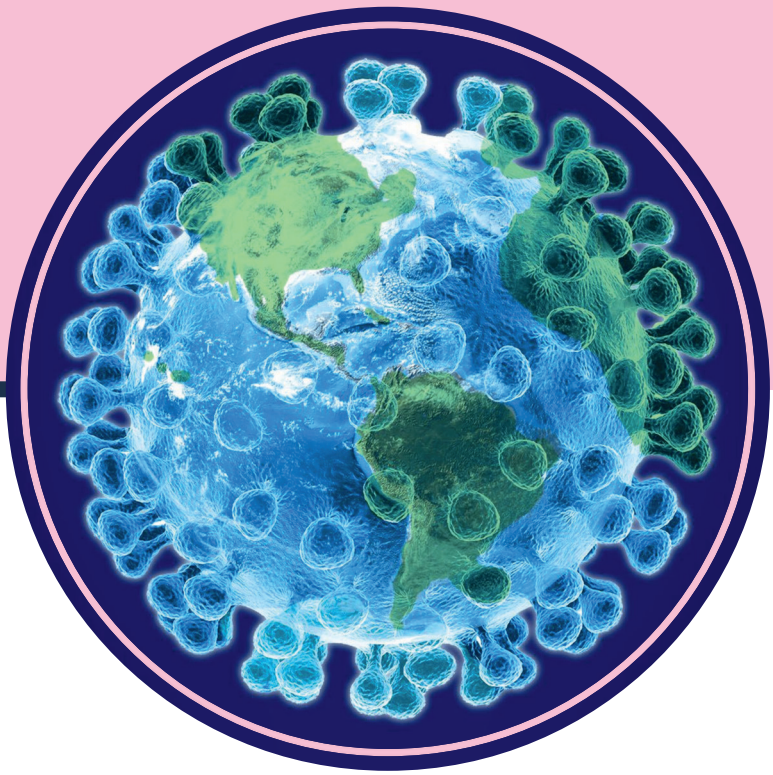
Coronavirus Disease (COVID-19)

Editors
Prof. Dr. Belgin SIRIKEN & Asst. Prof. Dr. Ayhan GULER



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PREFACE

In the historical process, there have been pandemic periods that affect the whole world from time to time. According to the definition of WHO (World Health Organization), a pandemic is considered to have started only when the following 3 conditions are met:

• The emergence of a disease that the population has not been exposed to before

• The causative agent of the disease infecting people and causing a dangerous disease

• Spread of the disease factor easily and continuously among people

A disease or medical condition cannot only be considered a pandemic because it is widespread and kills large numbers of people, but must also be contagious. For example, although cancer is a disease that causes many deaths in humans, it is not considered a pandemic because it is not contagious. There have been major epidemics in world history. Antoninus (Galen) Plague (165-180 AD), Justinian plague epidemic (AD 541-542) Black Plague (1346 - 1350), Fifth Cholera Pandemic (1879 - 1881), Modern Plague (third plague pandemic) (1894-1903) , Sixth Cholera Pandemic (1899-1923).

Approximately 75 million people died in these epidemics. Spanish Flu (1918-1920) More than 20 million people died. (H1N1), Asian flu (1957-1958), HIV / AIDS (1960), Hong Kong flu (1968-1969) and Corona virus pandemic (covid-19, 2019-2020.

It is also obvious that these pandemics, which affect the history and development of humanity, will cause bigger problems in the future with the increasing human population and the depletion of world resources. As scientists, this study aims to provide information to the public about the definition, development and spread of the virus that causes the current

Covid-19 pandemic and to present it as a book section to share with researchers.

We would like to thank the publishing house and our colleagues who contributed to the publication of this publication.

Best regards

Prof.Dr. Belgin SIRIKEN
Asst. Prof. Dr. Ayhan GULER

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Referees

Prof. Dr. Birgül IŞIK, Dicle University, Turkey

Prof. Dr. Hasan YELER, Cumhuriyet University, Turkey

Assoc. Prof. Dr. Rana ISIK, American Hospital, Turkey

Chapter I

A REVIEW: GENERAL OUTLOOK of CORONAVIRUS and SARS-CoV-2

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1.Introduction

SARS-2 CoV or COVID-19 coronavirus is a contagious disease seen recently in worldwide. Although most people infected with the virus will experience mild or moderate respiratory illness and healing without requiring special treatment, older people and people with chronic diseases and immunosuppressive problems such as cardiovascular diseases, diabetes, chronic respiratory disease, and cancer etc. are more likely to develop quite serious diseases even resulting in death (WHO,2020a,c).

Coronaviruses (CoVs) belong to Coronaviridae family (order Nidovirales). They are enveloped viruses, and contain extraordinarily large single-stranded RNA genomes ranging from 26 to 32 kb in length (Figure 1 and 2) (Zumla et al., 2016; Su et al., 2020). CoVs have been identified various animals such as avian hosts like bat, and mammalian such as camels, dogs and masked palm civets. Before 2002, it was considered that they caused mild diseases in the immunocompetent people. However, late of 2002, they

caused severe acute respiratory syndrome called SARS-CoV (Zhong et al., 2003; Drosten et al., 2003). Nowadays, for human, at least seven coronavirus species are identified as pathogens. These are HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1, MERS-CoV (Middle East respiratory syndrome), SARS-CoV and SARS-CoV-2 (CoVID-19). There is variation for pathogenesis among these 7 species. For instance, HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1lead to only mild upper respiratory disease. They seldom cause to disease for in infants, young children, and elderly people (WHO, 2020c). Remaining three species are more dangerous and can cause lower respiratory tract and trigger a severe respiratory condition in humans. SARS-CoV caused outbreak in 2002 and 2003 (Zhong et al., 2003; Drosten et al., 2003), and responsible for the Middle East respiratory syndrome (MERS-CoV), which emerged in 2012 and remains in the circulation in camels (Zaki et al., 2012). SARS-CoV-2, firstly emerged in December 2019 in Wuhan of China and a great effort is being undertaken to contain its spread.

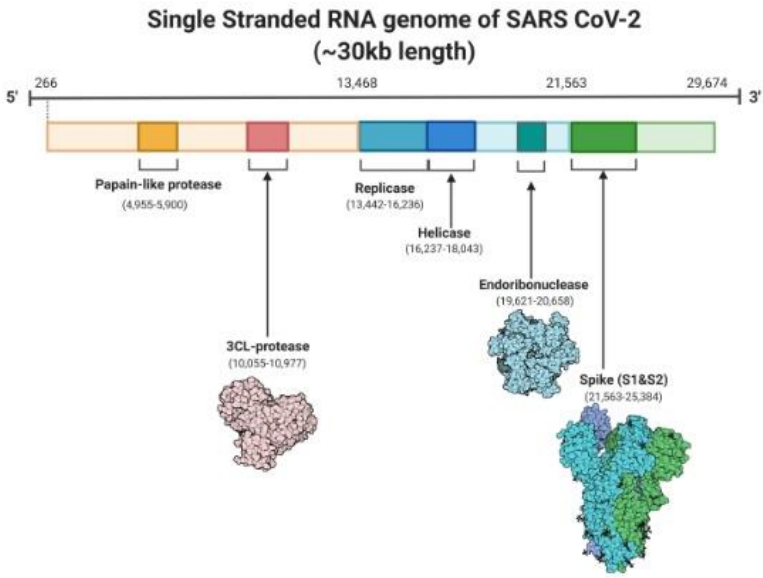

Figure 1. Single-stranded RNA genome of SARS-CoV2 (Rohan Bir Sing in Cascella et al., 2020).

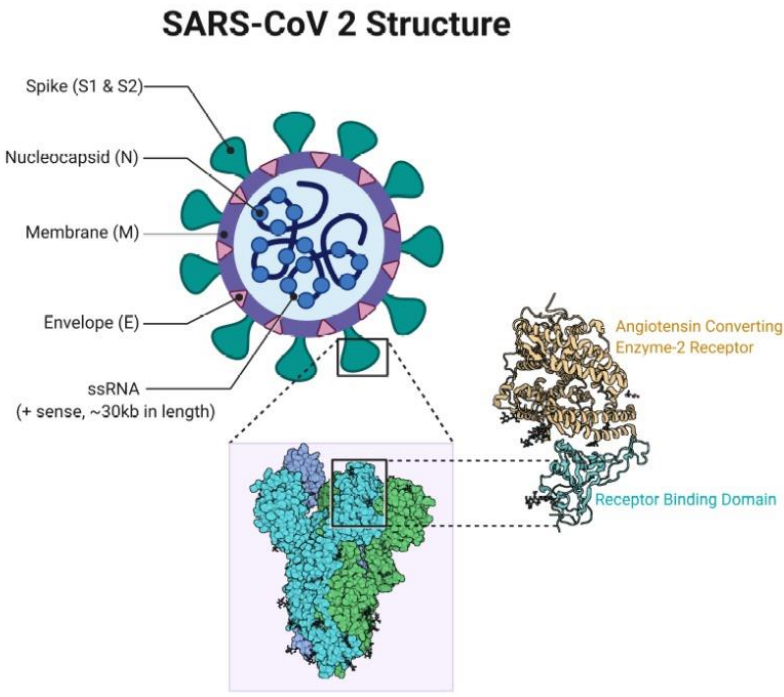

Figure 2. SARS- CoV 2 Structure (Rohan Bir Sing in Cascella et al., 2020).

Initially, the new virus was called 2019-nCoV (2019-novel coronavirus disease-COVID 19). Subsequently, the International Committee on Taxonomy of Viruses (ICTV) termed it the SARS-CoV-2 (the severe acute respiratory syndrome coronavirus-2) virus as it is very similar to the one that caused the SARS outbreak (SARS-CoVs) (Cascella et al., 2020; Zheng, 2020). The type coronavirus emerged from December 2019 in Wuhan, then has alarmed all over the world as of February 2020 (Zheng, 2020).

