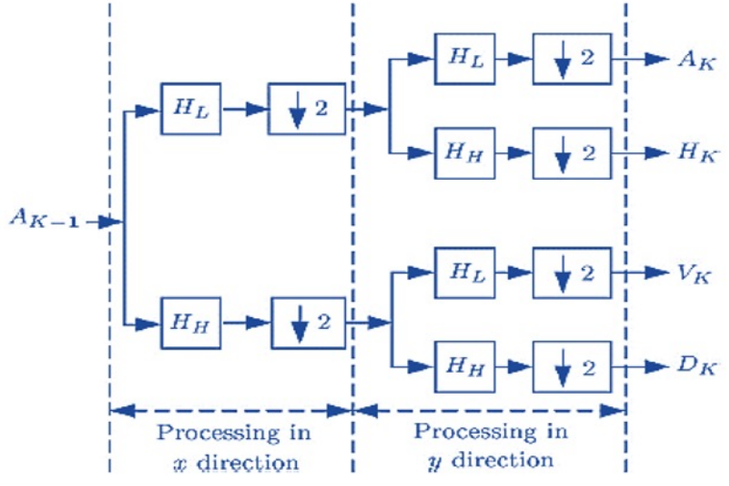
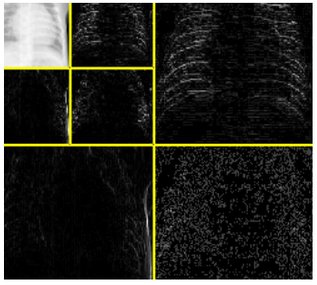


Figure 7. Two-dimensional DWT

Where are the approximation, horizontal, vertical, and diagonal detail images at the level, respectively. The decomposition process was applied many times on the approximation image since it contains more details. Figure 8 shows an example of Two-dimensional DWT decomposition of an image at the second level.

22 Strang, G. and Nguyen, T.: "Wavelets and Filter Banks", Wellesley-Cambridge Press, Wellesley, 1996.

(a)



(b)

Figure 8. Example of Two-dimensional DWT (a) original image (b) decomposed image

For an image, the wavelet energy of approximation, horizontal, vertical, and diagonal details at the level, is respectively, computed as [23]:

$$E_K^A = \sum_{x=1}^{M} \sum_{y=1}^{N} (A_K(x,y))^2 \quad (11)$$

$$E_i^h = \sum_{x=1}^{M} \sum_{y=1}^{N} (H_i(x,y))^2$$

$$E_i^v = \sum_{x=1}^{M} \sum_{y=1}^{N} (V_i(x,y))^2$$

$$E_i^d = \sum_{x=1}^{M} \sum_{y=1}^{N} (D_i(x,y))^2$$

These energies represent the strength of the details of the image at the decomposition level. So, the extracted features at the level can be expressed as follows:

$$v_i = (E_K^A, E_i^h, E_i^v, E_i^d)_{i=1,2,\ldots,K} \quad (15)$$

In this work, the wavelet energies at three decomposition levels are taken as image features. The energy of the approximation coefficient has been estimated once, whereas the energy of each of the three detail coefficients has been estimated at each level. Thus, the feature vector is a vector of dimensions 1×10 for each image.

Feature Fusion and Dimension Reduction

In this section, the fusion of multiple texture features is accomplished using a simple concatenation process. Let and denote feature vectors extracted via two different techniques. To avoid the problem of outliers in feature values, the feature values of vectors are normalized by the median normalization technique as follows:

$$x' = \frac{x - median(F_x)}{median(|(x - median(F_x))|)} \quad (16)$$

23 Wu X, Wang K, Zhang D, "Wavelet Energy Feature Extraction and Matching for Palmprint Recognition", Journal of Computer Science and Technology, vol.20, no.5, pp. 411-418, 2005.

Where is a feature value after normalization, and is the functions which produce x. Applying this normalization technique to all feature values results in normalized feature vectors and.

$$X' = \{x'_1, x'_2, \ldots, x'_m\} \text{ and } Y' = \{y'_1, y'_2, \ldots, y'_n\}.$$

After normalization, the resulted feature vectors are concatenated to form the overall feature vector.

$$Z' = \{x'_1, x'_2, \ldots, x'_m, y'_1, y'_2, \ldots, y'_n\}.$$

This fusion process results in high dimensional feature vectors which lead to poor performance in the classification phase. Therefore, we utilize the PCA technique to reduce the dimensionality of feature vectors. PCA finds a linear mapping of the data from a higher-dimensional space to a lower-dimensional space such that the variance of the data in the low-dimensional representation is maximized [24]. In PCA, we compute the sample covariance matrix , as given by:

$$C = n^{-1} \sum_{i=1}^{n} (X_i - \bar{X}_n)(X_i - \bar{X}_n)^T \quad (17)$$

where is the sample vector with dimensional , is the average of samples and is the number of samples. Next, we compute the eigenvalues and eigenvectors of . After that, we choose a dimension , and then we define the dimension reduced data as follows:

$$Y_{i=}T_K(X_i) = \bar{X} + \sum_{j=1}^{K} \beta_{ij}\, e_j \text{ , where } \beta_{ij} = (X_i - \bar{X}, e_j) \quad (18)$$

Multilayer perceptron (MLP) Classification

MLP is a supervised learning algorithm that consists of a set of neurons organized in layers (see Figure 9). The algorithm mimics the working of the human brain by employing the backpropagation (BP) technique to train its neurons [25]. Thus, MLP can solve very complex and nonlinear classification problems stochastically.

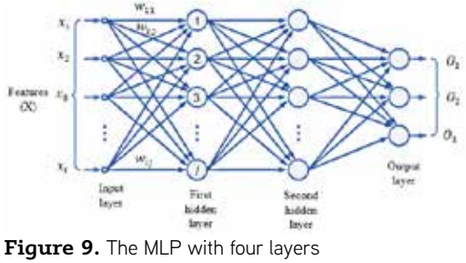


Figure 9. The MLP with four layers

The Stochastic BP algorithm can be summarized by the steps below:

24 Jolliffe IT. 2002 Principal component analysis, 2nd edn. New York, NY: Springer-Verlag.

25 S. Haykin, "Neural Networks- A Comprehensive Foundation", 2nd Edition, Prentice Hall, 1999, New Jersey.

Step1: Initialize the weights to small random values.

Step2: Randomly select training example and apply it to the input layer for all .

Step3: Propagate the signal through the network

$$V_i^m = f(net_i^m) = f\left(\sum_j w_{ij}^m V_j^{m-1}\right) \quad (19)$$

where is the activation function.

Step4: Compute the error terms at the output layer

$$\delta_i^M = f'(net_i^M)(t_i^d - V_i^M) \quad (20)$$

where is the desired output.

Step5: Propagate error backward to the preceding layer, m=M, M-1, ...,2

$$\delta_i^{m-1} = f'(net_i^{m-1}) \sum_j w_{ji}^m \delta_j^m) \quad (21)$$

Step6: Adjust all the weights

$$w_{ij}^{new} = w_{ij}^{old} + \eta \delta_i^m V_j^{m-1} \text{ , where } 0 < \eta \leq 1 \quad (22)$$

Repeat steps 2-6 until the stop criterion are satisfied.

Random Forest Classification

Random forest is a combination of decision trees such that each tree depends on the values of a random vector sampled independently and with the same distribution for all trees in the forest as shown in Figure 10. The decision trees output the class labels and the final class labels of the object are decided by using the majority voting. This classifier can work efficiently with large databases and even handle missing data [26].

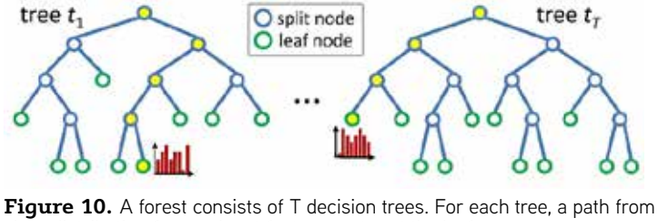


Figure 10. A forest consists of T decision trees. For each tree, a path from root to leaf, and a class distribution for one input feature vector at the leaf.

26 L. Breiman, "Random forests," Machine Learning, vol. 45, no. 1, pp. 5–32,2001

Multinomial Logistic Regression (MLR) Classification

MLR is a statistical model that uses the so-called softmax function to predict the probabilities of several classes or events [27]. The softmax function converts an arbitrary vector of real numbers into a discrete probability distribution by squashing all values to the range [0,1] and the sum of the elements to 1 as follows:

$$p(y = i|x) = \frac{e^{z_i}}{\sum_{j=1}^{K} e^{z_j}} \quad \text{for } i = 1, \ldots, K \quad (23)$$

Where is the discriminant function for class with the weight vector . Figure 11 illustrates the concept of Logistic Regression for K classes.

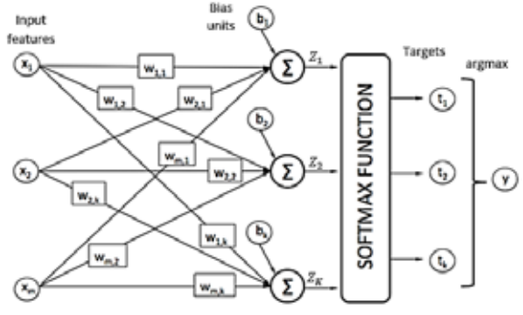


Figure 11. MLR for K classes

Performance Evaluation

The training and testing set were selected according to the five-fold cross-validation method as shown in Figure 12. The dataset contains 930 images and thus it was randomly split into two independent datasets with 744 images for training and 186 images for testing.

Figure 12. Five-fold cross-validation

To evaluate the efficiency of our algorithms, five criteria were used. These criteria are summarized in table 1:

27 Hosmer, D. W.& Lemeshow, S. (2000). Applied Logistic Regression (2nd ed.). New York: Wiley.

Table 1. Performance Metrics.

Measure (in %)	Equation
Accuracy	(TN + TP) / (TN + TP + FN + FP)100
Sensitivity/Recall	TP / (TP + FN)100
Specificity	TN / (TN + FP)100
Precision (PPV)	TP / (TP + FP)100
F1- Score	2x ((Precision x Recall) / (Precision + Recall))

Where TP, FP, TN, and FN represent True Positive, False Positive, True Negative, and False Negative, respectively. The accuracy represents the percentage of correctly classified test cases by the classifier, while sensitivity represents the proportion of correctly classified test cases to the total actual cases, specificity measures the actual negatives that the classifier correctly identifies, and precision refers to the proportion of correctly classified test cases to the total predicted cases, and finally, F1 Score measures the accuracy of the test [28].

III. Results and Discussion

The experiments were conducted on a dataset that contains three classes of chest X-ray images which are COVID-19, Pneumonia, and normal. The obtained results are shown in Table 2, Table 3, Table 4, and Figure 13, respectively. From the experimental result, it can be observed that the extracted texture features with different classifiers were successful in classifying the chest X-ray images with high performance. The LBP method with Multinomial Logistic Regression classifier surpasses all the other methods with an accuracy of 99.64%, whereas the HOG and wavelet features have the lowest accuracy nearly 92% with the same classifier. From Table 3, it can be noticed that the HOG features with Random Forest also give a significant performance with accuracy of 96.77% which is nearly equal to the accuracy of LBP features with Multilayer Perceptron. The fusion of different features remarkably improves the classification accuracy as shown in Figure 13. The classification accuracy of the Multinomial Logistic Regression classifier has increased and becomes 100% in the case of combining various texture features, whereas the performance of other classifiers has increased by about 2-3%. Consequently, it can be said that all classifiers achieve significant results when multiple features were used.

28 Han, J., Kamber, M., Pei, J.: Data Mining: Concepts and Techniques. (2012).

Table 2. Classifiers performance (%) on the LBP Features.

Classifier	Accuracy	Sensitivity	Specificity	Precision	F1 Score
Multilayer Perceptron	96.42	94.62	97.31	94.62	94.62
Random Forest	95.34	93.01	96.51	93.01	93.01
Multinomial Logistic Regression	99.64	99.46	99.73	99.46	99.46

Table 3. Classifiers performance (%) on the HOG Features.

Classifier	Accuracy	Sensitivity	Specificity	Precision	F1 Score
Multilayer Perceptron	94.62	91.94	95.97	91.94	91.94
Random Forest	96.77	95.16	97.58	95.16	95.16
Multinomial Logistic Regression	92.83	89.25	94.62	89.25	89.25

Table 4. Classifiers performance (%) on the Wavelet Features.

Classifier	Accuracy	Sensitivity	Specificity	Precision	F1 Score
Multilayer Perceptron	93.55	90.32	95.16	90.32	90.32
Random Forest	93.91	90.86	95.43	90.86	90.86
Multinomial Logistic Regression	92.47	88.71	94.35	88.71	88.71

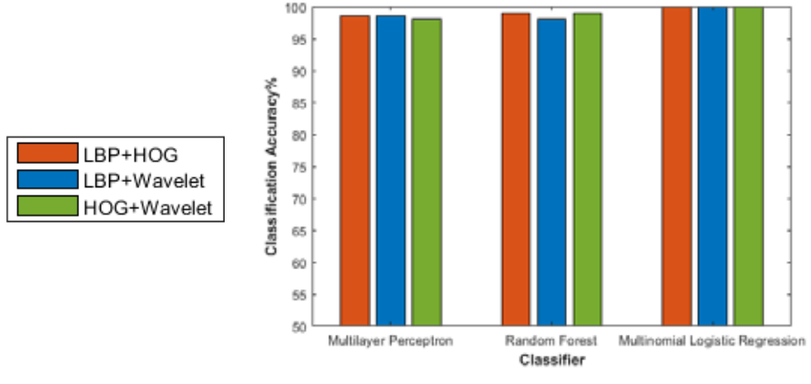


Figure 13. Classifiers performance on Multiple features

IV. Conclusion

In this research, we have extracted different types of features that describe the texture and the local structure of the chest. LBP and HOG are simple yet powerful techniques to extract meaningful texture features, whereas DWT offers a good representation of

the image in an effective way, since most of the image energy is concentrated in a small set of coefficients. The fusion of multiple features significantly improves the classification accuracy with promising results. However, the feature fusion process results in high dimensional feature vectors and this problem has been addressed by using PCA dimension reduction. The Multinomial Logistic Regression classifier has the highest performance with an accuracy of 100% on each of the following features: (LBP with HOG), (LBP with Wavelet) and (HOG with Wavelet), respectively. Other interesting results obtained by Random Forest and Multilayer Perceptron after combining different features. The experiments were conducted on publicly available datasets, and the performance of different classifiers shows that the extracted features were very essential to diagnose COVID-19 in X-Ray images.

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Gis-Based Modeling of COVID-19 Infection Risk in Turkey

Behnam Khorrami*

Abstract

The new coronavirus (COVID-19) emerged in China in December 2019 and became the world's mainstream challenge affecting all aspects of human life. Modeling the infection risk of COVID-19 is likely to provide preliminary information about the potential risky areas where higher priorities regarding protective measures should be given by the authorities. In this study, meteorological and socio-economic parameters were used to evaluate their association with the pandemic and incorporated in the proposed model. The results of regression modeling suggested that all considered socioeconomic variables including

Özet

Yeni koronavirüs (COVID-19), Aralık 2019'da Çin'de ortaya çıktı ve dünyanın insan yaşamının tüm yönlerini etkileyen genel bir sorun haline geldi. COVID-19 enfeksiyon riskinin modellenmesi, yetkililer tarafından koruyucu önlemlerle ilgili daha yüksek öncelik verilmesi gereken potansiyel riskli alanlar hakkında ön bilgi sağlayacaktır. Bu çalışmada, pandemi ile ilişkilerini değerlendirmek için meteorolojik ve sosyoekonomik parametreler kullanılmış ve önerilen modele dahil edilmiştir. Regresyon modellemesinin sonuçları, nüfus yoğunluğu, sosyal aktivite, havaalanı trafiği ve turizm gibi dikkate alınan tüm sosyoekonomik değişkenlerin

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population density, social activity, airport traffic, and tourism were highly correlated with COVID-19 transmission while only wind speed came out to be correlated among meteorological parameters. Other variables including precipitation, temperature, and humidity were not found to influence the disease in Turkey during the period of assessment. The defined influential variables at the second step were integrated based on the weighted linear combination technique to model the potential risk of the COVID-19 infection. The modeled infection risk map showed a high correlation with the cumulative positive cases of the disease suggesting that it can be used by decision-makers throughout the pandemic period to effectively control the disease.

