

## COVID-19: A Current Brief Review

### COVID-19: Güncel Kısa Bir Derleme

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#### ABSTRACT

Coronavirus infection has become an important public health concern because of its increasing prevalence, serious complications and mortality. The previous pathogenic coronaviruses severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) were mortal virus infections in past 15 years. Today the current epidemic caused by a new coronavirus (SARS-CoV-2) is called coronavirus disease of 2019 (COVID-19). The virus causes different illness, from upper respiratory tract infections like the common cold, to lower respiratory tract infections such as bronchitis, pneumonia, and SARS. The coronavirus can be transmitted through small infected droplets from a person with COVID-19 during coughs or exhales. Additionally, it can also be transmitted from contaminated environment or objects. A number of precautions to prevent transmission of COVID-19 have been applied to stop the current outbreak. There is no certain treatment of the disease but the studies on vaccines and treatment continue. In this review, we aimed to give a brief information about COVID-19.

Keywords: COVID-19, SARS-COV-2, pandemia

#### ÖZ

Koronavirüs enfeksiyonu artan prevalansı, ciddi komplikasyonları ve mortalitesi nedeniyle önemli bir halk sağlığı sorunu haline gelmiştir. Son 15 yıl içinde bundan önceki patojenik ölümcül koronavirüsler ciddi akut solunum sendromu koronavirüs (SARS-CoV) ve Orta Doğu solunum sendromu koronavirüs (MERS-CoV) enfeksiyonlarıydı. Bugün yeni bir koronavirüsün (SARS-COV-2) neden olduğu mevcut salgın 2019 yılının koronavirüs hastalığı (COVID-19) olarak adlandırılmaktadır. Hastalık soğuk algınlığına benzeyen üst solunum yolu enfeksiyonlarından bronşit, pnömoni ve hatta SARS enfeksiyonlarına kadar değişik derecelerde hastalığa neden olabilir. Damlacıklar veya doğrudan temas yoluyla insandan insana bulaşarak yayılabilir. Ayrıca kontamine olmuş cisimler veya çevre ile de bulaşabilir. Mevcut salgını kontrol etmek için; COVID-19'un kişiden kişiye bulaşmasını azaltmak önemli ve bunun için kapsamlı önlemler gerekmektedir. Hastalığın kesin tedavisi bilinmemektedir ancak aşılar ve tedavi ile ilgili çalışmalar devam etmektedir. Bu derlemede COVID-19 ile ilgili kısa bir bilgi verilmesi amaçlanmıştır.

Anahtar kelimeler: COVID-19, SARS-COV-2, pandemi

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## Introduction

Coronavirus was called first by June Almeida and David Tyrrell. They investigated and studied on human coronaviruses during 1930 when an acute respiratory infection of animals shown to be caused by infectious bronchitis virus [1]. Coronaviruses are big, spherical particles with surface projections. The diameter of the virus particles is approximately 125 nm. The diameter of the envelope is 85 nm and the spikes are 20 nm long [2]. In electron microscope the envelope of the virus seen as a distinct pair of electron-dense shells. The scientific name for coronavirus is Orthocoronavirinae or Coronavirinae [3]. They are grouped in two subgroups. Alphacoronaviruses and betacoronaviruses infect mammals. Gammacoronaviruses and deltacoronaviruses infect birds [4]. Even all these viruses have a genetic relationship; they can cause different diseases with different severities. Some can kill more than 30% of the infected patients such as MERS-CoV, and some are relatively benign, such as the common cold. Coronaviruses can cause colds with major symptoms, such as fever, headache and sore throat. Moreover; they can lead to pneumonia (viral pneumonia or secondary bacterial pneumonia) and bronchitis [4,5]. On the other hand, the coronavirus can also cause extrapulmonary disease such as cardiovascular, neurological, renal and hepatic diseases [6,7-9].

The World Health Organization office of China was informed of cases of pneumonia of unknown etiology in Wuhan City, Hubei Province, on the last day of 2019 [9]. A novel coronavirus currently termed coronavirus disease of 2019 was announced as the causative agent by Chinese authorities. According to the different reports, the COVID-19 symptoms ranged from mild to severe diseases that can ultimately lead to death. The symptoms usually appear in two weeks time after viral exposure which includes fever, cough, shortness of breath and pneumonia. The severe cases showed respiratory, hepatic, gastrointestinal and neurological complications that can leads to mortality. The transmission of COVID-19 can occur via respiratory droplets or from contaminated environment and objects [5,6,10-12].