2. Variation and Origin of Quite Pathogenic Coronaviruses

Coronaviruses contain four genera: 1) Alpha-coronavirus (alphaCoV) like 229E and NL63, 2) Beta-coronavirus (betaCoV), 3) Gamma-coronavirus (gammaCoV), and 4) Delta-coronavirus (deltaCoV) (Cui et al., 2019).

The betaCoV genus divides into five sub-genera or lineages (Chan et al., 2013). Genomic characterization has shown that while Gamma and Delta-coronavirus generally infect birds and occasionally humans, alfa and beta-coronavirus infect both human and animal (Cui et al., 2019). Among 4 genera, beta-coronaviruses are the most important group and the most highly pathogenic viruses against humans such as SARS-CoV-2, MERS-CoV and SARS-CoV (Su et al., 2016; Forni et al., 2017; Cui et al., 2019). Although pathogenic MERS and SARS coronaviruses originated from bats, the newly emerged SARS-CoV-2 still debatable (Wang et al.,2004; Cui et al., 2019). According to investigation findings, SARS-CoV strains determined in market civets were transmitted from horseshoe bats, and they found to be phylogenetically associated with SARS-CoV in bats from China, Europe, Southeast Asia, and Africa (Lau et al., 2005; Hu et al., 2017; Cui et al., 2019). Besides these, SARS-CoV strains isolated from humans were highly similar to those in bats in terms of genomic sequences except that S gene and ORF3 and ORF8 gene sequences. Because, it was detected some variation these genes regions. However, some regions in SARS-CoV from bats have major variations compared to from human's origin SARS-CoV (Song et al., 2005; Cui et al., 2019).

Camels origin MERS-CoV were found to be similar to human origin MERS-CoV. But there were some variations among S, ORF4b, and ORF3 genomic regions. According to genome sequencing -based researches have demonstrated that MERS-CoV strains from humans are phylogenetically related to those from bats (Cui et. al., 2019).

Different strains of MERS-CoV obtained from camels were found to be similar to those isolated from humans except for variations among the S, ORF4b, and ORF3 genomic regions. Furthermore, genome sequencing-based studies have revealed that the strains have identical genomic and protein structures except for the S proteins. In addition, recombination analysis of genes encoding orf1ab and S revealed that MERS-CoV originated from the exchange of

genetic elements between coronaviruses in camels and bats (Chu et al., 2018; Lau et al., 2013; 2018).

The zoonotic source of SARS-CoV-2 in not confirmed but according to genomic sequence of it showed that there was close relatedness (88% identify) with two bat-derived SARS-like coronaviruses (bat-SL-CoVZC45 and bat-SL-CoVZXC21). Obtained from phylogenetic analyses results of them, SARS-CoV-2 is genetically distinct from SARS-CoV and MERS-CoV (Zhou et al., 2020; Wu et al., 2020). However, both SARS-CoV and CoV-2 have similar receptor binding domain structure, whereas the primary protease is highly conserved between them. In conclusion, bats are the source of origin, while an animal sold at the Wuhan seafood market may represent an intermediate host facilitating the emergence of the virus in humans (Lu et al., 2020; Provincial et al., 2020).

3.Epidemiology and Clinical Characteristic of Human Coronaviruses

Coronaviruses cause respiratory and intestinal infections in humans. In 2002 and 2003, they caused the outbreak of severe acute respiratory syndrome (SARS) in Guangdong, China and rapidly spread around the World (Cui et al., 2019). During this outbreak, an epidemic of pneumonia with a high rate of transmission to other people occurred in the region, followed by subsequent outbreaks (138 people) in Hong Kong (Zhao et al., 2003; Zumla et al., 2016). In these outbreaks, SARS-CoV infected 8,098 people and caused 774 fatalities in 29 different countries by the end of the epidemic (Zumla et al., 2016). Then, during 2012, in Jeddah, Saudi Arabia, a patient with MERS-CoV died because of the severe pneumonia causing MERS-CoV (Zumla et al., 2016; de Groot et al., 2013). The same year, in Jordan, it was an outbreak causing MERS-CoV (Hijawi et al., 2013). MERS-CoV, then, was continued to spread to Middle East (Zumla et al., 2016). By 2020, it was seen 2,468 cases and 851 of them resulted from died in the World (Sheahan et al., 2020; Kilber et al., 2020). In Wuhan, China, during 2019, many patient

with atypical pneumonia were reported (Zhu et al., 2020). The first 6 weeks of the outbreaks, several patients were seen in more than 37 countries (WHO, 2019). Then the infection spread from Wuhan, China to across to World (Huang et al., 2019). SARS-CoV-2 caused 79,331 confirmed cases and 2,618 deaths around the World (WHO, 2019). However, COVID-19 caused 77,262 confirmed cases and 2,595 deaths inside mainland China alone. After China, Iran is secondary country, the highest fatalities, due to SARS-CoV-2 infection (WHO, 2020a,c).

4.Symptoms of Patient with Sars-Cov-2

A typical symptom of patient with SARS-CoV-2 infected is pneumonia, which is detected using by computer tomography (CT) or chest X-ray (Zhong et al., 2003; Zhu et al., 2019). At the beginning stage of disease, the patients showed the acute respiratory infection symptoms and sometimes quickly developed acute respiratory failure and other serious complications (WHO, 2020c). The first cases of coronavirus infection in the United States also showed basilar streaky opacities in both lungs by chest radiography. However, the pneumonia for this patient was only detected on the day 10 of his illness (Holshue et al., 2020).

Generally, the most common signs and symptoms of patients are fever and cough (Chen et al., 2020). Sometimes can show fatigue, shortness of breath or dyspnea, muscle ache, headache, chest pain, diarrhea, hemoptysis, sputum production, rhinorrhea, nausea and vomiting, sore throat, confusion, and anorexia were also observed in a proportion of the patients (Chen et al., 2019; Huang et al., 2020) (Figure 3).

Generally, SARS, MERS and COVID-19 cause severe acute respiratory syndrome. When compared to fatality rate of three types, COVID-19 causes much lower (2.3 %) than SARS (about 10 %) and MERS (about 36%) (Xu et al., 2020; Wu et al., 2020).

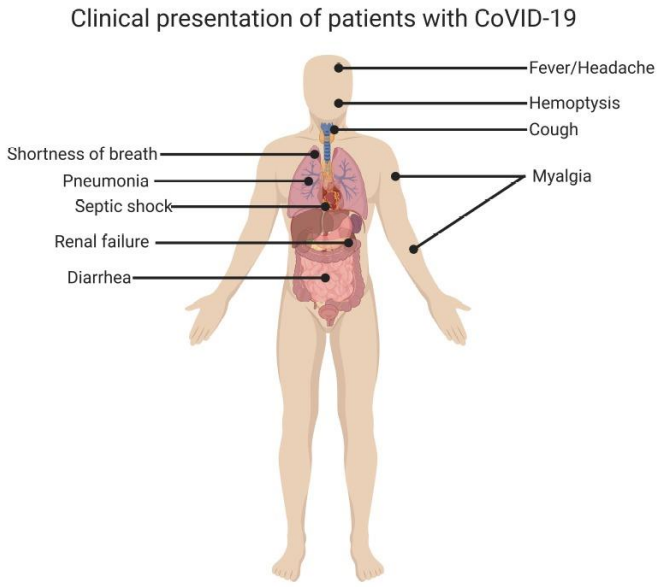

Figure 3. Clinical presentation of patient with SARS-CoV-2 (Rohan Bir Sing in Cascella et al., 2020)

5.Virus Transmission

SARS-CoV-2 can be transmitted by human-to-human through droplets, contact and fomites (Figure 4). SARS-CoV is commonly transmitted through indirect or direct contact with mucous membranes in the mouth, eyes or nose. It has been shown that unprotected eyes and exposed mucous membranes are vulnerable to SARS-CoV transmission. Average incubation period is 3 – 7 days, and continued up to 12 -24 days (Peiris et al., 2003; Belser et al., 2013; Chan et al., 2020; Guan et al., 2020; Li et al., 2020).

Sometimes, asymptomatic contact can also cause contamination of the SARS-CoV-2 viruses. According to the issue, a German businessman was found infected by SARS-CoV-2 after attending a conference together with a colleague with no signs or symptoms of infection but had become ill due to the SARS-CoV-2 infection later (Rothe et al., 2020). This case shows us that patient with the viruses but no symptom can spread the viruses. Therefore, it can preventive for measuring body temperature.

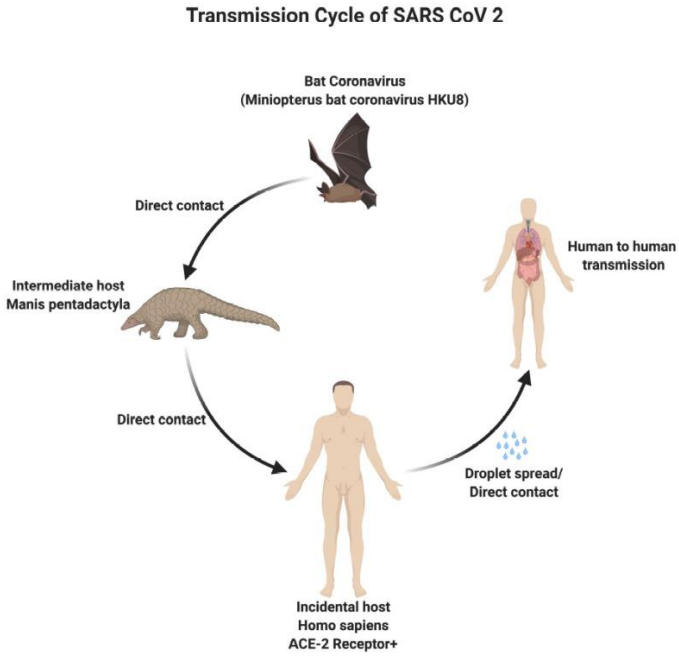

Figure 4. Transmission of SARS CoV-2 cycle19 (Rohan Bir Sing in Cascella et al., 2020).