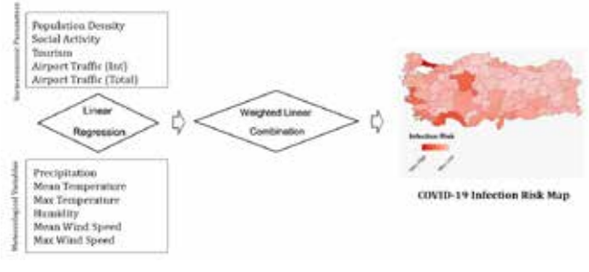
Keywords: *COVID-19, Infection Risk, Outbreak, Climatic Factors, Socioeconomic Factors, Turkey*

COVID-19 iletimi ile yüksek oranda korelasyon gösterdiğini, ancak meteorolojik parametreler arasında yalnızca rüzgar hızının korelasyon gösterdiği ortaya çıktı. Yağış, sıcaklık ve nem gibi diğer değişkenlerin değerlendirme döneminde Türkiye'de hastalığı etkilemediği görülmüştür. İkinci adımda tanımlanan etkili değişkenler, COVID-19 enfeksiyonunun potansiyel riskini modellemek için ağırlıklı doğrusal kombinasyon tekniğine dayalı olarak entegre edildi. Modellenen enfeksiyon risk haritası hastalığın kümülatif pozitif vakalarıyla yüksek korelasyon göstermektedir. Elde edilen sonuçlara göre, COVID-19 olası enfeksiyon risk haritası bu, hastalığın etkin bir şekilde kontrol altına alınması için pandemi dönemi boyunca karar verme mercileri tarafından kullanılabilecek etkili ve yararlı bir önlem aracıdır.

Anahtar kelimeler: *COVID-19, Enfeksiyon Riski, Salgın, İklimsel Faktörler, Sosyoekonomik Faktörler, Türkiye*

*

Graphical Abstract



Highlights

- COVID-19 is highly correlated with socioeconomic parameters in Turkey.
- Population density is the most influential parameter of COVID-19 infection.
- GIS-based modelling approach is an effective strategy to develop risk maps.
- An infection risk map can be used as a tool by decision makers.

I. Introduction

SARS-CoV-2 (later renamed Coronavirus disease COVID-19) was first detected in December 2019 in Wuhan city, Hubei Province, China. The virus started to spread among people at a very high pace, even faster than the spread of SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) in 2002 and MERS-CoV (Middle East Respiratory Syndrome-related Coronavirus) in 2012[1] inside China and later spread to the world primarily through human circulation. It is now believed that the human-to-human transmissibility of the virus caused the quick circulation of the disease among people leading to its spread in most of the countries just within two months.[2] The World Health Organization (WHO) announced a Public Health Emergency of International Concern (PHEIC) regarding the outbreak of COVID-19 on 30 January 2020.[3] On March 11, 2020, WHO declared a global pandemic announcement for COVID-19 outbreak.[4] As of 28 Aug 2020, coronavirus pandemic has left more than 24 million confirmed cases with above 836 thousand deaths.[5] Almost all the research centers and organizations around the world have started their work to discover a vaccine and/or an effective cure for COVID-19 to stop this one of the most horrific diseases of the modern history of the world.

Besides the great impact of the COVID-19 outbreak on public health,[6,7] it is also estimated that the continuation of this epidemic will have unprecedented negative impacts on international relations, global markets, and economy due to the restricted economic activities as a result of the protective measures including nationwide lockdowns and quarantine[8] which are currently seen as the only effective way for battling COVID-19 at least until an effective vaccine is found. The virus is new to human beings and enough

1 Boulos, Maged N. Kamel, and Estella M. Geraghty. "Geographical tracking and mapping of coronavirus disease COVID-19/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic and associated events around the world: how 21st century GIS technologies are supporting the global fight against outbreaks and epidemics.", 2020. pp. 1-12.

2 Wang, Chen, Peter W. Horby, Frederick G. Hayden, and George F. Gao. "A novel coronavirus outbreak of global health concern." The lancet 395, no. 10223, 2020. pp. 470-473.

3 WHO (2020a). World Health Organization Statement on the second meeting of the International Health Regulations Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV), Geneva, Switzerland, 30 January 2020. 2005. https://www.who.int/news-room/detai l/30-01-2020- statement-on-the-second-meeting-of-the-inter national-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov).

4 Cucinotta, Domenico, and Maurizio Vanelli. "WHO declares COVID-19 a pandemic." Acta Bio Medica: Atenei Parmensis 91, no. 1, 2020. pp. 157.

5 WHO (2020b). World Health Organization Coronavirus Disease (COVID-19) Dashboard https://COVID-19.who.int/?gclid=CjwKCAjwk6P2BRAIEiwAfVJ0rPqnPNtWM9axuzF3ThXvPnPX9YDDheSO3-NSJPapiafJIZR7RI7o0xo-C41MQAvD_BwE

6 Bai, Yan, Lingsheng Yao, Tao Wei, Fei Tian, Dong-Yan Jin, Lijuan Chen, and Meiyun Wang. "Presumed asymptomatic carrier transmission of COVID-19." Jama 323, no. 14, 2020. pp. 1406-1407

7 Sohrabi, Catrin, Zaid Alsafi, Niamh O'Neill, Mehdi Khan, Ahmed Kerwan, Ahmed Al-Jabir, Christos Iosifidis, and Riaz Agha. "World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19)." International journal of surgery 76, 2020. pp. 71-76.

8 Hamzelou, Jessica. "World in lockdown.", New Scientist, 245 (3275): 7. DOI: 10.1016/S0262-4079(20)30611-4.

information is not available regarding its characteristics and behavior, which requires more basic research on the issue.[9]

Since the onset of the pandemic, researchers have started to evaluate the disease from different perspectives. Spatial and statistical analysis of viral diseases and linking them to meteorological parameters have been one of the interesting issues around the world. The occurrence and outbreak of SARS and MERS, viruses of the same family of COVID-19, was linked to environmental and climatic factors.[10 11 12 13] Thus, it is thought that the spread and contagiousness of COVID-19 may also be associated with environmental and climatic factors [14] even though the accuracy of this idea has not yet been approved as a general scientific fact. While some researchers found that the virus is mainly impacted by meteorological parameters such as air temperature and humidity [14 15 16 17 18 19 20 21 22 23 24 25 26] others suggest that the impact of climate and weather parameters

9 Xu, Hao, Chonghuai Yan, et al. "Possible environmental effects on the spread of COVID-19 in China." Science of the Total Environment 731, 2020. 139211.

10 Cai, Quan-Cai, et al. "Influence of meteorological factors and air pollution on the outbreak of severe acute respiratory syndrome." Public Health 121, no. 4, 2007. pp. 258-265

11 Tan, Jianguo, Lina Mu, Jiaxin Huang, Shunzhang Yu, Bingheng Chen, and Jun Yin. "An initial investigation of the association between the SARS outbreak and weather: with the view of the environmental temperature and its variation." Journal of Epidemiology & Community Health 59, no. 3 (2005): pp. 186-192.

12 Altamimi, Asmaa, and Anwar E. Ahmed. "Climate factors and incidence of Middle East respiratory syndrome coronavirus." Journal of Infection and Public Health 13, no. 5, 202. pp.704-708.

13 Gardner, Emma G., et al. "A case-crossover analysis of the impact of weather on primary cases of Middle East respiratory syndrome." BMC infectious diseases 19, no. 1, 2019. pp. 1-10.

14 Ma, Yueling, Yadong Zhao, et al. "Effects of temperature variation and humidity on the death of COVID-19 in Wuhan, China." Science of the total environment 724 (2020): 138226.

15 Ahmadi, Mohsen, e.al.. "Investigation of effective climatology parameters on COVID-19 outbreak in Iran." Science of the Total Environment 729 (2020): 138705.

16 Şahin, Mehmet. "Impact of weather on COVID-19 pandemic in Turkey." Science of The Total Environment 728 (2020): 138810.

17 Sajadi, M.M., et al. "Temperature, Humidity, and Latitude Analysis to Estimate Potential Spread and Seasonality of Coronavirus Disease 2019 (COVID-19)". JAMA Network Open 3, e2011834. (2020). doi:10.1001/jamanetworkopen.2020.11834

18 Bukhari, Qasim, and Yusuf Jameel. "Will coronavirus pandemic diminish by summer?" Available at SSRN 3556998 (2020). DOI: 10.2139/ssrn.3556998.

19 Araujo, Miguel B., and Babak Naimi. "Spread of SARS-CoV-2 Coronavirus likely to be constrained by climate." MedRxiv (2020).

20 Hunter, Philip. "The spread of the COVID-19 coronavirus: Health agencies worldwide prepare for the seemingly inevitability of the COVID-19 coronavirus becoming endemic." EMBO reports 21, no. 4 (2020): e50334.

21 Xie, Jingui, and Yongjian Zhu. "Association between ambient temperature and COVID-19 infection in 122 cities from China." Science of the Total Environment 724 (2020): 138201.

22 Tosepu, Ramadhan, et al."Correlation between weather and COVID-19 pandemic in Jakarta, Indonesia." Science of The Total Environment 725 (2020): 138436.

23 Chen, Biqing, Hao Liang, Xiaomin Yuan, Yingying Hu, Miao Xu, Yating Zhao, Binfen Zhang, Fang Tian, and Xuejun Zhu. "Roles of meteorological conditions in COVID-19 transmission on a worldwide scale." MedRxiv (2020).

24 Wang, Mao, et al. "Temperature significant change COVID-19 Transmission in 429 cities." medrxiv (2020).

25 Qi, Hongchao et al. "COVID-19 transmission in Mainland China is associated with temperature and humidity: a time-series analysis." Science of the total environment 728 (2020): 138778.

26 Bashir, Muhammad Farhan, et al. "Correlation between climate indicators and COVID-19 pandemic in New York, USA." Science of the Total Environment 728 (2020): 138835.

on COVID-19 transmissibility rate is rather vague[27] or meaningless.[28 29] On the other hand, the relation of COVID-19 with socioeconomic and demographic parameters have been analyzed and confirmed by some studies. [30 31 32 33 34 35] Co-analysis of COVID-19 and other possible effective parameters will give insight into the spatial pattern of the transmissibility and spread of the virus making the monitoring of the pandemic much more convenient and precise. The results obtained from this assessment will eventually aid the decision-makers to put effective measures into force regarding the control of the risk associated with this contagious disease.

The first case of the new coronavirus in Turkey was detected on 11 March 2020. The pandemic continued to grow quickly so that by 1 April 2020 the virus has spread to the entire country.[36] As of 28 May 2020, Turkey had 160979 confirmed cases and the death toll has increased to 4461.[37] Sahin (2020)[38] analyzed the weather parameters and COVID-19 relation in Turkey and found that population, wind speed, and temperature are highly correlated with COVID-19 spread. To our knowledge, the socioeconomic parameters have not yet been analyzed in Turkey. By spatial integration of the effective factors on a disease agent, its behavioral characteristics can be modeled and the results will be extremely beneficial for the decision-makers. Based on this premise, the main purpose of the current study is to model the infection risk of COVID-19 in Turkey based on geographic information systems (GIS) and according to the explanatory variables selected through statistical analysis of meteorological and socioeconomic parameters in Turkey. The proposed methodology can be modified and used in all countries based on their existing conditions.

27 Cowling, Benjamin J., and Allison E. Aiello. "Public health measures to slow community spread of coronavirus disease 2019." The Journal of infectious diseases 221, no. 11 (2020): 1749-1751. DOI: 10.1093/infdis/jiaa123

28 Gupta, Sonal, Gourav Singh Raghuwanshi, and Arnab Chanda. "Effect of weather on COVID-19 spread in the US: A prediction model for India in 2020." Science of the total environment 728 (2020): 138860.

29 Jahangiri, Mehdi, Milad Jahangiri, and Mohammadamir Najafgholipour. "The sensitivity and specificity analyses of ambient temperature and population size on the transmission rate of the novel coronavirus (COVID-19) in different provinces of Iran." Science of the total environment 728 (2020): 138872.

30 Qiu, Yun, Xi Chen, and Wei Shi. "Impacts of social and economic factors on the transmission of coronavirus disease 2019 (COVID-19) in China." Journal of Population Economics 33, 2020. pp. 1127-1172.

31 Wu, Xiao, Rachel C. Nethery, Benjamin M. Sabath, Danielle Braun, and Francesca Dominici. "Exposure to air pollution and COVID-19 mortality in the United States." MedRxiv (2020).

32 Hou, Can, et al. "The effectiveness of quarantine of Wuhan city against the Corona Virus Disease 2019 (COVID-19): A well mixed SEIR model analysis." Journal of medical virology 92, no. 7, 2020. pp. 841-848.

33 Mollalo, Abolfazl, Behzad Vahedi, and Kiara M. Rivera. "GIS-based spatial modeling of COVID-19 incidence rate in the continental United States." Science of the total environment 728 (2020): 138884.

34 Siche, Raúl. "What is the impact of COVID-19 disease on agriculture?." Scientia Agropecuaria 11, no. 1 (2020): 3-6.

35 Evans, Olaniyi. "Socio-economic impacts of novel coronavirus: The policy solutions." BizEcons Quarterly 7 (2020): 3-12.

36 Turkish Ministry of Health."Coronavirus updates" (2020)., Accessed on 28 May 2020 at: https://COVID-19bilgi.saglik.gov.tr/tr/

37 Turkish Ministry of Health."Coronavirus updates"

38 Şahin, Mehmet. "Impact of weather on COVID-19 pandemic in Turkey." Science of The Total Environment 728 (2020): 138810.

II. Methodology

Data collection

To analyze the spatial transmission patterns of COVID-19 and its association with some effective meteorological and socioeconomic parameters in Turkey, the authors used the latest official updates on the confirmed positive cases and total death data of the pandemic in Turkey. The latest province-based statistics made available by the Turkish Ministry of Health is the cumulative data up to 03 April 2020 (Figure 1). The meteorological variables included in this study were selected to be air temperature, precipitation, humidity, and wind speed, which are previously reported to be influential in the dispersion potential and the infection power of the virus. The meteorological data were acquired from the earth observatory program of NASA.

TERRA is one of NASA's databases for reanalyzing the atmospheric remote sensing data based on the Goddard Earth Observing System Model, Version 5 (GEOS-5) with its Atmospheric Data Assimilation System (ADAS), version 5.12.4.[39] Many meteorological parameters are produced by the MERRA project (The Modern-Era Retrospective analysis for Research and Applications version 2) with a particular focus on the historical climate analysis, which is accessible via NASA's Giovani database portal (https://giovani.gsfc.nasa.gov/). The characteristics of the meteorological variables used in this study are given in Table 1.

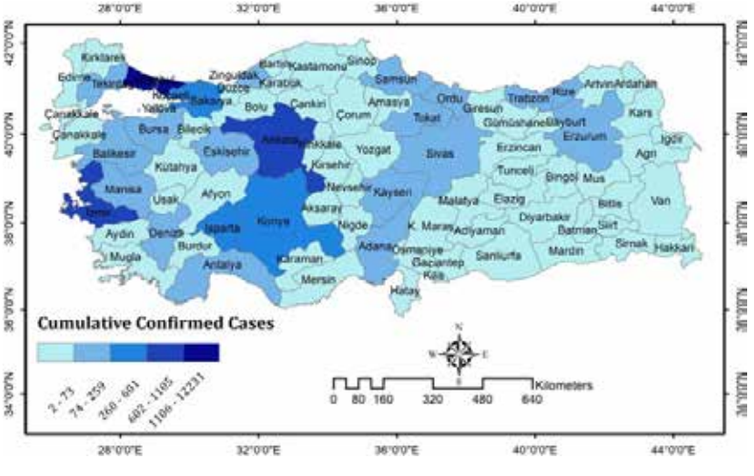


Figure 1. Spatial illustration of the cumulative confirmed cases of COVID-19 as of 03 April 2020 over Turkey.