## Epidemiology

The virus spreads rapidly more than 200 countries in a short time. Approximately 7 million infected cases of COVID-19 with a total of 400857 deaths were reported as of June 8, 2020. The numbers of infected cases and death associated with the disease increased daily (figure 1). In Turkey 170132 infected cases and 4632 associated deaths were reported (figure 2) [10,13]. A total of 2039194 tests were performed and 127943 patients recovered from disease. There are still 31429 patients with active disease. The number of disease is correlated with the number of tests performed. All these data can vary according to the regions, quality of healthcare system, treatment options, prevention methods, awareness of the people. The characteristics of the patients such as age, sex, and overall health also effect the results. The men, older people and patients with chronic diseases were reported as more prone to disease in some studies [14,15].

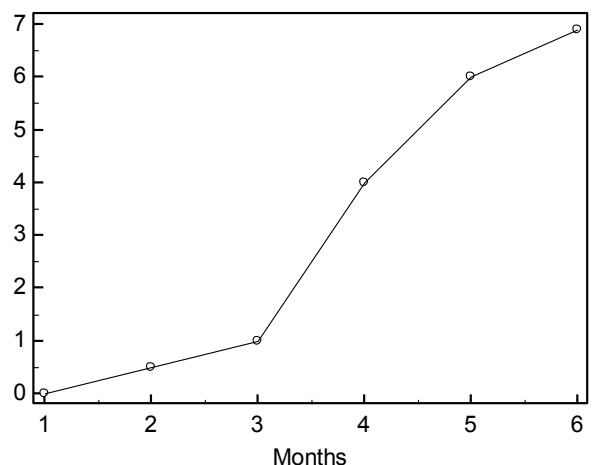


Figure 1: The total COVID-19 cases throughout the world between January 2020-June 2020. ( MedCalc v19.2.6, licenced to Şakir Özgür Keşkek) 1-6: January 2020 –June 2020 ([https:// covid19.who.int/](https://covid19.who.int/). Access date 08.06.2020.)

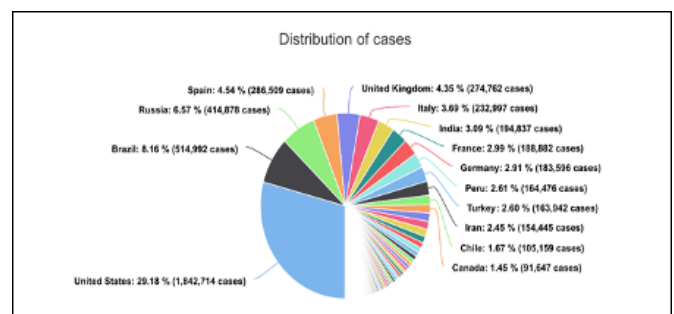


Figure 2: Distribution of cases according to the countries (<https://www.worldometers.info/coronavirus/#/countries>. Access date 01.06.2020.)

## Virus structure

Coronaviruses are enveloped, non-segmented, positive-sense single-stranded RNA virus genomes with size ranging from 26 to 32 kilobases. According to the best knowledge, today the biggest viral RNA genome is belonging to the coronavirus genome. It is characterized by club-like spike projecting from its surface [16]. The genetic analyses of SARS-CoV-2 genomes and classified out two prevalent evolution types of SARS-CoV-2, L type (~70%) and S type (~30%). The strains in L type, derived from S type, are more thrusting and contagious [17]. The virion has a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid protein. The interaction of receptor binding domain located in the S protein and target receptor on the host cell surface such as Angiotensin converting enzyme 2 (ACE2) are important for infection [4,6,17,18].

## Clinic

The symptoms of COVID-19 infection come out after an incubation period of near one week. The period from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days. The characteristics of the patient; age, sex, immune system and co-morbidities effect the incubation period [4,12,19]. Fever is the most common symptom, but it is highly variable according to the patient status. On the other hand, critically ill and older patients may not have fever. Most of the COVID-19 patients have similar symptoms, in addition to the fever such as cough, loss of appetite, fatigue, myalgia and headache (table 1). Sneezing, runny nose, sore throat, and skin lesions are less common symptoms. Loss of smell was reported in 30% of cases in some countries. Majority of patients with SARS-CoV-2 infection presented with mild flu-like symptoms and a few patients are in critical condition and rapidly develop acute respiratory distress syndrome, respiratory failure, multiple organ failure, even deaths [12,19-22]. A small number of cases do not have any symptoms associated with COVID-19 in any time [23].