6.The number of Coronavirus cases and death in the some of the country

According to Worldometers (2020), last updated June 18, has reported that more than 8,418,040 coronavirus cases and 451,664 death have seen so far around the world. The number of cases according to country; In the United State, it has been seen 2,221,000 confirmed cases and 119,484 death, and the number is the highest number of confirmed coronavirus cases. In Russia is second range, and the number of SARS CoV-2 cases is 561,091 cases. A total COVID-19 number are 7,660 death. and China with 83, 293 cases and 4,634 death, England with 299,251 and 42,153 death, Germany with 190,179 and 8,927 deaths, Brazil with 960,309 cases and 46,665 deaths, Iran with 195 cases and 9185 deaths, Spain with 291,763 cases and 27,136 deaths, Italy with 237,828 cases and 34,448 death, Pakistan with 160,118 cases and 2,093 deaths, France with 158,174 cases and

29,575 deaths, Canada with 99,853 cases and 8,254 deaths, Sweden with 54,562 cases and 5,041 deaths, Netherlands with 49,204 cases and 6,074 deaths, . In Turkey, 4,861 death and 182,727 cases were seen (Worldometer, 2020).

7.Preventive measure of SARS CoV-2

It was taken community measures against SAR-CoV-2 to control the spread of infection and diseases. To SARS CoV-2, there has been no vaccine vaccine and specific anti-viral drugs so far. Therefore, public health measures are considered as an effective tool for community. For this aim, hand hygiene, use of mask, hospital environment, droplet, airborne and contact precautions, institutional safeguard and standard measures.

The most important measure to control the spread of COVID-19 infection is frequent hand wash with soap and water or with an alcohol-based hand sanitizer. If hands are not visibly dirty, they should preferably have washed with alcohol-based sanitizer for at least 20 to 30 seconds (Siddharta et al., 2017). But, if hand dirty, they should wash with soap and water for 40-60 seconds (WHO, 2009). It must avoid to contracting person or other people, and hand must not contact eye or mount like that mucosa. Susceptible or infected surfaces and other surfaces must be clean with appropriate disinfection technique with 1.0% hypochlorite solution or 70.0% alcohol to limit the spread of infection (Khan, 2020). To prevent of infection spread by aerosol or droplet infection, it must mandatorily use mask. In the hospital, it is mandatory wear surgical mask. As air-droplet seldom crosses beyond 1 meter, within 1 meter between health and infected people, all health care workers must wear medical/ surgical mask along with face shield or goggles to protect eye from accidental spiting from patients. Personal protective equipment such as masks, gloves, gown, and goggles are necessary to prevent infection to health care workers. Dedicated instruments like stethoscope and thermometer) should be used for each patient however in case of sharing each instrument must be disinfected with alcohol

or hypochlorite solution. Health care worker must avoid touching their mouth, nose or eye, frequent hand wash (WHO, 2020c).

8.Conclusion

The CoVs have become the major pathogens of emerging respiratory disease outbreaks. They are a large family of single-stranded RNA viruses and can be isolated in different animal species. These viruses can cross species barriers and can cause, in humans, illness ranging from the common cold to more severe diseases such as MERS and SARS. The potential for these viruses to grow to become a pandemic worldwide seems to be a serious public health risk. In the last twenty years, several viral epidemics such as SARS-CoV in 2002 to 2003, and H1N1 influenza in 2009, have been recorded. Most recently, MERS-CoV was first identified in Saudi Arabia in 2012 (Cascella et al., 2020). Then, in 2009, SARS-CoV-2 emerged from Wuhan, China. It spreads quickly globally and can result in death of the infected patients. The mortality rate is 2.3% (Wu et al., 2020). The large number of patients within short period of time could result in the collapse of health care system. Thus, the mortality rate might be elevated. Anyone who has had close contact with a patient with laboratory-confirmed COVID-19 within 14 days of symptom onset or a history of travel from affected geographic areas (presently China, Italy, Iran, Japan, and South Korea) within 14 days of symptom onset (Cascella et al., 2020).

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Chapter II

COVID-19: UPDATE PATHOGENESIS AND CLINICAL EFFECTS

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Introduction

Covid 19(CoV-19) virus, severe acute respiratory syndrome (ARS) coronavirus 2 (SARS-CoV-2), which caused a worldwide pandemic, was first identified in Wuhan, China, on Jan 7, 2020. It has been found that, it is a member of the β koronavirüs family that is related to bat CoV type of viruses (Lu, R. et. al., 2020, Chan, J.F. et. al., 2020). Corona viruses (CoV) are single and positive strand RNA viruses that belong to Coronaviridae family and Nidovirales order (Qing Yeet. al., 2020). Due to its transmission from animal to human and then from human to human, it has started a severe pandemic around the world, and in our country.The more researches are carried out to examine the virus, its entry into human body and effects on human body, the more ways of protection from the virus, drugs and vaccines against the virus can be developed.

Covid 19 Pathogenesis

The research into the mechanism and effects of the virus have shown that corona virus has a round shape like a ball and some spike proteins in the focal areas. A careful examination was conducted by an electron microscope and a viral genome wrapped in the nucleocapsid is observed in the virus (Perlman S. et al., 2009). It has been found that there are 7 types of CoV virus. These are α- type HCoV-229E ve HCoV-NL63, β-type HCoV-HKU1, SARS-CoV, MERS-CoV, HCoV-OC43; and 2019-nCoV (Perlman S. et. al.,

2009). Previous studies revealed that while some of these virus types cause light symptoms, other types cause severe ARS or fatal acute lung injury (ALI). In a study, the mechanism of the virus was examined and found that the SARS-CoV virus entered the human body by binding to Angiotensin-Converting Enzyme-2 (ACE-2) and settled in the upper and lower respiratory tract (Qing Ye et. al., 2020). The same study also showed that the virus enters the cell cytoplasm through endocytosis after binding to the ACE-2 receptor. ACE-2 receptors in the human body are mostly found in the lungs, heart, kidneys, intestines, brain and testicles. Therefore, these organs were found to be target organs of the Cov-19 virus (Baig AM. et. al., 2020). The first line of defense of the human body against viruses is when the immune system is activated. However, it has been observed that excessive stimulation or overactivity of this system causes harmful effects on the human body (Channappanavar, R. et. al., 2016).

Research on CoV-19; showed that the virus plays a role in the pathogenesis of the disease by infecting the oral mucosa epithelium and stimulating its proinflammatory cells. Also, in the early stage of the infection, the virus settles in the respiratory epithelium and infects plasmacytoid dendritic cells and macrophages. As a result, the release of cytokines and chemokines is activated (Qing Ye et. al., 2020). This is followed by the release of interferons, Interleukin 1β (IN-1 β), Interleukin-6 (IL-6) and Tumor Necrosis Factor α (TNF-α), and then by an increase in the amount of blood neutrophils and macrophages.

Interferons are known to play an important role in viral infections at an early stage and have protective effects (A.G.-S et.al., 2006). However, studies on CoV-19 showed that delaying the release of interferon prevents the body's antiviral defense. The studies also showed that interferon, TNF, induced protein 10 (IP-) and monocyte chemotactic protein -1 (MCp-1) activation were detected in Covid 19 patients (Qing Ye et. al., 2020)

Covid 19 clinical effects

After CoV- 19 virus infects the respiratory mucosa, it stimulates the leukocytes and immune cells, especially T lymphocytes, to enter to the area. This causes excessive activation of T lymphocytes that play a role in the immune system. Viral peptides in CoV-19 virus are presented to cytotoxic T lymphocytes. While cytotoxic T (CD8) lymphocytes try to kill the virus, they cause an increase in virus-specific memory T lymphocytes.

As a result, while the overstimulation and excessive release of T helper (CD4) and T cytotoxic (CD8) lymphocytes decreases blood levels, the excessive release of cytokines and chemokines, neutrophils and macrophages increase the number of cells involved in other inflammation in a chain. This in return increases the blood values, especially neutrophils and lymphopenia.

In a study, a decrease was observed in the amount of blood eosinophils as a result of the excessive immune response in the human body due to the effect of the virus (Azkur, A.K. et. al., 2020). Excessive release of all these cells causes cytokine storm, apoptosis of airway and alveolar epithelial cells (Herold, S. et. al., 2008; Rodrigue-Gervais, I.G et.al., 2014). Apoptosis of endothelial cells and epithelial cells damages the pulmonary microvascular and alveolar epithelial cell barriers. Endothelial damage causes an increase in endothelial capillary permeability. As a result, it causes vascular leakage, alveolar edema and alveolar damage, which leads to hypoxia in the body.

Fluid accumulation in the alveoli prevents CO2 / O2 exchange. This causes an increase in O2 need and breathing difficulties in CoV-19 patients. Therefore, Inflammatory mediators play an important role in the pathogenesis of acute respiratory distress syndrome (ARDS).In some studies, it was found that cytokine storm was the main reason of ARDS and extrapulmonary multi-organ failure.

Wang, H.et al. (2008) and Xu et.al. (2020) conducted a post-mortal histopathological examination of lung tissue and they found widespread alveolar damage filled with fibro-myxoid exudate, a noticeable desquamation in pneumocytes, development of hyaline membrane, and mononuclear inflammatory cell infiltration, rich in lymphocytes, in interstitial distance. In addition, they detected an amphophilic granular cytoplasm due to a viral cytopathic effect and multinucleated syncytial cells characterized byprominent nucleoli and with atypically enlarged pneumocytes.