39 Gelaro, Ronald, Will McCarty, Max J. Suárez, Ricardo Todling, Andrea Molod, Lawrence Takacs, Cynthia A. Randles et al. "The modern-era retrospective analysis for research and applications, version 2 (MERRA-2)." Journal of climate 30, no. 14, 2017. pp. 5419-5454.

Table 1. Specifications of the meteorological variables received from MERRA-2 reanalysis

Variable Name	Description	Temporal Resolution	Resolution	Unit
T2MMean	Mean 2-m air temperature	Daily	0.5 ° x 0.625 °	°K
T2MMax	Max 2-m air temperature	Daily	0.5 ° x 0.625 °	°K
TPREC	Total precipitation	Daily	0.5 ° x 0.625 °	$kg.m^{-2}.s^{-1}$
SPEED	Surface wind speed	Daily	0.5 ° x 0.625 °	$m.s^{-1}$
SPEEDMax	Max surface wind speed	Daily	0.5 ° x 0.625 °	$m.s^{-1}$
QLML	Surface specific humidity	Monthly	0.5 ° x 0.625 °	$kg.kg^{-1}$

Besides the meteorological parameters, some socio-economic parameters were also included in the analysis to reveal their relationship with the pandemic. The new coronavirus is transmitted from human to human so social distance plays a critical role in its spread. Any activity and event requiring human gatherings should thus be included in COVID-19 related analysis to enrich the effectiveness of the results. From this viewpoint, the authors used data regarding human contacts. These factors are the social activity, tourism, airport passenger traffic, and population density of each province. Long-term (1995-2019) data regarding these parameters were obtained from the Turkish Statistical Institute (TSI) (http://www.turkstat.gov.tr). The averages of each parameter represent the accumulated potential and the current state of each province with regards to social contact that is considered critical for the analysis.

Linear regression modeling

A multiple linear regression analysis was performed to evaluate the strength of the relationships and define the potentially effective parameters on the spread and infection rate of COVID-19 over Turkey. Linear regression is one of the simplest and most widely used classical regression methods to model the linear and additive relations between explanatory (independent) variable(s) and a dependent variable (Yang et al, 2016[40]). The regression model can be expressed as:

$$Y_i = \beta_0 + \sum \beta_k X_{ki} + \epsilon_i \quad , i = 1,\ldots,n \qquad (1)$$

where Yi and Xki represent the dependent variable and independent variables, respectively; k represents the coefficients, and is the error term.[41]

40 Yang, Lingjian, Songsong Liu, Sophia Tsoka, and Lazaros G. Papageorgiou. "Mathematical programming for piecewise linear regression analysis." Expert systems with applications 44, 2016. pp. 156-167

41 Lewandowska-Gwarda, Karolina. "Geographically weighted regression in the analysis of unemployment in Poland." ISPRS International Journal of Geo-Information 7, no. 1, 2018. pp. 17.

In this study, an association analysis was conducted between the cumulative confirmed cases and the total death records of the COVID-19 pandemic reported for each province of Turkey. Explanatory variables were selected from meteorological variables and socioeconomic parameters that are theoretically assumed to influence the dispersion of the virus. Because the incubation period of the virus is reported to be 14 days,[42] the meteorological variables in this study were calculated to represent the average values of the preceding 14 days (from 21 Mar to 03 Apr) from the official declaration of the provincial statistics. The spatial maps of the explanatory variables are shown in Figures 2 and 3.

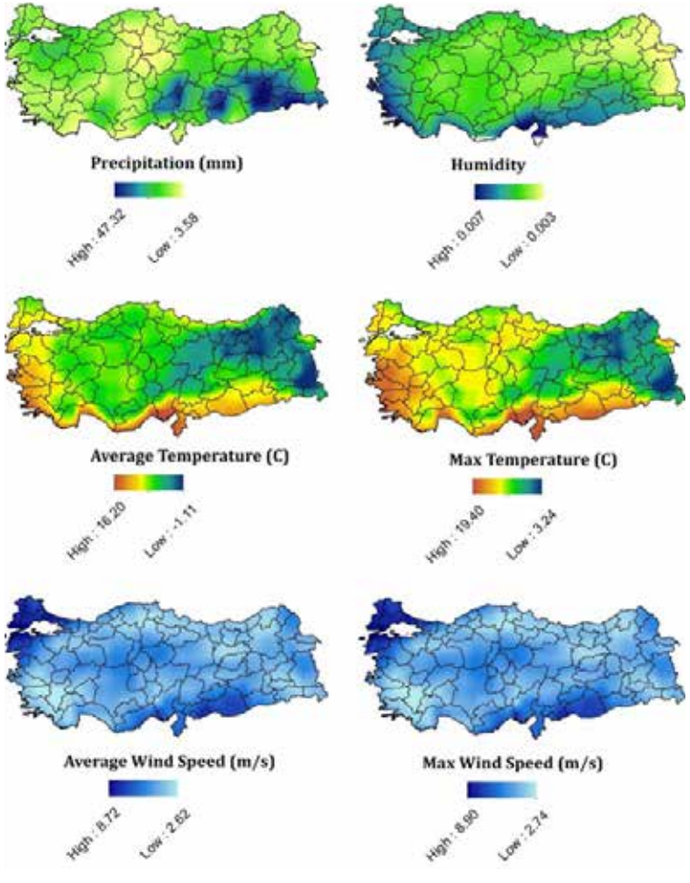


Figure 2. The spatial distribution of meteorological variables averaged for two weeks' period (21 Mar - 03 Apr 2020) over Turkey

42 Lai, Chih-Cheng, Tzu-Ping Shih, Wen-Chien Ko, Hung-Jen Tang, and Po-Ren Hsueh. "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges." International journal of antimicrobial agents 55, no. 3 (2020): 105924.

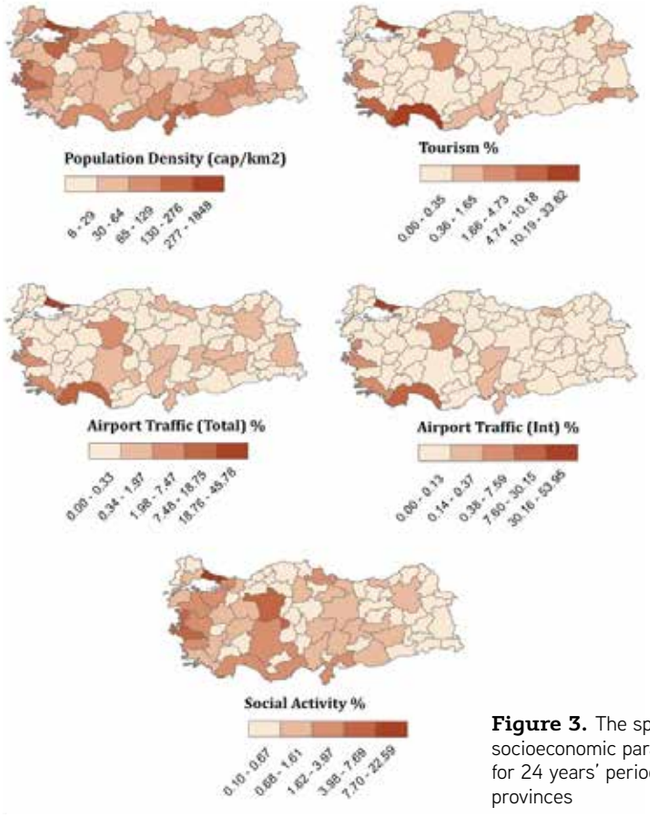


Figure 3. The spatial distribution of socioeconomic parameters averaged for 24 years' period (1995-2019) over provinces

Weighted Linear Combination (WLC)

Based on the regression analysis of different explanatory parameters to analyze the outbreak of COVID-19 over Turkey, a risk map of the pandemic was generated using the effective parameters based on the Weighted Linear Combination (WLC) approach. WLC is one of the most prevalent GIS-based decision models[43] through which, weights (showing the importance of the parameters involved) are added to each corresponding parameter (criterion) to produce the output. WLC is formulated as:

$$S = \sum W_i X_i \qquad (2)$$

where, Xi is the criterion of interest and Wi is its weight.[44]

43 Malczewski, Jacek. "On the use of weighted linear combination method in GIS: common and best practice approaches." Transactions in GIS 4, no. 1, 2000. pp. 5-22.

44 Drobne, Samo, and Anka Lisec. "Multi-attribute decision analysis in GIS: weighted linear combination and ordered weighted averaging." Informatica 33, no. 4 (2009).

III. Results and Discussion

The association between pandemic and the explanatory variables

COVID-19 is a newly emerged infection with rapid transmissibility. Yet, there is no comprehensive information about the virus in the scientific community to control the pandemic effectively. Thus, having the correct idea about the influential parameters on the dispersion of COVID-19 is of utmost importance to be able to bring it under. In this study, the authors applied a linear regression analysis to investigate the linear association of the variables and to define the effective parameters on the spread of the virus. The calculated correlation and regression coefficients (Table 2), gives an overview of the strength of the relations between each explanatory variable associated with the COVID-19 outbreak. Results indicated that the meteorological variables have a limited impact on the transmission of the pandemic over Turkey for the aforementioned period of analysis. Out of different meteorological variables used in this study, the only wind speed was correlated with COVID-19 cases.

On the contrary, all socioeconomic parameters were found to be influential on the pandemic in Turkey. Population density and social activity rate in each province were found to have the highest correlations with COVID-19, which is theoretically true since the high congestion of people in an area boosts the infection risk of the individuals and result in the spread of the disease. Airport traffic is also an effective parameter in COVID-19 transmission due to the incoming passenger traffic, particularly from foreign countries. The general status of each city regarding the rate of the traffic caused by the passengers coming into the country from abroad or traveling within the boundaries of the country will influence the dispersion of the virus. Tourism was also defined as an effective parameter. For a country like Turkey, which receives millions of visitors from outside and inside the country, the tourism factor also plays an important role in a pandemic like COVID-19.

Table 2. Linear Regression Modelling Results

	Confirmed Cases		**Total Deaths**	
	(R)	**(R^2)**	**(R)**	**(R^2)**
Population Density*	0.976	0.953	0.975	0.950
Precipitation	-0.093	0.009	-0.105	0.011
Temperature (Mean)	0.120	0.014	0.137	0.019
Temperature (Max)	0.035	0.001	0.046	0.002
Wind Speed (Mean)*	0.275	0.076	0.277	0.077
Wind Speed (Max)*	0.267	0.071	0.267	0.071
Humidity	0.137	0.019	0.153	0.023
Airport Traffic (International)*	0.864	0.746	0.860	0.740
Airport Traffic (Total)*	0.915	0.837	0.915	0.836
Social Activity*	0.930	0.865	0.934	0.872
Tourism*	0.770	0.594	0.769	0.591

* meaningful at 0.01 significance level

COVID-19 mortality analysis

Mortality rate or Case Fatality Ration (CFT) is an index commonly being used to describe the impact of a disease in a population.[45] In general, the CFT of a disease or pandemic is calculated as a ratio of total death to total cases. In this study, the province-based mortality analysis of COVID-19 was performed using the statistics of the top 10 critical provinces of the country regarding the number of deaths. As of 03 April 2020, the most death cases have been recorded for Istanbul, Izmir, Kocaeli, Ankara, Konya, Zonguldak, Balikesir, Trabzon, Sakarya and Adana provinces. Figure 4 shows the map of the total death and mortality rate of COVID-19 in Turkey.

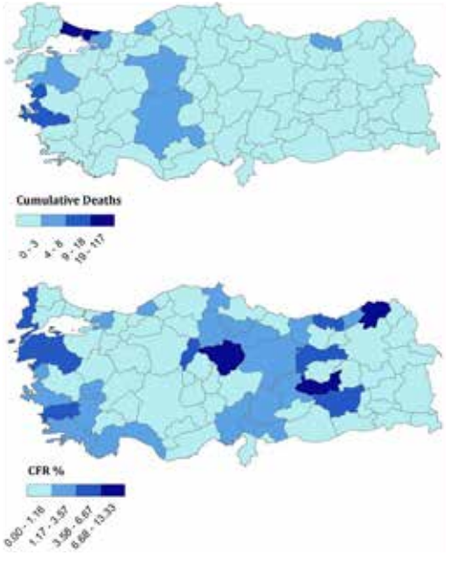


Figure 4. Spatial illustration of total deaths and mortality rate of COVID-19

45 Jacob, M. E., and M. Ganguli. "Epidemiology for the clinical neurologist." Handbook of clinical neurology 138, 2016. pp. 3-16.

According to the CFT map of the country, the mortality rate is highly concentrated in the smaller provinces especially those, which are located in the central and eastern parts of Turkey. The higher mortality in smaller provinces may be a result of the poor health infrastructures especially for those cities located in eastern Turkey where lower opportunities are available compared to the western areas. The other factor contributing to this pattern of mortality and life loss due to the COVID-19 pandemic may be relevant to the rate of the adult population of each province. It is stated by health officials that older adults (people aged over 65) are much more vulnerable to the pandemic. Thus, it is expected to witness higher mortality rates among these sensitive age groups.

In this study, the authors used three different parameters including the population of the vulnerable group, total number of patient beds in hospitals as well as the total number of health personnel data of the year 2018 available for top 10 provinces (Table 3), to analyze the associations between them.

Table 3. Province averages of health data (number of personnel, beds and vulnerable population) regarding the year 2018

City	CFR	Health Personnel	Patient Bed	Population (≥65 yrs)
Istanbul	0.956	34502	39328	1079196
Izmir	1.629	10093	11982	493673
Kocaeli	1.60	4083	4330	142644
Ankara	0.814	15702	18291	486783
Konya	1.165	5414	7527	211374
Zonguldak	2.538	1709	2195	75194
Balikesir	4.717	2798	3334	186472
Trabzon	5.747	2835	3247	99415
Sakarya	0.890	1863	1932	99494
Adana	1.245	5041	7033	186098

The statistical analysis of the parameters (Figure 5) resulted in a high correlation (0.768) between the number of vulnerable populations and the mortality rate of the virus, which indicates that elderly people are highly susceptible to loss of life in society. For the number of beds and health personnel, the negative correlations of -0.40 and -0.39, respectively, were achieved. These negative correlations justify the fact that the mortality rate of the virus depends also on the integrity of the health sector of the given area.

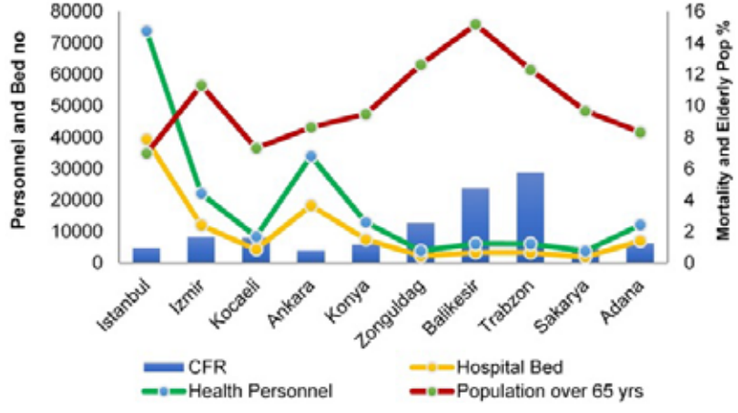


Figure 5. The schematic representation of the association of COVID-19 mortality rate and health parameters for the top 10 provinces regarding the death records

COVID-19 infection risk map

A potential map of COVID-19 infection risk was generated using WLC analysis through which, different layers are aggregated according to their importance, regarding the effect they have on the problem, to produce an integrated layer. In this study, the influential parameters (criteria) on the pandemic were identified through regression modeling. These parameters are population density, social activity, airport traffic (total), airport traffic(international), tourism, average, and max wind speed according to their importance (correlation value). The normalized correlation coefficient of each parameter was used as a weighing factor. Five classes were defined for each criterion based on the natural breaks classification algorithm and were ranked according to their priority level.

Table 4. The correspondent weight used for the explanatory variables

Category	Layer	Criteria	Ranking	Weight
Socioeconomic	Population Density	6.31-20.74	1	0.195
		20.75-56.86	2	
		56.87-129.10	3	
		129.11-273.56	4	
		273.57-1848.25	5	
	Tourism %	0-0.52	1	0.154
		0.53-1.59	2	
		1.60-4.63	3	
		4.64-10.20	4	
		10.21-33.82	5	
	Airport Traffic % (Int)	0	0	0.173
		0-0.20	2	
		0.21-3.38	3	
		3.39-7.61	4	
		7.62-53.95	5	
	Airport Traffic % (Total)	0-0.17	1	0.184
		0.18-1.79	2	
		1.80-7.35	3	
		7.36-18.66	4	
		18.67-45.78	5	
	Social Activity %	0.103-0.89	1	0.186
		0.90-2.12	2	
		2.13-3.89	3	
		3.90-7.68	4	
		7.69-22.60	5	
Meteorological	Wind Speed (Mean) m/s	2.61-3.69	1	0.055
		3.70-4.43	2	
		4.44-5.36	3	
		5.37-6.46	4	
		6.47-8.72	5	
	Wind Speed (Max) m/s	2.74-3.81	1	0.053
		3.82-4.59	2	
		4.60-5.53	3	
		5.54-6.64	4	
		6.65-8.90	5	

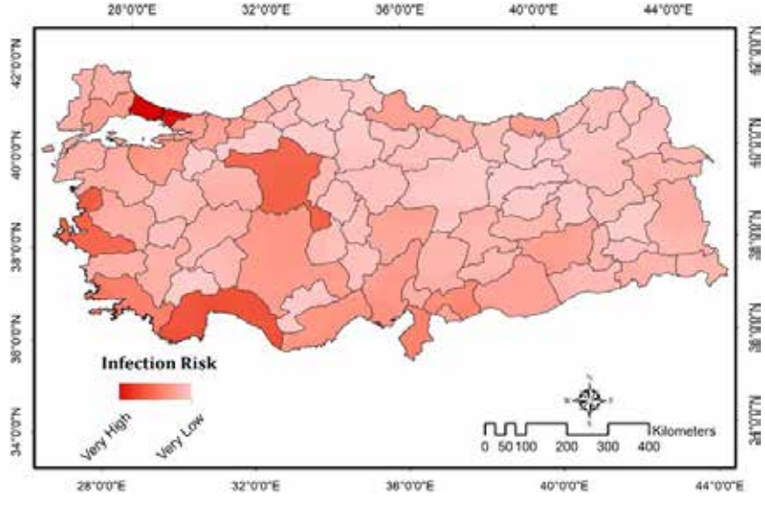


Figure 6. The potential COVID-19 infection risk map of Turkey

Table 4 gives the schematic view of the criteria and their correspondent weights used in WLC analysis.

The generated risk map of the COVID-19 pandemic (Figure 6) shows the possible areas of the country susceptible to the disease infection. From the visual interpretation perspective, the generated potential risk map mimics the map of confirmed cases of COVID-19 in Turkey (Figure 1). Istanbul has the highest infection risk and Antalya, Izmir, Ankara, Konya, Mugla, and Hatay provinces are defined as the risky areas of the country.

To verify the accuracy of the modeled risk map quantitatively, the statistical correlation of the zonal values derived from the two maps (confirmed cases and risk map) was performed. It is found that there is a high correlation (0.72) between the risk map and the map of confirmed cases in Turkey, which suggests that the modeled risk map can be used as an effective tool not only during the preliminary stages of the pandemic but also throughout the contagiousness phase as well by policy/decision-makers of the country to prioritize the required measures to control the pandemic. Such risk maps can provide an early warning with regards to the risky areas to achieve a better performance in the battle disease.

According to the risk map, 21 provinces were designated as risky areas (above mean). These provinces are Istanbul, Izmir, Ankara, Konya, Antalya, Adana, Mugla, Mersin, Samsun, Trabzon, Hatay, Gaziantep, Diyarbakir, Kayseri Duzce, Sakarya, Kocaeli, Bursa, Tekirdag, Balikesir, and Van. Out of these potentially recognized risky areas, 20 provinces (except Duzce) are among the 31 provinces for which provincial lockdown order was announced by the Turkish government[46] on 12 April 2020 in an effort to reduce the infection risk in the country. This fact indicates that the protective measure issued by the authorities was 0.64 in accordance with the modelled risk map of this study.

IV. Conclusions and Recommendations

Since its first case diagnosis in Wuhan city in China, the new coronavirus is continuing to hit the globe and is now turned into one of the biggest challenges of humanity with over 5.5 million positive cases as of the end of May 2020.[47] The pandemic has put not only the biosafety[48] of the human being in danger but also many other sectors, some of which, are yet to be discovered. The economy is one such sector and experts estimate the global economy to experience recession[49] in upcoming months due to the restrictions applied to the markets and economic activities all around the world. By linking the COVID-19 pandemic to different variables, the disease transmission mechanism[50] can be understood more clearly, which is central to battling the pandemic. In the current study, the authors used different parameters to investigate the extent of the relationship between each parameter with the COVID-19 reported confirmed cases in provincial Turkey. The regression results suggested that population density, social activity, airport traffic, tourism, and wind speed variables have a meaningful association with pandemic

46 Turkish Ministry of Interior Affairs. Curfew circular for two days. https://www.icisleri.gov.tr/2-gun-sokaga-cikma-yasagi. (2020).

47 Yang, Penghui, and Xiliang Wang. "COVID-19: a new challenge for human beings." Cellular & molecular immunology 17, no. 5, 2020. pp. 555-557.

48 Chen, Chien Chin, and Chia Yu Chi. "Biosafety in the preparation and processing of cytology specimens with potential coronavirus (COVID-19) infection: Perspectives from Taiwan." Cancer cytopathology 128, no. 5, 2020. Pp. 309-316.

49 Fernandes, Nuno. "Economic effects of coronavirus outbreak (COVID-19) on the world economy." Available at SSRN 3557504, 2020.

50 Graham, A. J., Peter M. Atkinson, and F. M. Danson. "Spatial analysis for epidemiology." (2004. Pp. 219-225.

transmission and fatality. The fatality analysis results also indicated that in the top 10 critical provinces of the country, the number of the elderly population (aged over 65) has the most impact on the mortality rate of the disease, which means that this vulnerable age group should be warier throughout the pandemic period. Health sector opportunities such as the number of health personnel and patients' beds in hospitals are the other influential factors in this regard. An infection risk map of the disease was also modeled based on the WLC analysis using the explanatory variables recognized through regression modeling. The generated risk map shows the potentiality of each province of Turkey regarding the susceptibility of its residents to the pandemic. The veracity of the modeled risk map was evaluated through a statistical comparison of the risk map and the map of confirmed cases of COVID-19 reported till 03 April 2020 for Turkey and it's found that the COVID-19 infection risk map is highly correlated with the reported infected people thus it can be applied by the health officials and other executive entities of the country through the period of the pandemic. The results also suggest that the same approach can be applied for other infectious diseases at the preliminary stages to be used as an effective tool to battle the pandemic.

Despite the high correlations achieved, the authors do not claim that the generated risk map is completely precise being aware that the number of effective variables used in this study is not the sole ones for the contagious COVID-19. Other parameters such as the social traffic (movement) data and the data showing the social hot spots (areas where normally attract a huge number of crowds in each province), some other demographic data regarding the education level of the residents, which may impact the obedience of the resident to the precautionary measures (such as social distancing, quarantine and mask usage) can also be added to the model to improve the accuracy of the spatial distribution of risk. By analyzing more parameters and by using more sophisticated decision-making techniques, the suitability and precision of the risk map can be improved.

Acknowledgements

Hereby I would like to convey my sincerest gratitude to the reverent academicians, Orhan Gunduz from Dokuz Eylul University and Khalil Valizadeh Kamran from the University of Tabriz, for their prolific and fruitful contributions without which the current research would not be fulfilled.

Author statements

The authors would like to state that there are no financial interests or connections that might raise the question of bias in the work reported or the conclusions, implications, or opinions stated.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure of the conflict of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Internet of Things During and After Pandemics

Aminu Yusuf*

Abstract

The world has seen several different pandemics and almost every pandemic is unique and required a novel approach to be tackled. Airborne transmitted pandemics are considered one of the most dangerous and frightening diseases. COVID-19 is an airborne transmitted virus that was declared a pandemic by the World Health Organisation. This virus has spread to almost every part of the world and has caused loss of lives and great damage to businesses. Researchers are working round the clock to ensure that safe and effective vaccines are found, however, until then, some majors need to be taken to reduce the

Özet

Dünya şimdiye dek birçok farklı pandemi gördü. Hemen hemen her pandemi benzersizdir ve mücadele edilmesi gereken yeni bir yaklaşım gerektirir. Hava yoluyla bulaşan salgınlar, en tehlikeli ve korkulan salgınlardan biri olarak kabul edilir. COVID-19, Dünya Sağlık Örgütü tarafından salgın ilan edilen havadan bulaşan bir virüstür. Bu virüs dünyanın hemen hemen her yerine yayılmış ve can kaybına ve işletmelerin büyük zarar görmesine neden olmuştur. Araştırmacılar, güvenli ve etkili aşıların bulunduğundan emin olmak için günün her saati çalışıyorlar, ancak o zamana kadar, virüsün bulaşma oranını azaltmak için bazı

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rate of transmission of the virus. The most common way in which COVID-19 is being spread is through coming in close contact with a COVID-19 carrier. This report shows that through effective use of the Internet of Things, the rate of COVID-19 transmission can be greatly reduced. 5G network which is the backbone of the Internet of Things (IoT) should be provided everywhere in the world. Using IoT, COVID-19 carriers can be traced, monitored remotely treated. Food and other essentials can be delivered without necessarily coming in contact with the carrier. Business and related transactions can be conducted online, class instructions can be delivered online and government officials can have virtual meetings.

Keywords: *5G network, Internet of Things, During, After, Pandemic*

büyük önlemlerin alınması gerekiyor. COVID-19'un yayılmasının en yaygın yolu, bir COVID-19 taşıyıcısıyla yakın temasta bulunmaktır. Bu rapor, Nesnelerin İnternetinin etkin kullanımı yoluyla COVID-19 bulaşma oranının büyük ölçüde azaltılabileceğini göstermektedir. Nesnelerin İnterneti›nin (IoT) omurgası olan 5G ağı dünyanın her yerinde sağlanmalıdır. IoT kullanılarak COVID-19 taşıyıcıları izlenebilir, izlenebilir ve uzaktan tedavi edilebilir. Yiyecek ve diğer temel malzemeler, taşıyıcıyla temasa geçmeden teslim edilebilir. İş ve ilgili işlemler çevrimiçi yürütülebilir, sınıf talimatları çevrimiçi olarak verilebilir ve hükümet yetkilileri sanal toplantılar düzenleyebilir.

Anahtar kelimeler: *5G ağı, Nesnelerin İnternet, Sırasında, Sonrasında, Pandemi*

*

I. Introduction

In December 2019, many cases of unknown viral diseases, which are associated with a respiratory disorder, were reported in Wuhan city, China[1]. The actual source of the virus was still unknown, but it was suspected that it came from bats. Within two months, this novel virus has spread to over thirty countries. In February 2020, World Health Organization (WHO) named it COVID-19. The name Covid is derived from three words, "corona", "virus", and "disease", and 19 represents the year it was discovered[2]. The virus was then declared a Global pandemic by WHO on 11th March 2020[3]. Some commonly seen symptoms of the virus include dry cough, difficulty breathing, diarrhoea, fever, fatigue, loss of taste or smell[4]. At present, there is no widely accepted cure, however, some vaccines have been approved by many countries. COVID-19 has been confirmed to be airborne transmission[5]. Sources of contraction are respiratory droplets

1 'COVID-19 Pandemic', in Wikipedia, 9 July 2020, https://en.wikipedia.org/w/index.php?title=COVID-19_pandemic&oldid=966805542."

2 'Coronavirus Disease Named COVID-19', BBC News, 11 February 2020, sec. China, https://www.bbc.com/news/world-asia-china-51466362."

3 'WHO Declares Coronavirus Global Pandemic', accessed 9 July 2020, https://www.aa.com.tr/en/health/who-declares-coronavirus-global-pandemic/1762632."

4 CDC, 'Coronavirus Disease 2019 (COVID-19) – Symptoms', Centers for Disease Control and Prevention, 13 May 2020, https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html."

5 'WHO Rethinking How Coronavirus Spreads in Air', BBC News, 8 July 2020, sec. World, https://www.bbc.com/news/world-53329946.

that can travel to about one meter and coming in contact with the virus carrier. This carrier can be human, animal or object.

Many countries conducted a number of mathematical modelling on the spread and containment of the virus. It has been confirmed that one of the major sources of which the virus spread is through the cluster. A cluster is formed when a virus carrier infects more than one person. That usually happens in crowded places where people live in close proximity such as in buses, planes, nightclubs, and beaches. Eliminating the clusters is considered one of the effective ways of hampering the spread of the virus. In doing so, many countries have banned all sorts of social gatherings, international flights grounded, enforced full or partial lockdown, and close down all religious worshipping centres, mandate the wearing of face masks.

There was no doubt that COVID-19 like previous pandemics has affected and changed our lives forever. It has left indelible memories in our lives especially to people who have lost family members. It brought psychological trauma to the frontline personnel and to the recovered persons. It has exposed our unpreparedness to a global pandemic despite many pandemics in the past. Many businesses have a temporary shutdown, downsized, or changed the way the business is done. Many workers have been furloughed and there is an imminent danger for global economic crises. As of 30th April 2020, 30 million Americans filed for unemployment benefits[6]. Also, for the first time in history, the price of oil in the US has turned negative[7]. This is due to a decline in the demand for oil that was caused as a result of countries shutting their borders and banning intercity travel or cross-border travel. Negative oil prices can be bad news to countries that heavily depend on oil exportation to fuel economic growth.

In the fight against COVID-19, many technological inventions have emerged or are being revived. These include the design of lifesaver ventilators, worldwide use of thermal cameras to check the temperature of individuals, design of social distancing applications. Others are the design of applications that gives real-time COVID-19 status of an area, automation in the application of disinfectant, increase use of drones and robots to deliver goods and services. This report is aimed at highlighting the use of the Internet of Things (IoT) in mitigating the effects of COVID-19 and other pandemics that will probably occur in the future.

II. 5G Network

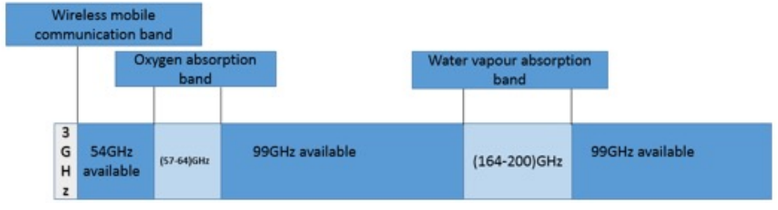
The wireless network uses radio frequency to communicate among computers and other electromechanical devices. 5G network refers to the fifth generation of wireless communication. One of its unique features is its utilization of a huge chunk of the millimeter-wave communication spectrum. As seen in figure 1, the present commercial wireless communication used spectrum in the range 300MHz-3GHz band. The two

6 '30 Million Americans Have Filed Initial Unemployment Claims since Mid-March - CNN', accessed 9 July 2020, https://edition.cnn.com/2020/04/30/economy/unemployment-benefits-coronavirus/index.html."