Patients with CoV- 19, have wide range of symptoms such as asymptomatic, mild clinical symptoms, digestive complaints and symptoms of severe respiratory distress. Previous studies have shown that these symptoms are followed most commonly by cough, fever, tiredness, nausea, vomiting, headache, diarrhea, anosmia, visual disturbance, chest pain, tachycardia, proteinuria, hematuria and thromboembolism.

Baig et.al. (2020) found that CoV-19 caused cerebral involvement via bloodstream. In addition, they stated that, the virus, that reaches the brain tissue, causes a neural effect by interacting with ACE-2 receptors, and a fatal neuronal damage following an endothelial damage. Inability to smell, severe headache, dizziness and hyposmia are seen as the clinical signs of brain involvement. However, neurological disorders such as acute cerebrovascular disease, ataxia, meningoencephalitis, and Guillain Bare were reported in a study(Chih-Cheng et.al., 2010).

All these symptoms and the sudden onset of symptoms such as cerebral edema is a condition that should be investigated.

Zhou F. et. al. (2020) found that an interesting result in their study, that when the researchers examined the blood values of the patients who need severe intensive care,in addition to lymphopenia, they found an increase in the levels of lactate dehydrogenase, D-dimer, ferritin and transaminases (Zhou, F. et. al., 2020).In another study, the blood values of

patients with severe CoV-19 in the intensive care unit and patients who had infection with milder symptoms were compared. It was found that, the patients in the intensive care unit had higherblood plasma levels of IL 2,7,10, granulocyte colony stimulating factor, IP 10, MCP1, Macrophage Inflammatory Protein 1 alpha (MIP1 alpha) and tumor necrosis factor (TNF)(Huang, C. et.al., 2020)

In a study, the ratio of lymphocyte and thrombocyte in the blood of patients with CoV-19 disease was investigated, and it was observed that the platelet levels were quite high as opposed to low lymphocyte levels (Cao, X. et. al., 2020). Considering the clinical course of the disease in this study, it was noted that high blood platelet levels increased the risk of embolism.In a study, it was observed that the susceptibility to thromboembolic events may increase in patients with SARS-CoV-2 virus (Ng, JJ.et. al., 2020).

In studies conducted by Shi, S. et. al. (2020) and Huang, C. et. al. (2020), cardiac symptoms were frequently observed in the patients with Cov-19.In another study conducted with 138 patients with CoV-19 in Whun state, it was found that lots of patients had myocarditis as cardiac involvement in addition to pneumonia (Wang, D. et.al., 2019). Similarly, Zhang, YY.et.al. (2020) observed that cardiac effect of CoV-19 virus is on ACE-2 receptor, and that a myocardial damage might occur as a result of cytokine storm causing changes in T lymphocyte ratios. In this study, other cardiac symptoms, such as 58% hypertension, 25% heart disease, and 44% arrhythmia were observed in patients with severe CoV-19 symptoms. It was also found that these symptoms were followed by heart failure.

Su et.al. (2020) conducted autopsy studies with 26 patients who died due to CoV -19. The researchers found histopathological diffuse proximal tubule injury in kidney tissue, loss of brushy edges and vacuolar degeneration.In this study, a significant result was foundwith a microscopic examination that, noticeable pointed coronavirus-like clusters

of particles were detected in tubular epithelium and podocytes.

Wong, SH. et. al. (2020) examined 1099 patients, and they found the signs of the involvement of the digestion system, such as nausea, vomiting, abdominal pain and diarrhea. They compared SARS-CoV and MERS-CoV and found that, the digestion system findings emerged with the SARS-CoV virus were seen less than the digestive system findings developed by the MERS-CoV virus. In addition, it was detected that there was an increase in patients' blood ALT (alanine aminotransferase), AST (aspartate aminotransferase), bilirubin and GGT (gamma - glutamyl transferase) levels. The researchers stated that the reason of the increase of these values, which are also indicative of liver damage, might be due to direct viral infection of hepatocytes, immune related injury or drug use.In a post-mortal study, the liver biopsy showed micro-vesicularsteatosis and mild lobular activity in hepatocytes.These histologicalchanges could be caused by SARS-CoV2 infection or drug induced liver injury. This issue needs to be investigated in further studies (Xu L et. al., 2020).

In a study of 73 CoV-19 patients, the expression of ACE-2 receptors was detected in the cytoplasm of the stomach, duodenal and rectum glandular epithelial cells, and CoV-19 virus was found positive in these patients' stool specimens. The duration of positive stool results may change from 1 to 12 days and this is important in viralcontamination (Xiao, F. et. al., 2020).

Conclusion

In previous studies, the effect mechanism of CoV -19 is found to be via ACE-2. However, the formation mechanism of some clinical findings is not fully clear.

Re-occurrence of the disease in some patients causes a lot of questions on the development of immunity. It is clear that the recovery time of the disease will be shortened by

solving this kind of problems. In addition, conducting further studies on the immune system strength and vaccine development, is important in terms of preventing the transmission and spread of the disease

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Chapter III

EPIDEMIOLOGY OF COVID-19

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1. Introduction

According to recent regulations by the international virus taxonomy committee (ICTV), Coronaviruses (CoV) are non-segmented positive-sense RNA viruses belonging to the largest enveloped genome (~ 30 kb) in the Riboviria regnum, the Nidovirales order, the Cornidovirineae suborder, and the Coronaviridae family. Morphologically, virion showing helical symmetry is ~ 125 nm in diameter. Its most important features are spike proteins located on the virion surface (Zhou et al., 2019; Li et al., 2020; Sen et al., 2020; Lai et al., 2020; Raoult et al., 2020) (Figure 1).

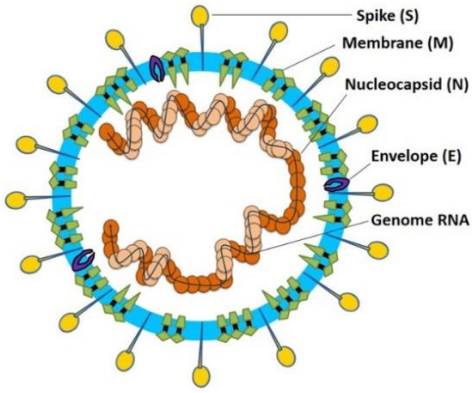

Figure 1. Schematic view of the coronavirus (Li et al., 2020)

Since these rod-like extensions on its surface are compared to the crown, the name coronavirus has begun to be pronounced with the word "corona" which means Latin crown (WHO, 2020b; T.C. Sağlık Bakanlığı, 2020b; Budak and Korkmaz, 2020; Ün, H. 2020). Coronaviruses are known as a virus family with a high probability of mutation and recombination. With its high mutation rate and high recombination frequencies of RNA genomes, it shows a good viral structure to quickly adapt to changing ecological conditions. This situation opens the way to adapt to new hosts by crossing the species barrier for family members (Ün, H., 2020).

The coronovirus, isolated from many animals (bats, pigs, cats, dogs, rodents and poultry etc.), is actually considered to be bats in its main reservoirs in nature (Fung and Liu, 2019; Yu et al., 2019; Bulut and Kato, 2020). Four different types of coronavirus are classified as Alphacoronavirus, Betacoronavirus, Deltacoronavirus and Gammacoronavirus. Among these, Alphacoronavirus and Betacoronavirus are called human coronovirus due to their ability to infect humans (HCoV) (Cupertino et al., 2020). HCoVs, which were accepted as one of the main viral infectious agents of the common cold and first described in the 1960s; Seven known HCoVs have been identified, including 229E, OC43, NL63, HKU1, SARS-CoV, MERS-CoV and coronavirus-2 (SARS-CoV-2) (Bulut and Kato,

2020). In HCoV; While 229E, NL63, OC43 and HKU1 cause typical mild and moderate respiratory diseases in humans, OC43 and NL63, which are known to cause epidemic especially in winter, are seen more frequently in children, and 229E is also caused by rare infections. Apart from these coronaviruses causing mild infections, SARS-CoV (Severe Acute Respiratory Syndrome) and MERS-CoV (Middle East Respiratory Syndrome) have been reported to cause severe infections (Wang et al., 2020). The SARS-CoV epidemic, which started in 2003 in live animal markets in Guangdong, China, detected viruses in 37 countries and regions within 9 months. In total, 8096 people were diagnosed and 774 deaths (9%) occurred. SARS mortality rate according to WHO; If the age is ≤ 24, it is reported as below 1%, if it is between the ages 25- 44, it is 6%, if it is between 45-64, it is 15%, if it is 65 and above it is 50%. It was reported that there were 2494 cases and 858 (34%) deaths infected with MERS-CoV, which was first seen in Saudi Arabia in September 2012, which affected 27 countries. The disease is transmitted from person to person by close contact. By touching the mouth, nose, and eyes with hands that have come into contact with the virus-contaminated surface and objects; The virus is transmitted to humans by inhalation of droplets thrown into the air during sneezing, coughing and speaking (Yeşil and Hacımustafaoğlu, M. 2020; TUBA, 2020).

In this review, we conducted a systematic review of the literature on control measures and epidemiology for handling information about the new type of coronavirus.

2. Epidemiology

The coronavirus, first seen in the city of Wuhan in Hubei province of China in 2019, has shown incurable pneumonia-like symptoms in people who have been in contact with the virus, unlike the previous known coronaviruses (Figure 2). It has been named as SARS-CoV-2 (Xu et al., 2020). The name of the disease caused by the virus was first named as 2019 Novel Coronavirus and later as COVID-19. It was declared epidemic by the World Health

Organization, as the situation aroused international concern. COVID-19 spread worldwide, causing more than 10 million cases and more than 500 thousand deaths (WHO, 2020c).