7 'US Oil Prices Turn Negative as Demand Dries up - BBC News', accessed 9 July 2020, https://www.bbc.com/news/business-52350082.

spectrums that cannot be used for wireless communications are (57-65) GHz and (164-200) GHz, which are for oxygen absorption and water vapor absorption bands, respectively. Hypothetically, there are about 252GHz millimeter (mm) wave communication spectrum which the 5G network is expected to fully exploit. Hence, understanding the mm-wave communication spectrum is essential for the implementation of the 5G network. Other features include the use of beamforming antennas in a spherical shape so that the total highly directional radiation will cover 360˚, the ability to transmit and receive on the same frequency simultaneously, and large-scale multi-input multi-output (MIMO) capability. Successful implementation of the 5G network will give birth to the Internet of Things (IoT), machine-to-machine (M2M) communication, device-to-device (D2D) communication and advanced vehicular communications. The scope of this report is on the IoT.

Figure 1. 3 – 300GHz milli-metre wave spectrum.



III. Internet Of Things

Internet of things (IoT) refers to the connection of a very large number of physical devices to the internet. Device refers to anything that can be assigned IP address and receive and send real-time data over a network. Many governments and organisations at various levels are using IoT to operate more efficiently, improve decision making and add value to the business. The idea of IoT has been around since the 1970s. IoT is formed from the convergence of the internet, wireless technologies, micro-services, and microelectromechanical systems (MEMS). One of the earliest examples of IoT is a Coke machine that was connected to the internet in 1982 at Carnegie Mellon University. Before deciding to make a trip to the machine, users could check the status of the machine using the internet and determine whether there would be a cold drink or not[8,9]. Supervisory control and data acquisition (SCADA) can be considered as one of the early stages of IoT. The system has remote terminal units that gather real-time information and send it to master control unit through communication channels. The master control unit processes the information and displays it to the operator. SCADA

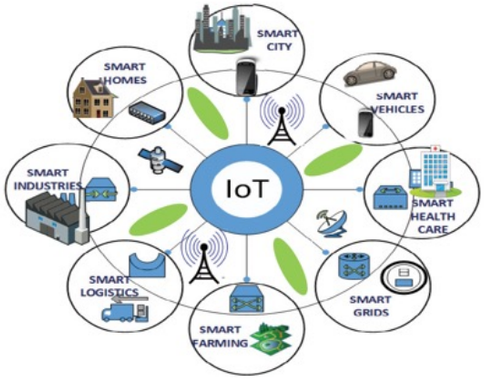
8 'The Little-Known Story of the First IoT Device', IBM Industries Blog, 7 February 2018, https://www.ibm.com/blogs/industries/little-known-story-first-iot-device/."

9 Gary Smith, 'From 1982 Coca-Cola Vending Machine to Latest Trend: What the Internet of Things Means for Business', Real Business, 15 July 2015, https://realbusiness.co.uk/from-1982-coca-cola-vending-machine-to-latest-trend-what-the-internet-of-things-means-for-business/."

has been successfully used in supervision and control of the national grid and in monitoring, control, and management of electric trains.

Despite the presence of systems like SCADA, the development of IoT can be characterized as a slow pace, this is because connecting billions of devices to the internet requires an enormous amount of data. To date, the bandwidth that will handle this enormous amount of data is not available. The IoT could only be achieved with the advent of high broadband 5G wireless network. 5G network proposes systematic changes in the architecture, networking, and multiplexing of the wireless network. It offers extended coverage anytime anywhere irrespective of the location of the user. It has low latency compared to the existing network as well as lower energy consumption. It is expected to have high throughput and high connection density. Implementation of IoT is complex, as it requires cooperation among enormous, distributed, autonomous, and heterogeneous components at various levels. The challenges associated with IoT are expected to be overcome in 2025. Typical functions of IoT are shown in figure 2. The world like never before is in need of the 5G network that will facilitate the realization of IoT.

Figure 2. Connecting anything to the internet[10].



Smart HealthCare

Some people contracted COVID-19 unknowingly simply by being at the hospital during the pandemic. Besides, a large number of healthcare personnel were infected when treating the COVID-19 patients. At the high peak of COVID-19, hospitals were overwhelmed, shortage of personal protective equipment (PPE) was reported in many countries. Smart healthcare can be provided by the IoT, which is a term that refers to remote real-time health monitoring. Effective remote health care monitoring systems that can be provided through IoT will ensure safety to the health personnel and will inhibit the overwhelming of the health facilities. Meaning that patients need not come to

10 Mamta Agiwal, Abhishek Roy, and Navrati Saxena, 'Next Generation 5G Wireless Networks: A Comprehensive Survey', IEEE Communications Surveys & Tutorials 18, no. 3, 2016. pp. 1617–55.extremely low latency, manifold increase in base station capacity, and signi-cant improvement in users' perceived quality of service (QoS

the hospital, but rather could be treated at home via virtual consultations and medicine delivery using drones. Hospitals often use IoT systems to carry out inventory management for medical instruments and pharmaceuticals. With a smart healthcare system, the existence of any potential epidemic could also be detected at an early stage, because new cases will be registered automatically on the central database. Globally, experts would have access to the database, through information sharing and counselling, the diseases will be kept under control before spreading further. Also, through a smart healthcare system, the right information will be disseminated directly to the individuals be it in the urban or rural areas, thereby blocking any sources of fake news.

Smart Farming

Recently, farming has been disrupted as many farmers cannot travel during the COVID-19 lockdown. Some of the farming essentials cannot be received, food supply cut, and markets see intermittent patronage. There were reports of panic buying which was as a result of fear of the unknown and as the demand is high, the price of primary consumables such as toilet rolls, sanitizers, and foodstuff goes high. These could have been prevented through IoT. It is known that automation in farming boosts efficiency. The farming could be done using advanced technology. Remotely, farmers can monitor the real-time situation of their farms and make informed decisions. Farm activities such as ploughing, harrowing, planting, weeding, pest control, and harvesting can be done through smart farming. Anomalies in crops can be detected and eliminated without losing the entire crop. Smart farming can also be used to monitor the general health status and feeding order of individuals or groups of animals. Using smart vehicles, farm products can then be transported to the food processing industries, markets, and to consumers' destinations. Issues of panic buying will not have arisen if there were continuity in the delivery of food and essentials to consumers' doorsteps. Also, IoT can play a vital role in ensuring food security.

Smart Industries

In industries where jobs are performed by humans and that jobs require skilled labor, industries often face slow production until the personnel are properly trained and got used to the job. Also, in a production chain where the line of production is a sequence, any delay at one stage caused by a human error will affect the successive stages. To ensure continuity, better quality, precision, and large-scale production, automation through IoT should be implemented. A large number of industries are already semi or fully automated. Incorporating IoT in industries means having more sensors and electronic devices that will process, control, and supervise the production processes. The system can detect and rectify faults along the production line. IoT will not only ensure continuity of production during the crisis but will ensure large scale production at a relatively lower cost.

Smart Meetings

During the COVID-19 pandemic, many schools and colleges have resorted to virtual classes. Commercial platforms such as Zoom, Skype, and Google are frequently being used for virtual meetings. Students receive classes and get to interact with the teachers

and receive feedback online. Continuous assessments and exams are all conducted online. To some level, even laboratory classes are taught online. Harvard[11] and Cambridge[12] have announced that course instructions will be delivered online for the 2020/2021 academic session. This is to ensure the safety of both the staff and students. Before now, there are already distance learning programs run by some colleges. Governments and organisations typically United Nations (UN), World Health Organisations (WHO), European Union (EU), African Union (AU) use virtual meetings to deliberate on important issues. It can be concluded that in years to come, there is a strong possibility of virtual meetings and classes replacing the conventional way of gatherings. Of course, this could easily be achieved with IoT connecting anything anywhere anytime.

Smart Business

With our day to day activities turning to social media, billions of people have active social media accounts such as Facebook, WhatsApp, Twitter, Instagram, and WeChat. Individual daily usage of these platforms ranges from few minutes to hours. Using that to their advantage, businesses have turned to woo customers online. According to Facebook, more than 140 million businesses use their app every month[13], that is, a huge revenue is being generated by Facebook through these businesses. Businesses use those platforms to advertise and sell their products. The advertisement can be done through internet influencers and celebrities or through direct pop-up ads. Through the use of IoT, small, medium, and large businesses can survive during and after the pandemic. And, it is expected that the online market will continue to attract more revenue in years to come.

IV. Conclusion

As the world is battling COVID-19, many lives are being lost. COVID-19 has affected our daily lives and changed the world forever. It has caused governments to impose partial or complete lockdown, issue social distancing guidelines, and compulsory use of facial masks. Travel bans were also imposed. Many businesses have recorded losses as a result staff has been retrenched. It will take some time to mitigate the negative impacts it has caused. During the pandemic, virus carriers can be traced using IoT, food and essentials delivery can be done easily, health can be monitored remotely, business and related transactions can be done online, class instructions can be delivered online and government officials can have virtual meetings. It has been shown that by effectively using IoT, the effects of COVID-19 will be mitigated. Activities could be done much faster, easier, and more convenient than before.

11 'Harvard Goes Online, Tuition Costs Unchanged | Fox Business', accessed 9 July 2020, https://www.foxbusiness.com/lifestyle/harvard-online-learning-school-year."

12 Stephen Castle, 'Cambridge University Will Hold Its Lectures Online Next Year', The New York Times, 19 May 2020, sec. World, https://www.nytimes.com/2020/05/19/world/europe/cambridge-university-coronavirus.html."

13 'Company Info', About Facebook (blog), accessed 9 July 2020, https://about.fb.com/company-info/."

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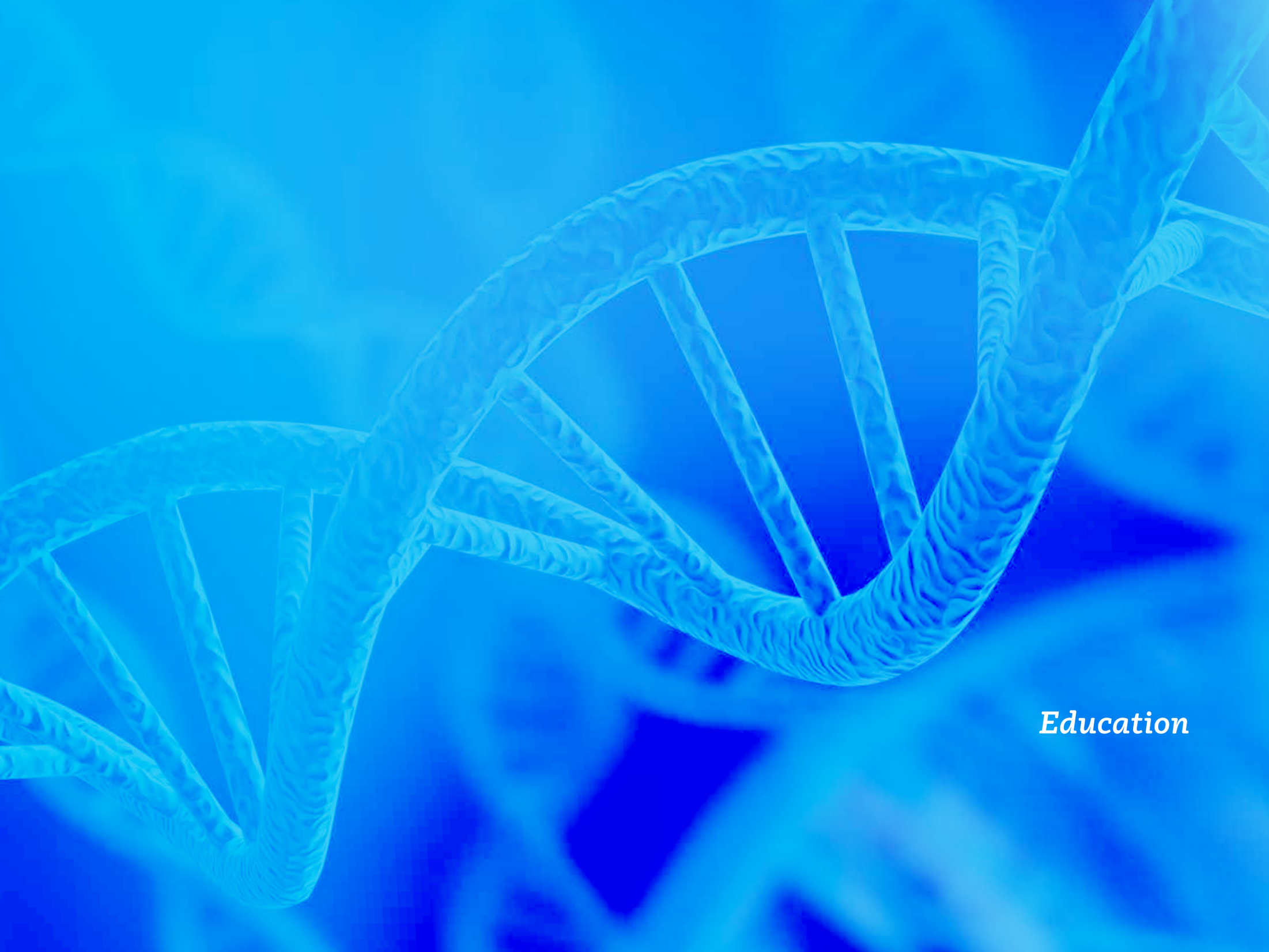

Education

The Effect of Lockdown Caused by COVID-19 Pandemic on Postgraduate Students of Natural and Applied Sciences at Turkish Universities

Abir Nasir* Muhammed Assaf* Firas Ibrahim*

Abstract

Today, the world faces one of the most destructive diseases that threaten human life, which is called COVID-19. This ongoing global pandemic led governments around the world to make a quick decision for starting lockdown and quarantine to curb the spread of COVID-19. The higher education sector is one of the most affected sectors because most of the universities worldwide suspended their academic activities; their works have been limited to online learning, and most scientific events, including national and international conferences, symposiums, workshops, and training programs have been canceled or postponed.

Özet

Bugün insan hayatını tehdit eden en yıkıcı hastalıklardan biri olan COVID-19 ile karşı karşıyayız. Bu devam eden küresel salgın, dünya genelinde devletlerin COVID-19'un yayılmasını engellemek için karantina ve sokağa çıkma yasağı başlatma konusunda hızlı bir karar almaya yönlendirmiştir. Yüksek Öğretim sektörü en çok etkilenen sektörlerden biridir çünkü dünya çapındaki üniversitelerin çoğu akademik faaliyetlerini askıya almış ve çalışmaları uzaktan eğitim ile sınırlılandırmıştır. Ulusal ve uluslararası konferanslar, sempozyumlar, çalıştaylar ve eğitim kursları dahil olmak üzere çoğu bilimsel etkinlikler iptal edilmiş

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The master's and doctoral students from different science fields encounter the most difficult situation because unlike the students of social sciences; they need to conduct their experiments at the laboratories. Therefore, most of them had to freeze their registrations or suspend their experiments. And in some cases of scholarship students had to deal with the reduction or even cancelation of their scholarships. The results of this research showed that the shift to online learning was ineffective, but it may be suitable for theoretical lessons during this emergency period. Also, the universities have to improve their online learning platforms and facilitate students' attendance to the online lessons by providing them digital devices and free access to the internet. On the other hand, the lockdown period was useful for some students. They found an efficient time to write up their theses, reading research, and publishing articles.

Keywords: *Coronavirus, COVID-19, Pandemic, Postgraduate Student, Scientific Sectors*

Farklı bilim alanlarından yüksek lisans ve doktora öğrencileri sosyal bilimler öğrencilerinin aksine deneylerini laboratuvarlarda yapmaları gerektiğinden zor durumla karşılaşmışlar. Bu öğrencilerin çoğu kayıtlarını dondurmak veya deneylerini askıya almak zorunda kalmıştır. ayrıca bazı durumlarda burslu öğrenciler burslarının azaltılması ve hatta iptal edilmesi söz konusu oldu. Sonuç olarak bu süreç, uzaktan eğitime geçişin başarısız olduğunu ancak böylesi bir acil durumda teorik dersler için uygun olabildiğini bizlere göstermiştir. Ayrıca üniversiteler uzaktan eğitim platformlarını geliştirmesi ve öğrencilerin çevrimiçi derslere katılımını dijital cihazları ve internete ücretsiz erişimi sağlayarak kolaylaştırması gerekmektedir. Diğer taraftan, karantina süresi bazı öğrenciler için faydalı olmuştur. Tezlerini yazmak, araştırmaları okumak ve makaleleri yayınlamak için verimli bir zaman bulmuşlardır.

Anahtar kelimeler: *COVID-19, Korona Virus, Lisansüstü Öğrenci, Pandemi, Fen Bilimler*

*

I. Introduction

Nowadays, the world faces one of the most destructive diseases which threaten human life, which is called COVID-19. It is caused by a novel coronavirus (SARS-CoV-2) of probable zoonotic origin. COVID-19 arose in December 2019 in Wuhan, China, and pervaded everywhere around the world as a lethal pandemic.[1] This ongoing global pandemic led governments around the world to make a quick decision for starting lockdown and quarantine to curb the spread of the pandemic. Furthermore, this pandemic suspended most of the human activities worldwide and negatively affected most of our life sectors such as the health, economy, and education sectors.[2]

The higher education sector is one of the most affected sectors because most universities worldwide suspended their academic activities, and their works were limited

1 Jie Li et al., "Game Consumption and the 2019 Novel Coronavirus." The Lancet Infectious Diseases 20, no. 3. 2020.

2 Andria Pragholapati, "COVID-19 Impact on Students,". 2020.

to online learning.[3] The scientific communities have been negatively affected by the COVID-19 pandemic; which didn't only impact the lab works in the universities, but also led to cancel or postpone most scientific events, including national and international conferences, symposiums, workshops, and training programs. These events were converted into virtual forms which led to creating many difficulties such as logistical issues, time zone differences for attendees, internet connectivity issues.[4]

The master's and doctoral students of natural and applied sciences disciplines encounter the most difficult situation because they need to conduct their experiments at the laboratories unlike other faculties like law, economy, arts, and social sciences. Unfortunately, their lab experiments were suspended which led those students to the critical situation.[5] So, these students were forced to wait for an undetermined time to start or resume their works.[6] The suspension of academic scheduled activities in universities led to substantial financial impacts due to the cancellation of visas, or travel tickets, losing allowance of accommodation at campuses, and the cancellation of funding or scholarships.[7] Additionally, the closure of universities and lockdown caused by the COVID-19 pandemic adversely affects the mental health of students; it may have caused psychological stress, tension, anxiety, or depression to many students [8].

The result of closing scientific workplaces and labs will extend the research time, and, in some cases, will lead to re-starting entire experiments, putting the experiments on hold, or downscaling them to a bare minimum. Also, maybe the scheduled work in the labs will be crowded after closure due to shifted works.[9] Additionally, the ongoing pandemic may adversely affect the funding of research, which is generally funded by governmental or private agencies, as the funding has been stopped or redirected to fund COVID-19 researches.[10] However, despite stopping academic activities in labs some master's and doctoral students invest their time during the closure in reading more articles related to their research for widening their knowledge, writing and analyzing data of their previous experiments, preparing their own articles, and publishing them.[11] In this study, we focused on the impact of COVID-19 on postgraduate students in the

3 Duygu Aydemir, and Nuriye N. Ulusu. "Commentary: Challenges for PhD Students during COVID-19 Pandemic: Turning Crisis into an Opportunity." Biochemistry and Molecular Biology Education, .2020.

4 Nadia Drake, "How the Coronavirus Is Hampering Science" Scientific American, last modified March 10, 2020, https://www.scientificamerican.com/article/how-the-coronavirus-is-hampering-science/.; MIT News Office, "Events Postponed or Canceled as MIT Responds to COVID-19.", MIT News | Massachusetts Institute of Technology, last modified March 9, 2020. https://news.mit.edu/2020/events-postponed-canceled-COVID-19-0309.

5 Duygu Aydemir, and Nuriye Nuray Ulusu. "Identifying and Solving Scientific Problems in the Medicine: Key to Become a Competent Scientist." Turkish Journal of Biochemistry 45, no. 2, 2020.

6 Maya M. Hammoud, Taylor Standiford, and J. Bryan Carmody. "Potential Implications of COVID-19 for the 2020-2021 Residency Application Cycle." JAMA 324, no. 1, 2020.

7 Supram Hosuru Subramanya, Bhupendra Lama, and Krishna Prasad Acharya. "Impact of COVID-19 Pandemic on the Scientific Community." Qatar Medical Journal 2020, no. 21, 2020.

8 Pragholapati, "COVID-19 Impact on Students."

9 Lei Su, "My Lab Is Closed to Me Because of the Coronavirus. Here's How I'm Planning to Stay Productive." Nature, (2020), accessed August 23, 2020.

10 Subramanya, Lama, and Acharya, "Impact of COVID-19 Pandemic on the Scientific Community."

11 Aydemir and Ulusu, "Commentary: Challenges for PhD Students during COVID-19 Pandemic: Turning Crisis into an Opportunity."

fields of natural and applied sciences at Turkish universities; how it affects the research work in labs, their academic productivity, scholarship, and funding.

II. Methodology

The research has been carried out at Turkish universities in 2020 between June and August. A literature review was conducted using available reports and previous articles to set up the questionnaire's main themes and questions. This research is based on an empirical approach investigating the impact of closure caused by the governmental arrangements to curb the spread of the COVID-19 pandemic on the conducting research of postgraduate students and shift to online learning. Both qualitative and quantitative data were collected from master's and doctoral students of natural and applied sciences in Turkish universities via evaluative questionnaires and semi-structured interviews with academics who work at Turkish universities.

Online questionnaire: the questionnaire was developed by the research team and was tested through a pilot survey of 10 respondents to collect feedback for further improvement and question form adjustment, and informed consent was got from the participants. The questionnaire was designed using the Google Forms tool; and the questions have been written in three languages (Turkish, Arabic, and English) that helped students from different nationalities to fill in the questionnaire. After that, the final version was distributed online through WhatsApp groups and other pages of social media. The questionnaire contains 23 variables concerning the impact of shifting to online learning and lockdown on scholarship, labs work, and other scientific activities. In total, there were 110 enrolled respondents of more than 50000 postgraduate students from different science departments at 23 Turkish universities.

Online Key informant interviews: Eight semi-structured key informant interviews were carried out through Zoom application with academics who work as supervisors on postgraduate students at Turkish universities. Before conducting the interviews, they were scheduled for participants and the researchers explained the study objectives and procedures to eligible participants. Additionally, the informed consent and the approval for a voice recording of participants were taken before the beginning of the interview with conditions to maintain privacy and not share personal information. Every interview lasted for 45 minutes and was carried out in Turkish, then translated and transcribed into English. The questions of interviews focused on the main three points:

- The effectiveness of the online learning process and the difficulties encountered by graduate students in the lesson stage.
- The effect of the lockdown caused by the COVID-19 pandemic on the graduate students in the research stage in the applied science departments.
- Recommendations regarding the difficulties faced by students in light of the current COVID-19 pandemic.

Data analysis: The qualitative data (from interviews) have been analyzed thematically, and the quantitative data (from the questionnaire) have been analyzed by using the SPSS v.25 application for discussing the relationship between the different variable factors. Additionally, significant differences between all variables were identified by using the Chi-square test. Moreover, we excluded all samples of the survey which are not completed.

III. Results and Discussions

In this study, 110 postgraduate students who study in different science fields have enrolled. Most of them (65%) are Turkish students and others from different nationalities. The proportion of participant doctoral students was 38% and the proportion of students at the thesis stage was 65% (Table-1).

Table 1. Summary of participant students.

Participant students	Study	Nationality		Gender		Study stage	
		Turkish	others	Female	Male	Lessons	Thesis
Master	68	44	24	34	34	30	38
Doctorate	42	29	13	16	26	8	34
Total	110	73	37	50	60	38	72

- The effectiveness of the online learning process and the difficulties encountered by graduate students in the lesson stage.

By practicing online learning for postgraduate students in the coursework stage, the participants generally asserted that it was an ineffective and unsuccessful method and didn't fulfill the role that traditional learning does, especially in the sciences fields, as most of the lessons need practical applications to clarify the theoretical ideas.

"In theoretical disciplines such as law or literature, perhaps we can say that online education can be successful, but for the faculty of sciences such as chemistry or biology fields or even in different engineering departments, we cannot ever say that online education was successful because education in these colleges depends mainly on the practical lessons", as one of the participants said.

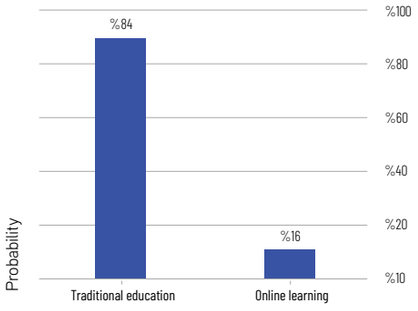

Figure 1. Preferred method of learning.

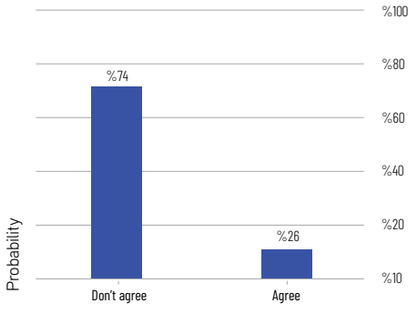

Figure 2. Successful of online learning experience.

The participants agreed that many difficulties faced the postgraduate students in the online learning process. These difficulties were limited by the weakness of the internet in most cases, the lack of access to the internet especially for students who live in the countryside, and the lack of computers and other devices, such as tablets, that help students to access the internet.

"In one lesson for Master students program at the Faculty of Sciences, 12 out of 26 students entered the program! Because of the weakness of the Internet often, and some of the students don't have computers", as one of the participants said.

In addition, among the difficulties were the weakness of the university's electronic platform and the lack of skills of students and professors in using online education programs such as Zoom and other online meeting Apps, because they have recently started using it.

Also, one of the effects was on some scholarship students who had to extend their education time, forced the reduction of their scholarships, and others lost it completely because of different reasons related to the lockdown. Furthermore, some students may suffer from congestion at home, also may need a private room or a private computer and that is not available for most families especially if there is more than one student at home and everyone receive online education.

As one of the participants said:

"The face-to-face traditional lesson is completely different from the online lesson. The traditional lesson involves direct communication and eye connection, in which the teacher knows how well the student understands from his facial expressions. In addition to that, in online education, the students may prefer to avoid showing their images or may forgo asking about any idea they didn't understand"

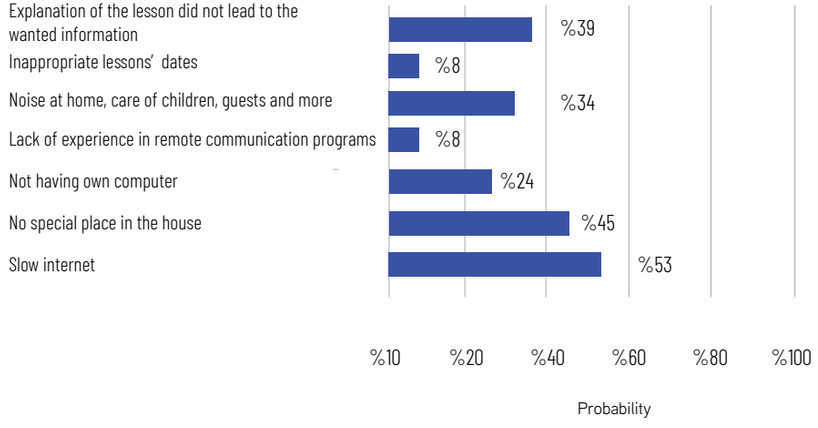

Figure 3. Difficulties faced during the online education process.

Some of The students were evaluated by homework and some of them by projects. Most of the participants assured that the evaluation process could not be considered fair at all due to the absence of some students from the lessons. Some of them considered it was fair, because they divided the mark within learning stages, including attendance of the lesson, assessment of their homework, short quizzes after lessons, and the final graduation of their projects.

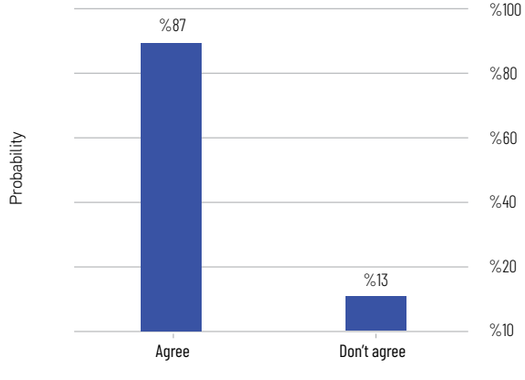

Figure 4. Using the university platform easily.

Finally, despite the participants' agreement that the online learning process was not successful, there were some benefits returned to students in this process. Including, the student was able to attend his lessons from home without the need to go to university, which helped him to save the costs of transportation, university accommoda-

tion, and a lot of other material costs. In addition to that, students learned to search for information themselves and to find the sources of knowledge that help them to do their homework and prepare their projects. Furthermore, the online learning method provides the possibility of recording lessons, which allows the students to attend the lessons many times and follow them at any time.

-The effect of the lockdown caused by the COVID-19 pandemic on the graduate students in the research stage in the applied science departments

Participants agreed that the lockdown of universities caused by COVID-19 greatly affected the research of postgraduate students. Mainly, the laboratory work was disrupted due to the inability to come to the laboratory, hence contributed to the failure to submit the semi-annual reports of research. Some students needed to extend the research period and some were forced to delay the discussion of the thesis. Furthermore, the lockdown disrupted the sample collection process in the research of biology, agriculture, and biodiversity disciplines for many students, which in turn affected adversely on the continuity and the duration of the research.

"We weren't able to pick the plant samples which are necessary for the experiment of one of my students. The suitable time for collecting plant material was in May, and in that month there was lockdown, so we have to wait one year for the next season", as one of the participants said.

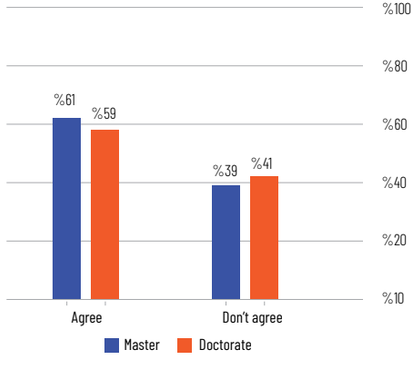

Figure 5. Need to extend the study period.

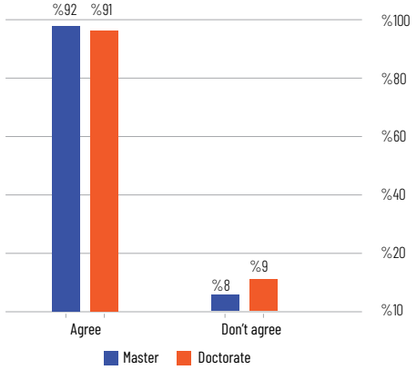

Figure 6. The effect of lockdown on work lab.

One of the participants, who lives and works in the same city, indicated in his interview that he found in the empty laboratory an opportunity to complete many kind of research in a short period. This was as a recommendation for the students who can benefit from such an opportunity to do researches and publish articles.

Most of the sciences activities such as conferences have been suspended during the lockdown period, this adversely affects the postgraduate who was supposed to participate in them. Despite the launch of online conferences, the participants agreed that

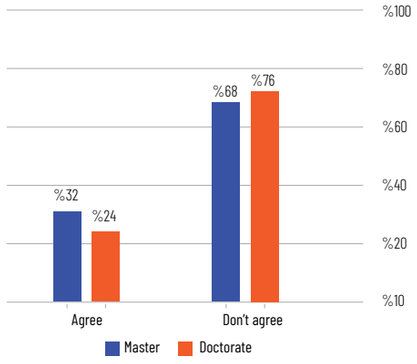

Figure 7. The ability to go to university during lockdown.