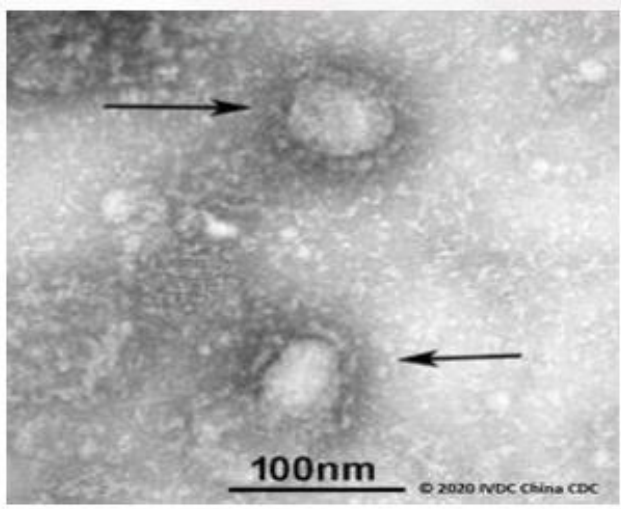

Figure 2. SARS-CoV-2 (Betacoronavius) electron microscope image (T.C. Sağlık Bakanlığı, 2020; URL_1)

It is known that COVID-19 can be transmitted through zoonotic passage such as SARS-CoV and MERS-CoV. It is determined that the natural host of SARS-CoV are musk cats (Guan et al., 2003). In MERS-CoV, it has been shown that they can switch from camels to people, and the main mansion is reported to be a bat. (Alagaili et al., 2014; Li et al., 2020). For COVID-19, the origin is thought to be a bat due to its genetic structural similarities (Malik et al., 2020). In genomic studies, it has been reported that COVID-19 is 86-89% similar to bat SARS viruses, 79% similar to SARS-CoV and approximately 50% similar to MERS-CoV. (T.C. Sağlık bakanlığı, 2020; Chen et al., 2020; Lu et al., 2020). Phylogenetic analysis suggests that the betacoronavirus strain of COVID-19 is from the Sarbecovirus subtype and has a similar receptor (angiotensin converting enzyme 2 receptor) binding site structure, which is genetically different with SARS-CoV, so it is similar to SARS-CoV. has been revealed

to cause (Yeşil, E., ve Hacımustafaoğlu, M. 2020; Zhu et al., 2020). In another study, the genome homology between SARS-CoV and SARS-CoV2 is 79.5%, while the homology between SARS-like viruses isolated from bats and SARS-CoV2 is 96% (Wang ve ark., 2020; Zhou ve ark., 2020).

The known symptoms of COVID-19 so far are dry cough, fatigue, muscle pain, shortness of breath and high fever. Some patients rarely experience headache, loss of taste and sense of smell, stuffy nose and diarrhea (WHO, 2020b). These symptoms appeared to occur on the fifth day of the disease. In some cases it has been determined that it may vary between two and fourteen days (Hopkins, 2020). Research shows that the incubation time of COVID-19 is similar to MERS and SARS, but slightly longer than influenza. In addition, most of the cases have survived the disease without requiring a significant medical intervention; It has been stated that people with chronic immunocompromised risk group (individuals with chronic diseases such as diabetes, high blood pressure, lung and heart diseases and elderly people) have a severe course of the disease (Budak ve Korkmaz, 2020). It has been shown that this disease is transmitted from person to person, especially adults are sensitive to COVID-19, and the severity of the disease is related to age. In addition, in a structural study, in a study that examined 99 patients hospitalized in the same hospital with the diagnosis of COVID-19, they showed that older men were more likely to become infected and quickly entered acute respiratory distress syndrome (ARDS), creating a life-threatening condition (Chen et al., 2020).

In all confirmed cases of Coronavirus detected in humans, direct or indirect links to infected individuals or regions are observed. Droplet and direct patient contact is considered as the most likely transmission route (Lu ve ark., 2020).

In the uncontrollable contamination and spread, particular emphasis is placed on super propagation or super infectious agents. These infected individuals cause the virus

to spread uncontrollably across countries, regions and continents (Hilgenfeld ve Peiris, 2013). The disease was rapidly transformed from a regional epidemic to a global pandemic and officially declared a pandemic by the WHO (TUBA, 2020).

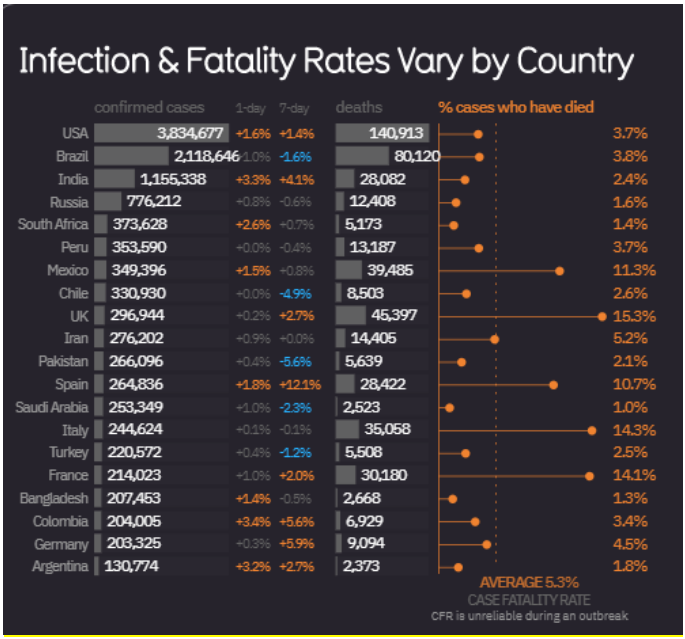

Figure 3a. Top 20 countries by total number of cases and deaths as of July 22 (URL_2)

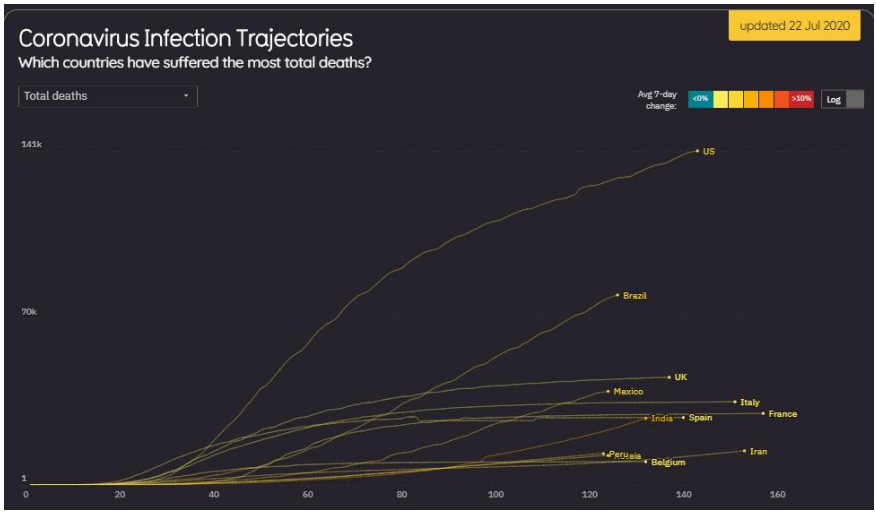

Figure 3b. Countries with the highest mortality rate as of July 22 (URL_2)

While trying to take the precautions to stop the epidemic in China for the first time, the epidemic spread to the world has shown its effect especially in Europe. Figure 3a shows the data of the 20 countries with the highest number of cases, especially July 22, 2020, in the world. (URL_2). As seen in the figüre 3a, depending on the population surplus, the USA is the country with the highest number of cases and deaths due to some problems in the implementation of the measures. Brazil, which is located in South America, is in the 2nd place in terms of both parameters (Cupertino et al., 2020). As seen in the graphic, it takes place in the 3rd and 4th places in terms of number of cases and deaths in India and Russia in Asia. The epidemic in India has spread rapidly and has affected many people. Among the European countries, Italy has also increased rapidly in terms of number of cases and deaths and ranks 5th in terms of number 14 deaths (Figure 3b). In Germany, another European country, it ranks 19th in terms of the number of cases. The first case was detected while China ranked 26th in the number of cases, at the end of July, Turkey, China has increased through 7 as well. In the early stages of the outbreak, South Korea ranks 69th in terms of the number of cases, due to the fact that too

many tests and quarantine processes are carried out in accordance with the rules (URL_2; URL_3). Factors such as virulence, spread characteristics of the epidemic, host resistance, screening policy, treatment services, age and gender affect the fatality rate of the case (Gordis 2009; Memikoğlu and Genç., 2020).

Conclusion

As a result, as of July 22, there were more than 15 million cases worldwide and over 600 thousand deaths in the world. The number of cases over the last 200 thousand and 5 thousand deaths by Covidien-19 outbreak in Turkey has continued to be a major problem all over the world and in our country. In order to keep the outbreak under control as soon as possible, it is extremely important to prevent transmission routes and to prevent contact with patients. This epidemic should be managed by all countries with an approach focused on preventing incidents and deaths in line with epidemiological data.

Conflict of Interest

None.

Author Contributions

CB drafted the manuscript, compiled information from the literature. CB, BS and AG drafted the manuscript and gathered information from the literature. BS supervised and reviewed the manuscript.