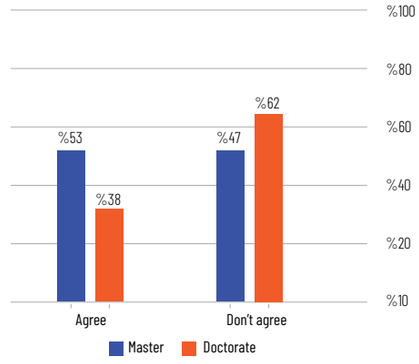

Figure 8. The ability to continue experiments during the lockdown.

these are till now unsuccessful by comparing to traditional conferences; because the online conferences can't provide the same opportunity to gain new information or to meet other researchers. Online conferences are considered a new experience, some researchers have a preconception about them.

"I have not participated in any teleconference, and don't think about that! Because I think it is an unsuccessful method", as one of the participants said.

Furthermore, some students have suspended their studies to avoid losing their university registration; this led to losing more time for the student in their current research work.

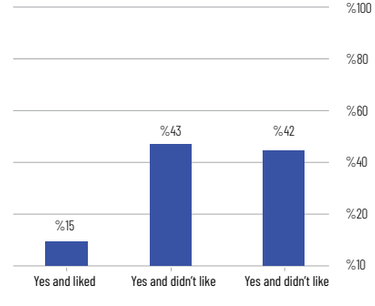

Figure 9. Attendance to or participation in an online conference.

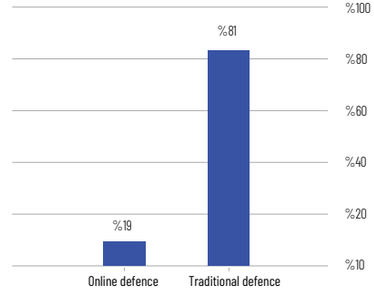

Figure 10. The preferred way for thesis defense.

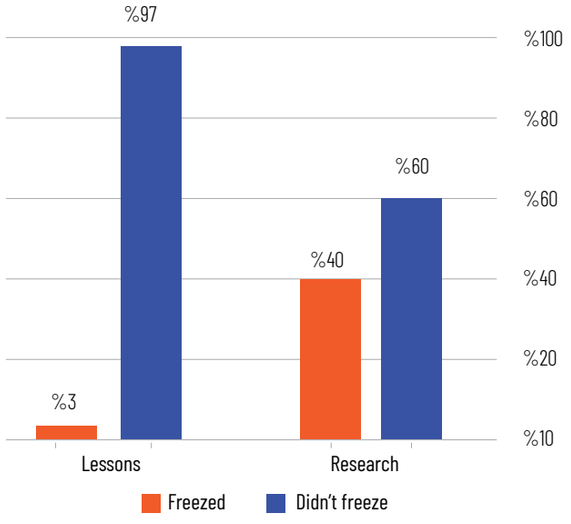

Figure 11. The proportion of postgraduate students who freezed their university registration.

Finally, Most of the participants in the research confirmed the importance of benefiting from the lockdown period for the postgraduate students. The students were able to complete writing their theses while staying at home, read many articles related to their topics, prepare and publish articles, or even attend online conferences.

-Recommendations regarding the difficulties which students have faced during the COVID-19 pandemic

According to the ongoing situation of the COVID-19 pandemic and increasing in the number of infected cases daily; some participants suggested continuing closure of universities in order to preserve the health of students, as one of the participants says:

"The rate of 40% of online learning indeed isn't sufficient, but it should be 100%. Although it is ineffective, we are adhered to shift to it at the current, in order to preserve the health of students and teachers."

Other participants suggested that online learning should be resuming for theoretical disciplines, while applied sciences lessons should be carried out face to face, also the continuation of online learning should be related to the developments of the pandemic, with adhering to the directives proposed by the specialists, in order to preserve the public health of students.

"We can change decisions according to the status of the COVID-19 infection. If the number of infected cases increases greatly, we can stop face-to-face learning and depend only on the online learning method", as one of the participants says.

Furthermore, the participants suggested providing postgraduate students with computers or smart tablets, and free internet access, also, improving the digital learning platform with advanced settings, and providing efficient training for students and academics to use it professionally. Besides, some of the participants suggested training academics to prepare the lessons as videos and upload them to the platform of the university.

Moreover, another participant suggested that the lessons and work lab should be compensated during the holiday of summer according to the current situation of the COVID-19 pandemic and the governmental arrangements; he also suggested resuming the work lab with taking the precaution arrangements whatever the current situation of COVID-19 and the lockdown, because the students can easily maintain social distancing in the labs due to their small number.

IV. Conclusions

Higher education is one of the most important sectors, which was undergone a sudden forced shift towards virtual learning methods due to the lockdown and governmental quarantine arrangements caused by the COVID-19 pandemic. This shift to online learning is mostly has affected adversely. This study focused on the effect of COVID-19 on postgraduate students in different science fields. It shows clearly that some participants agreed in several aspects despite the difference in their departments. The lockdown led to a delay in the planned time table for the experiments of all students, as a result of their effect on lab work, collecting samples, completing experiments, or submitting reports and thesis; therefore, freezing the registration of students, or suspension their research was one of the alternatives solutions. Additionally, the physical conferences were also suspended or canceled due to the lockdown and shift to online conferences at the current period. The results showed the online conferences were an unsuccessful method and didn't play an effective role for both students and academics compared with physical conferences.

Furthermore, the scholarship students have been affected adversely due to lockdown; it was noticed that they lost some time of their scholarship, and their graduation has been suspended and delayed, also, most of them had to extend their study period, which means decreasing in the funding of their scholarship. Moreover, some of the participants got some benefits during the lockdown of the COVID-19 pandemic such as reading articles, attending online conferences, publishing articles, and writing in their theses.

Finally, although several months have passed since the forced shift to online learning, many participants still consider it as an unsuccessful method compared to face-to-face learning; whereas some of the participants thought it a partially suitable method for this

emergency period. Also, there still is a glimmer hopes to succeed the online learning at least for theoretical lessons, and the need to develop virtual methods for the practical lessons of applied sciences such as in silico methods.

Acknowledgement
We would like to thank Dr. Abdulkarem Lakmes for his help in the data analysis of the research.

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Education During and After the COVID-19 Pandemic: Anatomy Education

Gkionoul Nteli Chatzioglou*

Abstract

Anatomy education is the cornerstone of medical and health education traditionally taught by dissection and didactic courses. However, due to today's COVID-19 pandemic, technology-based education is becoming increasingly important. This article examines the advantages and disadvantages of educational methods used from past to present. It is seen that computer-based education methods (three-dimensional part printing-3B, virtual reality glasses -Virtual Reality-VR, augmented reality - Augmented Reality - AR, anatomy, magic mirrors - Magic Mirrors, videos, social media, online sources) come to the

Özet

Anatomi eğitimi geleneksel olarak diseksiyon ve didaktik derslerle öğretilen tıp ve sağlık eğitiminin temel taşını oluşturmaktadır. Ancak günümüzde yaşanan COVID-19 pandemisi sebebiyle teknolojiye dayalı eğitim giderek daha büyük önem kazanmaktadır. Bu makalede geçmişten günümüze kadar kullanılan eğitim yöntemlerinin avantajları ve dezavantajları incelenmiştir. Pandemi boyunca ve pandemi sonrası bilgisayara dayalı eğitim yöntemlerinin (üç boyutlu parça basımı-3B, sanal gerçeklik gözlükleri -Virtual Reality-VR, arttırılmış gerçeklik - Augmented Reality - AR, anatomaj, sihirli aynalar - Magic Mirrors,

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forefront during and after the pandemic. Innovative and technological applications emphasized will be a guide for anatomists to determine the most appropriate method in the field of clinical, academic and education.

Keywords: *Anatomy Education, Innovations, Technology, COVID-19, Pandemic*

videolar, sosyal media, çevrimiçi kaynaklar) ön plana çıktığı görülmektedir. Vurgulanan yenilikçi ve teknolojik uygulamalar; anatomistlerin klinik, akademik ve eğitim alanında en uygun yöntemi belirlemelerinde bir kılavuz olacaktır.

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I. Introduction

Today, anatomy education has gained an important place both in the medical education curriculum and in all branches related to the health field. The ongoing coronavirus (COVID-19) pandemic has had a great impact on anatomy education (practice and theoretical education).[1]

The anatomy education before the pandemic was carried out as a practical course on cadavers, especially in medical faculties, or with cadaver dissection practices.[2] After the pandemic and during the pandemic, it was not possible to conduct applied anatomy education with cadavers.

Anatomy education with cadaver dissection from the 17th century to the present day is known as the 'gold standard' learning and teaching technique.[3] Scientific studies support the fact that it is useful in reinforcing the information learned in theory, such as three-dimensional perception of structures by cadaver dissection method and examination of their neighborhoods.[4] However, the necessity to maintain social distancing with The COVID-19 pandemic does not make one-on-one education with cadavers possible. For this reason, anatomists and academicians have evaluated alternative education methods. Although there are many anatomists who think that there is no education method that can replace cadaver dissection education, many kinds of technology-based learning techniques are actively used today.

1 Mohamed Estai and Bunt Stuart, "Best teaching practices in anatomy education: A critical review ", Annals of Anatomy-Anatomischer Anzeiger, 208 (2016), pp.151-152.

2 Esther M Bergman, "Discussing dissection in anatomy education", Perspectives on medical education, 4:5 (2015), p.211.

3 Sabine Hildebrandt, "Lessons to be learned from the history of anatomical teaching in the United States: The example of the University of Michigan", Anatomical sciences education, 3:4 (2010), pp.202-204.

4 M. Ashraf Aziz et al., "The human cadaver in the age of biomedical informatics", The Anatomical Record: An Official Publication of the American Association of Anatomists, 269:1 (2002), p.25.

The use of technology in the pandemic process has become more popular by students and has been preferred more because it increases the interaction between both students and academicians. In addition, many studies conducted[5] in[6] the world have shown that students are prone and interested in using technologies such as augmented reality and virtual reality. These technological possibilities enabled the student to observe anatomical structures in three dimensions and accelerate learning by evaluating neighboring structures. In general, the opportunities offered by technology in the field of education also emerge as an alternative education model in anatomy education. Brenner et al. presented 6 different learning techniques for anatomy education in[7] 2003: i) amphitheater courses given with presentations, ii) cadaver dissection, iii) process (dissected cadaver parts), iv) use of different models, v) computer-based education (VR, AR and 3D) and vi) live anatomy education and radiological anatomy education.

II. Discussion

Cadaver Dissection

For almost 400 years, anatomy education has been suggested to be the best learning method by dissecting on cadavers.[8]

There are undoubtedly many advantages of dissecting on human cadavers; deep learning enables the gaining of experiences such as preparing the student for the clinic, preparing him/her to face the dead, patient privacy and approach to the patient, improving hand skills and establishing the relationship between the symptoms of patients and pathophysiology. However, it teaches the importance of teamwork and coping with stress.[9]

Many anatomists still think that anatomy education with cadaver dissection is the ideal learning method today. According to[10] the results of Patel and Moxham (2006),69% of the academicians stated that they chose the dissection method and subsequently, the more appropriate learning method was the process method.

In the study[11] conducted by Stephan et al. in 2019, the results of the analysis on the contribution of cadaver dissection to modern anatomy pedagogy were found to be

5 Bernard J Moxham and Plaisant Odile, "Perception of medical students towards the clinical relevance of anatomy", Clinical Anatomy: The Official Journal of the American Association of Clinical Anatomists and the British Association of Clinical Anatomists, 20:5 (2007), pp.560-561.

6 Claire France Smith and Mathias Haydn Socrates, "What impact does anatomy education have on clinical practice?", Clinical Anatomy, 24:1 (2011), pp.113-115.

7 Brenner E et al., "General educational objectives matched by the educational method of a dissection lab", Ann Anat, 185:173 (2003), p.229-230.

8 Samy A. Azer and Eizenberg Norm, "Do we need dissection in an integrated problem-based learning medical course? Perceptions of first- and second-year students", Surgical and Radiologic Anatomy, 29:2 (2007), pp.173-175.

9 Birgit H. Fruhstorfer et al., "The use of plastinated prosections for teaching anatomy - the view of medical students on the value of this learning resource," Clinical Anatomy, 24:2 (2011), pp.246-248.

10 K. M. Patel and Bernard J. Moxham, "Attitudes of professional anatomists to curricular change", Clinical anatomy, 19:2 (2006), p.137.

11 Georgina C. Stephens, Charlotte E. Rees, and Michelle D. Lazarus, "How does donor dissection influence medical students' perceptions of ethics? A cross sectional and longitudinal qualitative study", Anatomical sciences

very important. In the study, it was revealed that there is a strong synergy between anatomy education and ethical perceptions of students and the potential of anatomy to be integrated into medical ethics education. Participants in this study showed that 5 main themes related to cadaver dissection and medical ethics of donated organs: reputation, usefulness, volunteering, justification for the need for dissection, and the dilemma between objectification and personalization were better perceived. Therefore, anatomy education with cadaver dissection teaches students respect and importance for simultaneous cadaver as well as being effective and useful.

However, with The COVID-19 pandemic, the obligation to maintain physical distance does not make one-on-one education with cadavers possible. For this reason, anatomists and academicians had to evaluate alternative education methods.

On the other hand, whether it is possible to dissect a whole body by students has been discussed in scientific studies. Especially considering the low cadaver donation in our country and the high cost of obtaining a whole cadaver from abroad, it is seen that the current education is not possible by every institution.[12] This situation leads to inequality in the educational opportunities offered between institutions.

Prosection

The prosection is the dissection of cadavers or part of a cadaver by an experienced anatomist in order to demonstrate for students anatomic structure. During the Middle Ages and early Renaissance, anatomy education was considered very popular by the process method.[13] Before the COVID-19 pandemic, this method was preferred in most universities in our country due to the limited number of cadavers and low cadaver donations. When the effect of cadaver dissection education method and process method education was investigated, it was shown that there was no significant difference between the two education methods, and they contributed to almost equal learning.[14]

Plastination

The plastination method was first developed by Gunther von Hagens in 1977. Today, it has been one of the best techniques developed for the protection of the dead human body.[15]

education, 12:4 (2019), pp.332-340.

12 İlke Ali Gürses, Osman Coşkun and Adnan Öztürk ", Current status of cadaver sources in Turkey and a wake up call for Turkish anatomists", Anatomical sciences education, 11:2 (2018), pp.155-160.

13 U. Enke, „Historische Anmerkungen zu Anatomie und anatomischem Unterricht an den hessischen Universitatten von 16. Bis zum 18. Jahrhundert", Hess. Arztebl, 122 (2005), pp. 820.

14 Vernon L. Yeager, "Learning Gross Anatomy: Dissection and Prosection", Clinical Anatomy, 9 (1996), p.58.

15 Gunther von Hagens et al., "The current potential of plastination", Anatomy and embryology, 175:4 (1987), 412. doi:10.1007/BF00309677

Plastination samples are frequently preferred by anatomists because they are odorless, easy to provide and easy to use.[16] Studies have shown that[17] [18] plastic samples are considered useful by students and can meet their needs at various levels.

Although anatomy education with placentation samples has many advantages, it also has many disadvantages. For example, although dissected cadavers can be preserved by plastination method, there are many disadvantages such as tissue loss, discoloration and shrinkage.

In addition, the use of chemicals that will be harmful to human health during the preparation of plasticized samples creates anxiety in terms of human health safety. Additionally, although variants of living humans can be seen in plastinated samples, there is no chance of discovering or dissecting new variants. Therefore, the student can only examine variations (if any) in the plasticized sample. Another important disadvantage is the obligation for students to gather physically in a common area, as in both the cadaver dissection method and the process method. However, it seems that this is not possible due to today's pandemic.

Live Anatomy

Today and in the past, artists have always shown great interest in the living body.[19] Live anatomy education has many advantages over cadavers. With live anatomy education, the student can palpate the model patient and have the chance to evaluate with occlusion and percussion methods. It can also be painted to represent the body, muscles or organs of the person being used.[20] Although anatomy education is possible with the staining method, educational experience similar to this method has not been defined in the literature in our country.