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Chapter IV

EFFECT OF ACEIs (ANGIOTENSIN-CONVERTING ENZYME INHIBITORS) AND ARBs (ANGIOTENSIN II RECEPTOR BLOCKERS) ON AS CORONAVIRUS DISEASE 2019 (COVID-19)

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1.Introduction

Unknown cause of pneumonia was emerged in Wuhan, China in December 2019 (Sayın et al.,2020). In these patients, the pneumonia agent was found to be 'severe acute respiratory syndrome coronavirus 2 (previously known as SARS-CoV-2; 2019-nCoV) (Alimoglu and Erol, 2020). This disease was identified by the World Health Organization (WHO) in February 2020 as Coronavirus Disease-2019 (Corona Virus Disase 2019; COVID-19) (Givi et al., 2020). On March 10, 2020, it was announced that the first SARS-CoV-2 positive case was seen in our country (https://covid19.saglik.gov.tr). Infection occurs through airway and contact. Although the virus has been noted in urine and feces, fecal-oral transmission is still controversial. The virus affects everyone regardless of race, gender, age, and country, but it does more harm in the elderly, smokers, patients with hypertension and those with chronic disease. (Jin et al.,2020; COVİD-19 (SARS – CoV2) Enfeksiyon

Rehberi,2020). The average half of patients have comorbid diseases such as hypertension, diabetes and cardiovascular disease (https://www.facs.org/about-acs/covid-19).

2.Clinic and Research

The incubation period is between 2 and 14 days. The clinical picture has three stages (Mason,2020).Stage I: Asymptomatic period (first 1-2 days). The inhaled virus sticks to the nasal cavity epithelial cells and begins to multiply. Binding is done with ACE 2 (angiotensin converting enzyme 2) receptors. The spread in this process is not so great. However, these patients are probably the most dangerous group because they are not contagious without testing. In this process, it is the most suitable diagnostic method to show the virus in the nasal swab by PCR method. Stage II. Upper airway period: The virus begins to move down in the next few days. The patient begins with fever, fatigue and constant cough. In laboratory tests, leukocytosis, neutrophilia, lymphopenia, CRP elevation are remarkable. In this process, CXCL 10 can be considered a good marker. This marker will have an important place in the assessment of COVID-19 patients over time. 80% of COVID-19 cases are in stage I and II. It is recommended to follow these cases at home (COVİD-19 (SARS – CoV2) Enfeksiyon Rehberi,2020). Stage III. Lung involvement period: 20% of cases experience this period.The virus immediately descended to the alveoli and damages type II pneumocytes. As a result of the occupation of the virus by binding to the ACE 2 receptor, an environment consisting of alveolar damage, fibrin-rich hyaline membrane and a small number of multinuclear cells is formed.The patient has intense mucus secretion that is excreted by coughing. Rapid viral proliferation and virus damage progress as a result of ACE 2 down regulation, antibody dependent development and extensive infiltration and cytokine storm as the virus binds. How cytokine storm is triggered is still an important topic of debate. This event became clear in primary HLH. Due to their genetic mutations (HLH 2-5, RAB 27, XIAP, LYST, etc.), NK and CD8 T cells are activated and cause cytokine

storm, killing power decreasing or decreasing. Activated macrophages phagocyte cells and cytopenias begin. Macrophage activation syndrome (MAS) has similar mechanisms in cases such as HLH, rheumatological diseases, infections, malignancies, and some metabolic diseases, but genetic predisposition of some hypersitokinemia has been demonstrated (in some cases, heterozygous performance mutations have been shown). The incident is thought to be caused by very severe (immunosuppressive use, heavy viral load, cancerous tissues). The situation in COVID-19 patients is slightly different from the nucleus (neutrophil exellellet traps) caused by the initial leukocyte counts, but they weave virus residues like cocoon, but their increase (viral load) causes hyperactivation of T cells(Barnes et al.,2020).

3.Use of COVID-19 and angiotensin converting enzyme inhibitors and receptor blockers

The coronavirus disease outbreak 2019 (COVID-19) is caused by a new coronavirus infection, officially called the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) (Coronaviridae Working Group of the International Committee for Taxonomy of Viruses).

Among the COVID-19 patients admitted to a hospital, the resulting data suggest that hypertension may be associated with an increased risk of COVID-19-related mortality(Guan et al.,2019;Zhou et al.,2020).

ACEIs (angiotensin converting enzyme inhibitors) and ARBs (angiotensin II receptor blockers) are part of the reninangiotensin-aldosterone system (RAS) inhibitory agents and are considered one of the first-line drugs for the treatment of the majority of patients with hypertension. (Flack and Adekola,2020 ;Kovell et al.,2015).

However, continued use of ACEI / ARB is controversial in the COVID-19 environment. The reason for this discussion is that the use of ACEIs and ARBs can increase the expression of the ACE2 receptor in animal-based studies(Igase et al.,2008;Ferrario et al.,2005). It is a necessary

entry point for the known cellular receptor and SARS-COV-2 infection (Wu et al.,2020).

Conversely, ACE2 expression after SARS infection has been shown to be downregulated, causing RAS over-activation and severe pneumonia progression(Kuba et al.,2005).

There is an interesting method of reasoning about the increased expression of ACE2 and virus entry into the cell through this receptor. Generally, it is believed that increased ACE2 expression should result in direct direct delivery of virus particles to the cell. According to popular speculation, ACEi causes a decrease in angiotensin II, leaving ACE2 receptors available for coronavirus access. However, the same ACEi leads to an increase in angiotensin I and it is well known to be a substrate for ACE2.As a result of angiotensin I – ACE2 interaction, angiotensin 1-9 is produced. Little is known about the functional aspects of this product. Although initially thought to be just an intermediate step in converting angiotensin I to angiotensin II, recent evidence has shown significant cardiovascular bioactivity (Flores et al.,2020). In addition, a number of active agents such as apelin-13, dynorphin A 1-13, des-Arg9-bradykinin, neurotensin 1-13 and kinetensin were metabolized by ACE2(Vickers et al.,2002).

In this multicenter retrospective study, the in-hospital use of ACEI / ARB has found to be associated with the risk of COVID-19 all-cause mortality compared to the use of ACEI / ARB or the use of a different class of antihypertensive agents among hypertensive patients. Although unmeasured mixing is thought to have contributed to the observed protective relationship, these data suggest that the in-hospital use of ACEI / ARB is not associated with increased mortality in COVID-19. These findings provide clinical evidence to support have been recently published guidance statements from several international communities to continue ACEI / ARB in patients with COVID-19(Available at: https://www.hfsa.org/,2020; Available at:

https://ishworld.com/news/a/A-statement-from-the-International-Society-of-Hypertension-on-COVID-19/. Accessed March 5, 2020). Given the retrospective nature of this work, these data need further validation in geographically diverse, prospective, cohort studies. Randomized controlled trials are needed to examine the effectiveness of ACEI / ARB use in hypertension and COVID-19 patients. Previous clinical studies have shown that hypertension is a risk factor for higher mortality in patients with SARS and Middle East Respiratory Syndrome(Morra et al.,2018;Matsuyama et al.,2016).

As a result, increased ACE2 expression can increase infection in the body due to COVID-19.

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Chapter V

COVID-19 and FOOD SAFETY

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1. Introduction

As a result of the genomic analysis performed by the World Health Organization in the seafood market in Hubei province of Wuhan city of China, it was understood that the factor was a new type of virus called “SARS-CoV-2”. SARS-CoV-2 infection has been named as Coronavirus (CoV-Coronavirus) Disease 2019 (COVID-19) by the World Health Organization (WHO). COVID-19 quickly spread to many countries and continents and was officially declared as a pandemic by WHO as it killed more than 4000 people till March 11, 2020. (Park, 2020; Tuba 2020).

This ~~nomenclature~~ naming was made based on the abbreviation of the word COVID-19, corona (corona-CO), virus (VI) and diseases (D). It has gained an international dimension, which first appeared in China and later spread to the world, especially Asian countries, and therefore this disease has been evaluated as an “epidemic” (TUBA, 2020).

Coronaviruses (CoV) are single chain, positive polarity, enveloped RNA viruses in the Coronaviridae family, which are located in the Orthocoronavirinae subfamily, causing

serious respiratory disease. Coronaviruses are positive single-stranded and enveloped RNA viruses, the RNA size ranging from 26 to 32 kb. Both α- and α-CoV strains are known to infect mammals.

2. Symptoms

Though many pathogenic coronaviruses for humans often cause mild clinical symptoms, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) are zoonotic coronaviruses within the genus β-CoV and cause severe acute respiratory syndrome (Lu et al., 2020; Memikoğlu and Genç, 2020). Coronaviruses have been identified for several mammals including camels, bats, mice, dogs, cats in many birds (Cavanagh, 2007; Ismail et al., 2003) as well as humans. Today, mammalian coronaviruses have been regularly identified (Lu et al., 2003). For example, HKU2- bat coronavirus was blamed for fetal acute diarrheal syndrome in 2018 (Zhou et al., 2018).

They cause a wide variety of respiratory infections, ranging from the common cold to pneumonia (pneumonia) in humans. Incubation period is 3-5 days. The disease is self-limited within 4-6 days and patients recover quickly. In severe cases and in the risk group, pneumonia occurs. Symptoms of disease caused by coranavirus are cold, with a 35% percentage sore throat, dry cough, runny nose, weakness and fatigue. It is generally seen every year in autumn and winter months (Tuba 2020). Lu et al. (2020) The most common symptoms of COVID-19 were determined as fever, cough and difficulty in breathing. Sore throat, diarrhea and nausea are observed in 5% of all cases where vomiting observed in 1-2%. Pneumonia, severe acute respiratory failure, multiple organ failure and death were observed in patients with advanced course. DUZELTİLMELİ.

3. COVID-19's Ability to Stay Alive in Outdoor Environments

SARS-CoV-2 (coranavirus 2), formerly referred to as HCoV-19, is a severe acute respiratory syndrome and the

ability of virus resistance in the external environment depends on many environmental factors such as ambient temperature, humidity ratio in the air and surface conditions (T.C.Ministry of Health, 2020), as well as it depends on the specific type of virus and amount of the virus. In general, the human coronavirus cannot survive on dry surfaces. Inactivation of the virus in dry environments usually ranges from a few hours to a few days. In a study conducted by the American Working Group it was reported that SARS-CoV-2-nn was able to survive for 3 hours in the air, 4 hours on copper surfaces, 24 hours on cardboard and 2-3 days on stainless steel and plastic surfaces, Up to 3 hours of survival in the air also indicates that the virus can be transmitted by inhalation. In laboratory studies, due to the controlled atmosphere and high contamination rate, it was observed that Corona virus SARS-CoV-2 is less resistant as compared to other pathogens and various non-enveloped viruses or bacterial spores In natural environments, due to changes in temperature and humidity, daylight and lower contamination levels, their durability in natural environments is much lower compared to studies conducted in laboratory environments. (American Working Group, 2020).

4. Foodborne COVID -19

Food-borne microorganisms such as bacteria, viruses and parasites in Germany cause about 100,000 cases every year. Coronaviruses that infect animals can occasionally spread to humans, though rarely. Coronovirus cannot grow in food as it needs a live host for reproduction and development (BfR 2020a, b, WHO, 2020). Just like SARS, no data on the foodborne spread of CoVID-19 among humans and an no outbreak caused by oral-faecal transmission have been identified (Mullisa et al., 2012).

Coronavirus factor; turns to be inactive after 10-15 minutes at 56 ° C, a few days at 37 ° C, and a few months at 4 ° C (Siddell et al., 1983). However, the agent is resistant to freezing and can survive for years without losing its infection ability at -60 ° C (Andries et al. 1978; Siddell et al., 1983).

The human coronavirus is highly sensitive to the dry surface and stays alive for up to 3 hours on the dry surfaces of the hospital (Sizun et al., 2000).

Bakery products: Bakery products (such as pastries, pies) or vegetables and fruits can be directly contaminated by Coronavirus during sneezing or coughing of infected people. However, viruses cannot reproduce in foods. Retail bakery products are generally prevented from contamination often prevented by using a splash barrier (protective equipment) from contamination caused by sneezing or coughing consumers (BfR 2020a, b).

Vegetables and fruits: When vegetables and fruits are prepared, general hygiene rules, such as direct washing of food or frequent hand washing, should be followed (BfR, 2020a).

Frozen foods: To date, there is insufficient evidence for SARS-CoV-2 contamination by food infection. Previous coronaviruses, SARS and MERS, are cold-resistant and can remain intact in frozen-form for up to 2 years at -20 ° C and even -60 ° C. Therefore, the general hygiene rules must be observed (BfR 2020a).

Imported foods: Limited data are available regarding the spread of this virus to foods, imported products (such as mobile phones and toys), tools such as door handles and tools, and plates and tableware (such as knives and forks) (BfR, 2020b). There is no evidence to suggest that imported animals or animal products pose a risk for the spread of the 2019 novel coronavirus in the USA (BfR 2020a).

Food packaging: COVID-19 factor SARS-CoV-2's duration of staying alive outside the living organism may change depending on the environmental conditions. Despite the fact that SARS-CoV-2 lives on cardboard for a maximum of 24 hours and in experimental environments under controlled relative humidity and temperature for steel, plastic and similar hard surfaces virus can remain live for a few days, no data available for contaminated packages exposed to

different environmental conditions and temperatures transmit the infection. However, there is no risk of contamination of the respiratory system by contact with the mucous membranes of the virus found in the skin of contaminated people (for example, by touching the face). Concerns can be raised if people who intervene in packaging, including consumers, comply with regular and effective handwashing and effective general hygiene rules by public health officials (European Commission, Cyprus, 2020).

The European Commission ~~has~~ published an Internet document on the subject "Cyprus, Food Safety and COVID-19" (European Commission Cyprus, 2020). In this, document following information was revealed.

Food workers: Food operators are responsible for the implementation of adequate hygienic measures by their employees, according to EU food safety legislation. General hygiene practices should be applied by food companies and food workers. Additional measures must be taken by business owners and relevant authorities under COVID -19. Within the scope of these measures, keeping the social distance between people or using plexiglass, preventing contact between truck drivers and food facility, prevention of excessive usage of hand disinfectantsmay be stated. The number of employees should be minimized also. Precautions should be taken against being an asymptomatic carrier working in the food business. Within the scope of these precautions, high personal hygiene (none hygienic behaviors such as sneezing or coughing while producing or processing food must be prevented and regular hand washing must be observed), including wearing appropriate, clean and protective clothing when necessary and consistently applying ~~good~~ proper hygiene rules . while handling food products minimize the risk of transmitting viruses. In addition, if an employee's virus test is positive, additional sanitary measures should be taken, depending on the level of risk. In general, food workers should wash their hands frequently with soap and, if necessary, use antiseptic. Food operators should train their employees on how to properly use personal protective

equipment and remind how important it is to comply with the rules for personal hygiene and social distancing rules. (European Commission, Cyprus 2020; Galanakis 2020).

To date, there is no data on the presence of the COVID-19 spreading on food products~~,~~. Likewise, there is no evidence that food is a source or tool of infection. However, theoretically, as door knobs or other surfaces touched by infected people may cause spread of virus, food products if handled by infected people may cause contamination (European Commission, Cyprus, 2020; Galanakis 2020; WHO 2020). Therefore, everyone should follow the advice of public health officials on washing hands. General hygiene rules should be followed when retailers treat food products. Personnel who need to contact food at the supermarkets (for example, cutting meat, slicing meat or dairy products, cleaning fish, packing fruits and vegetables) should wear gloves and change gloves frequently or otherwise wash their hands frequently. Consumers should also fulfill their responsibilities. As a good practice of hygiene in general, customers in stores should not touch food other than what they want to buy to avoid contamination with any pathogens they may have (European Commission, Cyprus, 2020; Desai and Aronoff, 2020).

At home, food should be properly stored and contact between cooked food and raw food must be avoided, , food should be stored after removing the outer packaging, fruit and vegetables should be systematically cleaned and washed thoroughly, cross-contamination between knives, forks, plates and foods should be avoided, and foods to be cooked should be exposed to necessary temperature during enough time period, hands should be washed thoroughly with soap after contact with food and refrigerator and kitchen surfaces should be cleaned frequently (European Commission, Cyprus, 2020; Galanakis 2020).

As a result, in line with current information, the oral-digestive system, in other words, the esophageal-gastrointestinal tract does not play a role in SARS-CoV-2

outbreaks. The main source of transmission is through droplet infection during coughing and sneezing. These droplets are absorbed by the respiratory system, mouth and eye mucous membranes of other people and contamination occurs. In the laboratory studies of SARS coronavirus it was proven that virus has become fully inactivated after 5 minute-contact with conventional detergents at room temperature. Although it is unlikely that this virus will be transported with contaminated food or imported products, regular hygiene rules must be observed every day, such as regular hand washing and compliance with hygiene rules during food preparation (BfR, 2020a). Since this virus is heat sensitive, the risk of infection can be reduced by applying heat to foods (BfR 202b). Widespread hygienic measurements, proper and frequent washing with soap and regular surface cleaning, washing and cleaning of standard home surfactant-based door handles should be practised (BfR 2020a). In enveloped viruses, the surrounding of the genetic material is covered with a layer of fat. Therefore, an enveloped virus is highly sensitive to degreasers such as alcohol or surfactants containing soap and dishwashing detergents. These substances inactivate the virus, causing damage to the envelope layer of the virus. Although no work has been done in this regard, if the dishes or cutlery, are washed in the dishwasher at 60 ° C or above, this virus will most likely be inactivated (BfR, 2020b). In washing with cold water, dense and suitable detergent should be used but detergent should not be applied for long time, and washed materials should be dried immediately (Lai et al., 2005).

5. Methods of Protection from COVID-19

1. Frequent washing of hands: Hands should be washed frequently. This washing procedure should be done especially after cleaning your nose, when you cough or sneeze, when you go to the bathroom and before eating or preparing food (BfR 2020a, b).

Wash your hands immediately with soap and water for at least 20 seconds. If there is no soap or water, your

hands should be cleaned with an alcohol-based hand sanitizer containing at least 60% alcohol. Eyes, nose and mouth should not be touched with unwashed hands (BfR 2020a, b).

2. Cleaning and disinfection: If the surfaces are dirty, they should be cleaned. Detergent or soap and water should be used before disinfection. The use of the most common EPA registered home disinfectants should be preferred and the surface suitable-disinfectant should be selected. Bleach should be diluted. For example; Use 5 tablespoons (1/3 cup) of bleach for 3,785 liters of water or 4 teaspoons of bleach for a quarter of water. Alcohol solutions should contain at least 70% alcohol. Surfaces used on ~~a~~ daily basis should be disinfected frequently (tables, door handles, light switches, countertops, handles, tables, phones, keyboards, toilets, taps and sinks) (BfR 2020a, b). For surface cleaning, 62-71% ethanol, 0,5% hydrogen peroxide, 0,1% sodium hypochlorite should be applied for 1 minute for SAES, MERS and HCoV. But it is not known for COVID-19. However, these agents can be used (Kampf et al.2020).

3. Item sharing: Dishes, glasses, food containers, towels or bedding in your home should not be shared with other people. After using these materials, they should be washed thoroughly with soap and water or put in the dishwasher and washed (BfR 2020a, b).

4. Laundry and textile products: No concrete information is available as to how long the SARS-CoV-2 virus remains live in the textile or washing machine. Textile products such as clothes, bed linen, bedding, towels and underwear of the sick people contaminated with the body fluids of infected people, should be washed in the washing machine with a dense detergent at least 60 ° C and then should be dried. While hand-washing textile products of contaminated people, the textiles touching directly to the skin or exposed to body fluids of sick people should be avoided (Robert Koch Institut, 2020). Widespread hygienic measurements, proper and frequent hand-washing with soap

and regular surface cleaning, disinfecting standard house surfactant-based door handles should be applied (BfR 2020a).

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Chapter VI

"COVID-19" IN THE FRAMEWORK OF A DYSTOPIAN ELEMENT

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Nothing is there to come, and
nothing past, But an eternal
"now" does always last.