Computer-Based Education

Although a computer-based education model was used before the COVID-19 pandemic in our country, it was not very common. However, due to the ongoing pandemic process, computer-based education opportunities are evaluated by all institutions and trainers. Computer based education models used in anatomy education in the world:

- 3D part printing

16 D. Gareth Jones and Maja I. Whitaker, "Engaging with plastination and the Body Worlds phenomenon: A cultural and intellectual challenge for anatomists", Clinical anatomy 22:6 (2009), 772.

17 Fruhstorfer, Birgit H. et al., "The use of plastinated prosections for teaching anatomy - the view of medical students on the value of this learning resource." Clinical Anatomy 24.2 (2011): 246-252.

18 Rafael M. Latorre et al, "How useful is plastination in learning anatomy?", Journal of Veterinary Medical Education, 34:2 (2007), p.174.

19 Michael J. Griksaitis, Marina A. Sawdon, and Gabrielle M. Finn. "Ultrasound and cadaveric prosections as methods for teaching cardiac anatomy: A comparative study. " Anatomical sciences education 5:1 (2012), 20-26.

20 Paul G. McMenamin, "Body painting as a tool in clinical anatomy teaching", Anatomical sciences education, 1:4 (2008), 140.

- Virtual Reality (VR)
- Augmented Reality (AR)
- Anatomy
- Magic Mirrors
- Videos
- Social media (Youtube, Twitter, Facebook)

Three-Dimensional Part Printing (3d)

3D printing (3D) digital models can be made of various materials such as plastic, nylon plastic (polyamide), alumide, ceramic, wood, metal and carbon fiber filaments.[21]

Fasel et al. (2016) suggested[22] that 3D samples had a very good quantitative and excellent qualitative correlation with anatomical reality so that 3D could be included in a undergraduate anatomy curriculum.

Many researchers have compared the 3D group with other tools (e.g. Text, atlas, 2D images, examples of plastine) and most concluded that group 3D was more likely to receive higher scores[23].[24],[25]

Chytas et al. (2020) concluded that learning through[26] 3D is generally perceived as fun and effective; however, there is limited evidence of its educational effectiveness compared to the cadaver dissection method, so further scientific studies on the effectiveness of 3D in education are needed.

Virtual Reality (VR)

One of the most interesting aspects of virtual reality is that users can interact with the virtually created environment.[27] Although some studies have encouraged the use of VR, the structures[28] that VR focuses on can affect the results. Birbara et al. (2019) compared anatomy perceptions using[29] 3D cranium (skull) models and suggested that

21 İlknur Reisoğlu et al., "3D virtual learning environments in education: a meta-review", Asia Pacific Education Review, 18:1 (2017), 81.

22 Jean HD Fasel, et al., "Adapting anatomy teaching to surgical trends: a combination of classical dissection, medical imaging, and 3D printing technologies", Surgical and radiological anatomy, 38:3 (2016), 366.

23 Shi Chen, et al., "The role of three-dimensional printed models of skull in anatomy education: a randomized controlled trail", Scientific reports, 7:1 (2017), 10.

24 Monique Garas et al., "3D Printed specimens as a valuable tool in anatomy education: A pilot study", Annals of Anatomy-Anatomischer Anzeiger, 219 (2018), p.60.

25 Claire F. Smith et al., "Take away body parts! An investigation into the use of 3D printed anatomical models in undergraduate anatomy education", Anatomical sciences education, 11:1 (2018), p.49.

26 Dimitrios Chytas et al., "Three-dimensional printing in anatomy teaching: current evidence", Surgical and Radiologic Anatomy, 42 (2020), pp.839 840.

27 Santiago González Izard, Juan A. Juanes Méndez & Pablo Ruisoto Palomera, "Virtual Reality Educational Tool for Human Anatomy", Journal of medical systems, 41:5 (2017), p.76

28 Jingjie Zhao et al., "The effectiveness of virtual reality-based technology on anatomy teaching: a meta-analysis of randomized controlled studies", BMC Medical Education, 20 (2020), p.8.

29 Nicolette S Birbara, Claude Sammut, Nalini Pather, "Virtual reality in anatomy: a pilot study evaluating different delivery modalities", Anat Sci Educ, 13:4, p.449.

a desktop might be appropriate to provide VR resources. Interestingly, the authors emphasized that the more important factor was preliminary information.

Augmented Reality (AR)

Augmented reality is a next-generation 3D visualized technology that is defined as "interacting with both of them simultaneously by digitally placing virtual objects on physical objects in real space." Recently, its effect on anatomy education has been examined in scientific researches.[30], the most distinguishing feature[31] of AR is that the user can represent an anatomical model in three dimensions without losing his/her sense of environment.[32] One study showed that AR yielded better results than traditional presentation courses and dissection, although students preferred traditional methods.[33] In another study, it was observed that students using mobile AR had significantly higher scores than those using two-dimensional pictures, graphics and text ($p < 0.05$).[34] The results of the current research on AR in anatomy education are relatively limited. AR tools used in anatomy education: MagicMirrors and Anatomage Tables. Magic Mirrors are screen-based systems that allow users to discover anatomical structures in relation to their own bodies along with medical images. The total cost of the hardware components of magic mirrors is about €1000 (or $1138), which includes an imaging device, a computer, and a surveillance camera.[35]

Anatomage dissection platform (Anatomage Inc., San Jose, CA) is a virtual dissection platform used in anatomy education. Anatomy tables have been integrated into macroscopic anatomy courses in some countries and students' perceptions have been evaluated. In fact, according to the results obtained from some studies, Anatomy can replace radiological anatomy courses as well as cadaver dissection courses. Comparing the cost of Magic Mirrors and Anatomy, it is seen that the cost of the Anatomy table is quite high (80,000 €about 91,000 US Dollars). The reason is that it includes two combined high-resolution, life-size touch screens and a computer in a single enclosure. Bork et al. investigated the effect and efficiency of Magic Mirrors, Anatomy and theoretical courses on students.[36] In the study, volunteer participants were evaluated by performing a pre-test (theoretical post-course test) and then a post-test (Magic Mirrors, Anatomy and theoretical course) containing text and pictures. According to the results, it was noted that the participants of all three study groups scored higher than

30 Christian Moro et al., "The effectiveness of virtual and augmented reality in health sciences and medical anatomy." Anatomical sciences education 10:6 (2017), 549-559.

31 Bridget M. Kuehn, "Virtual and augmented reality put a twist on medical education", Jama 319:8 (2018), 756-758.

32 Katerina Bogomolova et al., "The effect of stereoscopic Augmented Reality visualization on learning anatomy and the modifying effect of visual spatial abilities: a double center randomized controlled trial", Anatomical Sciences Education, 13 (2019), p.559-567

33 Diana Coomes Peterson and Gregory SA Mlynarczyk, "Analysis of traditional versus three-dimensional augmented curriculum on anatomical learning outcome measures", Anatomical sciences education 9:6 (2016), 529-536.

34 Sevda Küçük, Samet Kapakin and Yüksel Göktaş, "Learning anatomy via mobile augmented reality: Effects on achievement and cognitive load", Anatomical sciences education 9:5 (2016), 411-421.

35 Felix Bork et al., "The benefits of an augmented reality magic mirror system for integrated radiology teaching in gross anatomy", Anatomical sciences education 12:6 (2019), 585-598.

36 Bork, "The benefits", 585-598.

the posttest. While the scores for all participants were 48.87% ± 13.17% in the pretest, they increased to 56.77% ± 17.17% in the posttest. The scores of the pre-test and post-test with picture and text content of all three participant groups were evaluated. It was observed that the students in the Magic Mirrors group had higher painting scores than the students in the other group (Anatomy and theoretical courses). In the pretest and posttests of the text contents, it was found that the students in the theoretical course group were more successful than the other groups. As a result, it is seen that the technological possibilities offered can be useful in anatomy education. In terms of cost, the use of Magic Mirrors stands out. Especially during and after the pandemic, these opportunities are provided by the Institutions and have the potential to be used by students and academic staff.

Video

In a study conducted in Ege University, Department of Anatomy, the opinions of students about learning and perception of videos used in[37] anatomy applied courses (Web-based Computer Supported Education Packages) were asked to interpret positively or negatively with open-ended expressions. The effects of videos on students are summarized below:

1. Ability of trainers to edit and revise videos at any time
2. Having the opportunity to work on the next subject
3. Opportunity to repeat the lessons
4. Preparing for practical exams as well as ensuring that the current knowledge is more memorable
5. Equal opportunities for all students

Students using Web-based Computer Aided Learning Packages have shown that videos help and meet their expectations.[38] The availability of this method during and after The COVID-19 pandemic has provided a great advantage.
Several studies on dissection videos showed that anatomy exam scores did not increase, on the contrary, they obtained lower results.[39]

Another study showed that students in the field of osteology scored higher than the traditional method with visual support (video) method.[40] Overall, students tend to the method of education with videos and report that this increases their learning satisfaction.[41]

37 Mehmet Asim Ozer, Figen Govsa and Ayse Hilal Bati, "Web-based teaching video packages on anatomical education", Surgical and Radiologic Anatomy 39: 11 (2017), 1253-1261.

38 Ozer et al., "Web-based teaching", 1253-1261.

39 Noelle A. Granger and Diane Calleson, "The impact of alternative dissection on student performance in a medical anatomy course: are dissection videos an effective substitute for actual dissection? ", Clinical Anatomy: The Official Journal of the American Association of Clinical Anatomists and the British Association of Clinical Anatomists 20: 3 (2007), 315-321.

40 Angela A Viswasom and Jobby Abraham, "Effectiveness of video demonstration over conventional methods in teaching osteology in anatomy", Journal of clinical and diagnostic research: JCDR, 11:2 (2017), 9-11

41 Mitchell B. Alameddine, Michael J. Englesbe and Seth A. Waits, "A video-based coaching intervention to improve surgical skill in four-year medical students", Journal of surgical education, 75:6 (2018), 1475-1479.

However, Langfield et al. (2018) stated that[42] anatomy videos alone did not improve students' learning outcomes, but instead created a tendency to passive learning. As a result, they suggested that videos should be used as active learning tools. Grosser et al. (2019) emphasized that the key to successful education using[43] videos is to strengthen the link between clinical and anatomical knowledge.

Social media (Youtube, Twitter, facebook)

Anatomists who gained popularity in social media anatomy education also developed Facebook pages to help students learn.[44]

Interestingly, Jaffar and Eladl's (2016) study showed that students who performed well on their Facebook pages participated in the discussions more deeply. Students who contributed with a single "like" or comment performed lower. The authors emphasized that Facebook could be an appropriate platform for engaging students in the context of education rather than a distraction, where performers engage more deeply.[45]

Another Facebook survey showed that 86.7% (254/300) of respondents' cadaver videos were not beneficial enough for viewers without cadaver experience (Rai et al., 2019).[46] It has been noted that a Twitter hashtag created by Hennessy et al. (2016) helps students learn and provides simple/easy and fast communication between students and educators using Twitter[47]. Students also actively use YouTube videos to learn anatomy, so their effectiveness was also examined.[48]

However, it is very important that photographs and videos of educators' cadaver or cadaver materials are processed in a precise (resolution sufficient) manner.[49] Nevertheless, many anatomists argue that the best way to learn and teach human anatomy is through cadaver dissection. However, people who want to learn anatomy and are outside of medical education (such as dentistry, nursing, health vocational schools)

42 Tracey Langfield, Kay Colthorpe, and Louise Ainscough, "Online instructional anatomy videos: Student usage, self-efficacy, and performance in upper limb regional anatomy assessment", Anatomical sciences education, 11:5 (2018), 461-470.

43 Johannes Grosser et al., "Acquiring clinical knowledge from an online video platform: A randomized controlled experiment on the relevance of integrating anatomical information and clinical practice", Anatomical Sciences Education, 12:5 (2019), 478-484.

44 William Pollock, and Paul M. Rea, "The Use of Social Media in Anatomical and Health Professional Education: A Systematic Review", Biomedical Visualization. Springer, Cham, (2019), 149-170.

45 Akram Abood Jaffar and Mohamed Ahmed Eladl, "Engagement patterns of high and low academic performers on facebook anatomy pages", Journal of medical education and curricular development, 3 (2016), JMECD-S36646.

46 Rabjot Rai et al., "Social media and cadaveric dissection: A survey study", Clinical Anatomy, 32:8 (2019), 1033-1041.

47 Catherine M Hennessy et al., "Social media and anatomy education: Using twitter to enhance the student learning experience in anatomy ". Anatomical sciences education, 9:6 (2016), 505-515.

48 Ayman G Mustafa et al., "Using YouTube to Learn Anatomy: Perspectives of Jordanian Medical Students ", BioMed Research International (2020).

49 Catherine M. Hennessy et al., "Social media guidelines for anatomists", Anatomical sciences education, 13:4 (2020), 527.

have limited access to such facilities, so social media has the ability to fill the large gap in education.[50]

Medical Imaging Techniques Based Education

The use of medical imaging techniques (CT, MRI, USG) in anatomy education provides the opportunity to visualize the structure and physiology of human anatomy in vivo as well as the follow-up of pathological processes. With the development of Computerized Tomography (CT), Magnetic Resonance Imaging (MRI) and Ultrasonography (USG), three-dimensional imaging of the human body has become possible.

As a result of the fact that technology has gained an important place in our lives and has continuously improved, imaging techniques have been asked to be integrated into the medical curriculum, especially in medical faculties. The only study on this subject in our country is in the Department of Anatomy of Faculty of Medicine of Gata University. According to the survey study, it was seen that the rate of participation in the recommendation that radiological anatomy courses should be in the medical education curriculum was 60% in the 2nd grade, 90% in the 5th grade and 95% in the 6th grade. The biggest advantage of this method, which is preferred by both students and instructors, is that it can be integrated even during the pandemic process and is sustainable with distance education.[51]

Education with Presentation

Since the 16th century, anatomy education has been integrated into the medical curriculum as theoretical and practical courses. In the studies conducted in 2000 and 2004, it was claimed that such an educational approach was ineffective, outdated and passive learning. Instead, the promising hybrid education model was proposed by Graham et al.[52]

Hybrid education model is an education model in which online teaching methods are integrated as well as the traditional face-to-face education model presented. With this teaching model, it has become especially attractive due to the availability of internet resources, including audio and video, in any subject. One of the most important features of this model is that it is not attendance-based teaching, but rather the potential to facilitate active learning and increase academic performance. It is understood that the Higher Education Institution rapidly prepared for the mixed education system during and after the pandemic.[53]

50 Rabjot Rai et al., "Social media and cadaveric dissection: A survey study", Clinical Anatomy, 32:8 (2019), 1033-1041.

51 İsmail Nadir Gülekon, "The place of radiological and clinical anatomy in anatomy education: Student opinions", Gazi Medical Journal, 28:3 (2017).

52 Charles R Graham, "Blended learning systems." The handbook of blended learning: Global perspectives, local designs, (2006), 3-21.

53 The decision on the teaching of courses through distance education with digital facilities was examined at the Meeting of the Executive Board of Higher Education dated 27.05.2020. YÖK (Higher Education Institute) has acknowledged that in accordance with Article 44/e of the Law No. 2547, courses in primary and secondary education programs can be given by distance education up to 40%, at least 10% of the courses in the first and second education programs, which are approved by the senates of the relevant higher education institutions before the start of the academic year, are strongly recommended to be given only by digital means and by distance education, that these courses to be given by distance education in formal education on the basis of each semester or whether they should be given simultaneously with the spread of the whole program will be given by higher education institutions and these courses to be given through digital opportunities and distance education as the Higher Education Council have been accepted by YÖK, where it is especially important to give a relatively greater place in the fall semester program of the 2020-2021 academic year.

III. Conclusion

As a result, the advantages and disadvantages of anatomy education methods used from past to present have been compiled. Although cadaver dissection is considered the best anatomy education method in applied anatomy education, it is unfortunately not effective in cases such as pandemic and natural disaster. Therefore, it will be very important to evaluate and investigate the new techniques presented for technology-based anatomy education in our country. In addition, with the use of new technologies compiled in the post-pandemic world, both academics and students will contribute to the Internationalization of Higher Education in Turkey.

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ISBN 978-975-17-4879-9