Abraham Cowley

Introduction

Artistic forms of human and nature have changed the perception of reality with their development. "How realistically was this painting drawn! How beautifully the painter reflected the generational difference and the battle scenes! It is impossible to separate the people in the picture from the truth! " We started to use sentences like "We are entering a very beautiful garden by saying " Like the Monet Table. " We associate violence, action, adventure, videos with movie scenes.

The concept of "dystopia", which we encounter in fictional products such as novel, can be an example to the situations mentioned above. Based on them, we can also say that the "pandemic" process is like a movie or a novel and that this movie or novel is "dystopic". To say this, we need to study dystopia and its link to the pandemic process.

"Dystopia" means "bad place". Dys / dis, a Greek prefix, means "bad", "sick" or "abnormal". The word is considered to be the opposite of "utopia". Utopia means "good place". Dystopia comes from the word "Eutopia" which means "a beautiful place that does not exist" and means anti-utopia. " (STEEL, 2015, P.60). Poorly ruled,

oppressive, dictatorial environments are dystopian scenes. For dystopian writers, Mina Urgan states that she took her source from utopia, but unlike utopia, she received her source from pessimism and evil. These books, which reflect a dark pessimism, are called 'dystopia'. Utopian writers used to be progressive. 'The situation is bad; If we follow this or that method, the situation would improve. " current dystopia writers are conservative, even reactionary. They think, "The situation is bad, since there is no remedy to improve the situation, it will be a thousand times worse in the future" (Urgan, 1984: 94).

While utopia promises an inaccessible dream, we cannot go beyond the movies, but the reason we are likely to be experiencing "dystopia" may be the basic rules of physics, sociology, and theology. As with the concept of "entropy", as the system gets worse, human communities deteriorate. Dystopic works describe the worsening and "dark" aspect of humanity. According to Nail Bezel, utopias describe a kind of heaven on earth, while dystopias describe the hell created by people trying to build their dream paradise. Utopias suggest harmony for happiness, but dystopias describe fear and pain caused by so-called harmony (Bezel, 1993: 17).

From the past to the present, the most commonly used phrases to manage communities are fears from threats and security measures to be taken against them. This threat can be an invasion, a drought hazard, a health concern or an economic disaster. Managers can sometimes use these threats as a trump card to consolidate their strength. Individuals may sometimes agree to renounce their rights to protect themselves from threats. Power and government are related. Societies feed on issues such as nationalism, belief difference, gender difference in order to strengthen this relationship.

Dystopia writes a scenario to destroy our hopes for the future. Every scenario is about a pessimistic world. Why does dystopia want to instill the concept of "bad place"? Is dystopia describing the world we live in, or is it preparing for

bad prospects? Totalitarian governments may come to mind when the concept of dystopia is mentioned. Because disrupted societies are capital for dystopia. April Spisak says that dystopias characterize societies that are governed by a limited, powerful authority. (Spisak, 2012: 55). Dystopia was first put into literature by John Stuart in 1868. However, examples of true meaning emerged in the twentieth century. This was caused by events and changes in the twentieth century. At that time, humanity, who met technology, met pessimism. These developments affected all fields including literature. Space studies, atomic and nuclear bomb studies, developments in cloning or chemistry have led people to question the new world more deeply. This has been the subject of literary works.

A Dystopian Element "Pandemic"

Dystopia has preserved its existence and turned into a perception thanks to the capitals that life has given to it over a hundred years. This perception is in the form of an external siege. Huxley also mentions a framework for dystopias other than human existence: "There is an externality that has a negative impact on the potentials of the individual, such as internal security, happiness, mind and capacity to love." This siege is thanks to technology, but it can be defined as the dominance, not the use of this technology. Human beings have to survive. For this, while humankind once fought with primitive weapons, it now benefits from the greatest blessings of technology without the need for these weapons. So why has man become the material of dystopia? First of all, it is necessary to answer this. While trying to survive in the early ages, mankind, who hunts for animals and intervenes in the disasters of nature as much as he can, has to share the blessings he has as he grows over time; because as it multiplies, it needs more food, more shelter, or more safety. This situation increased competition among people and turned into wars when this competition place came. After the separation between the growing human population began, conflicts, quarrels, betrayals and deaths also occurred and

human beings began to find solutions to get out of this situation with the least damage.

The individualized person starts to care about his existence and struggles for his life and that of his loved ones at the expense of being alone. While fighting this struggle, he also has instinctive fears and this situation puts people in a defensive position. Such threats have normalized ordering people. Indeed, lately experienced pandemic process exemplifies this situation. After a virus originated in Wuhan city of China, a pandemic process has been launched all over the world as a result of the death of patients with weak immunity, especially chronic diseases and the transmission of a virus which is thought to be produced from private laboratories or transmitted from a bat or mice. Although it was horrifying to see the people who collapsed on the roads, vehicles, at workplaces via social media or on TV, scientists gave promising news to those who strive for getting rid of this virus over time. Social distance rule was one of the first measures put forward to get rid of this process. Though this rule first started between people, it continued between countries and ended with border closures. Solutions such as the closure of public living spaces were applied. Mankind first astonished that their usual single-order life turned into a movie scene, then they got accustomed to this new situation day by day. The strange thing was how they got used to this situation, which affects even their spiritual value sharing, in such a short time. There was only one reason for this: People think as individuals and live as individuals. With this thoughts, people do not want to help someone who has been injured or even died with the fear of having trouble. As people became more individualized, their fears increased and as their fears increased, they agreed to be systematically registered from birth. Moreover, when concepts such as family, homeland, culture, religion stay in the background, the concept of "Self" came to the fore, and then we found ourselves in a dystopian Covid-19 world. People who already individualized became even more individualized in this pandemic process, becoming even afraid of his wife or child.

These fears forced people to obey authority. Otherwise, disobeyment would cause unwanted results for societies. “Life movement in today's societies can be summarized as“ people’s moving from family to school, from school to military barracks, from barracks to factories or employers, to hospitals when they are sick, and to prisons when they somehow object to comply with rightful or unfair rules ”.

Preparedness For the Pandemic Process

While the thought of pandemic is utopian, living this process has made the self-centered person the center of the world. This is a proof that the world that dystopias offer us is not far from reality. We have seen a situation threatening the world and the measures taken by countries that do not want to be affected by this situation. The measures taken by the countries had to restrict fundamental rights, freedoms and needs, and people voluntarily contributed to this dystopic situation by ranking their need for health before their need for freedom. They had to do this, since there were many official rules and restrictions taken by the central government to avoid further losses. The skill of the state structure to protect the society and the power of providing public services is important at that point. The Covid-19 process has shown all the countries that are caught unprepared for this situation that managed the process and that cannot manage the process correctly. For whatever reason, in societies created in dystopias, bureaucratic administration, religious values or technologic developments control masses: In dystopias, society is sometimes under the control of a philosophical or religious authority, sometimes a capital group, sometimes the bureaucratic system and sometimes the technology.

Changing time has also shown its effect on generations. It is not surprising that the first generation to keep up with the pandemic process are today's social media users. In fact, they are the ones who welcome the house closure measure while they are the ones who like to be out of their houses before the pandemic. This shows us how generations integrated into developing and changing living conditions and that it is

easier than expected to work from home via using IT tools. So how should we assess that none of us act to change the future when dystopia depicts a dark pit to us? Dystopia makes people get accustomed to what has happened so far. Therefore, people are not expected to hope to change today despite the darkness of future and great risks which people are familiar with. What is expected of dystopias is voluntary obedience. Pandemic process shows us this voluntary obedience even at our homes. "What is important in the dystopia system is everybody's volunteerism. The ability to receive all kinds of services that can be reached with a single touch of a screen and even to fulfill its duties has gradually connected the society to the house. , The perception of the virtual outside world has manipulated the family institution in the families using online services. These facilities hurled family members to other worlds controlled by the system, even when they were all in the same house." The place where this obedience takes place may even be a room rather than a house. Foucault, who sees the society in a room, claims that all these thoughts emerged within the framework of permanent truths or under their effects. After all, the house or the room shows us that there is no need for space for the obedience that starts within the human self.

Conclusion

The concept of colonialism that started with the Industrial Revolution continues to exist even today, and technological, psychological, economic or cyber wars continue between countries. The only difference between the wars of today and the past is that they take place more systematically and more effectively depending on technological developments. These developments have added words such as manipulation, mass control, artificial intelligence, coding and information to the literature of dystopian works that marked the 20th century. If we count the new words engraved in our memory in the pandemic process, it is almost impossible to remove dystopia from our lives. Within the framework created by the dystopias with a pessimistic approach, the heroes gradually become a part of

the system and non-questioning, thinking, obedient individuals. We see these figures in Orwell's works. The hero of 1984, for example, loves the person or system that runs the country unconditionally and accepts that two plus two equals five instead of four. Similarly, In Huxley's Brave New World, people are not aware of what they laugh at or why they stop thinking. There is no phenomenon of self in Zamyatin's work called "We" and people have no name. An obedient society that does not question and think submits all kinds of dangers and continues their lives with the thought of "I shouldn't face any danger" rather than seeking solutions to the danger. Although the pandemic process is not fictional, it created that feeling. We got all the news from a single screen and became afraid of even our shadows. We were shocked and thought about conspiracy theories. Moreover, our shock of the process was not only about the disease itself. The news of earthquakes, meteor falling, grasshopper invasions and tsunami rumors have caused a great uncertainty among people. Whatever the reason, unfair sharing created by wars of interest has individualized people and this individuality has proved itself in every element that threatens humanity. The figures in dystopic works show that the truth and fiction are intertwined also in pandemic process. In fact, we are always inclined to build fiction and then live it. To live what we have built in our fiction, we apply to technology. While we need the technology to be the most powerful, we agree that the technology is more powerful than us and we let it rule and control us.

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