Symptomatic, pre-symptomatic and asymptomatic transmissions are three ways for transmission of COVID-19. Symptomatic transmission occurs via close contact through respiratory droplets, contact

with the infected individuals or from environment due to the contaminated objects and surfaces. Pre-symptomatic transmission may occur when viral load is high enough to enable transmission just before the symptoms appear [18,20].

Table 1: Frequency of symptoms in COVID-19 [17].

Symptom	Range
Fever	83–99%
Cough	59–82%
Loss of appetite	40–84%
Fatigue	44–70%
Shortness of breath	31–40%
Coughing up sputum	28–33%
Muscle aches and pains	11–35%

The complications of the disease are pneumonia, acute respiratory distress syndrome, multi-organ failure, septic shock, and death [24]. Cardiovascular complications may include heart failure and arrhythmias. Increased blood coagulation may be a hematological manifestation [25]. One of four patients with COVID-19 have elevated liver enzymes due to the liver injury [26]. Central nervous system complications may include seizure, stroke, encephalitis, and Guillain Barre syndrome [27].

## Diagnosis

Identification, examination and confirmation of pathogens can be achieved by laboratory studies. For diagnosis of coronavirus, respiratory materials including nasopharyngeal swabs, oropharyngeal swabs, stool sample, tissue biopsies, blood sample, urine sample can be tested. Real-time Reverse transcription PCR (RT-PCR) is the best way for the detection of virus today [19].

Blood samples of COVID-19 have included lymphopenia with reduction of CD4 and CD8 lymphocytes, prolonged prothrombin time, elevated lactate dehydrogenase, d-dimer, alanine transaminase, ferritin and creatinine kinase [4,5]. Patients with severe illness had higher plasma level of cytokines [25]. There are some difficulties for the diagnosis of COVID-19 because laboratory detections and radiographic images are not always in agreement with clinical features and contact histories of patients [19].

Radiological findings of COVID-19 pneumonia

are multiple lung opacities, multiple types of the opacity. Especially bilateral lower lobes of the lungs are involved [26]. Diagnosis of COVID-19 has to be depend on detailed understanding of clinical features, radiographic features, and laboratory detection [19].

### Treatment

Today, we have no any effective approved vaccine or anti-viral therapeutic agents to treat COVID-19. The disease management focuses on supportive care which may include fluid therapy, oxygen support, and supporting other affected vital organs. Lifestyle management with healthy diet, exercise and body hygiene are recommended to improve immunity. Many type of medications are being evaluated for the treatment of COVID-19 including remdesivir, favipiravir, chloroquine, hydroxychloroquine, lopinavir/ritonavir, and lopinavir/ritonavir combined with interferon beta [27].

The effective treatment options against COVID-19 can either based on the use of broad-spectrum anti-viral drugs. Remdesivir is an RNA polymerase inhibitor and inhibits SARS-CoV-2 in vitro tests and clinical recovery was observed in patients treated with the remdesivir [28].

Favipiravir is an RNA dependent RNA polymerase inhibitor. It exerts an antiviral action more potent than lopinavir/ritonavir in the treatment of COVID-19, and that there are no serious adverse reactions reported for this drug [29].

Chloroquine, an antimalarial agent with anti-inflammatory and immunomodulatory activities, has achieved to an important position as a potential therapeutic option for the management of COVID-19 [30]. Chloroquine increases endosomal pH of the cell and block virus infection.

Tocilizumab, also known as atlizumab, is an immunosuppressive drug. It is a monoclonal antibody against the interleukin-6 receptor. Tocilizumab can prevent cytokine storm in severe coronavirus disease [31].

Peptidic fusion inhibitors, antiSARS-CoV-2 neutralizing monoclonal antibodies, anti-ACE2 monoclonal antibodies and protease inhibitors may be a choice in the future [32-34].

Antibodies of the patients recovered from COVID-19 is being investigated for a passive immunisation. The FDA has approved the using of blood plasma from patients who have recovered from COVID-19 [35].

### Prognosis

The symptoms, clinical properties of COVID-19 can differ in wide spectrum. The disease may occur with a few or no symptoms, similar with other common respiratory diseases infectious such as the common cold. Non serious cases may recover in two weeks time, while those with severe diseases may take three weeks to two months to recover. The duration of the disease from the onset of the symptoms to death has ranged from two to eight weeks [36].

Hypertension, diabetes mellitus, obesity and cardiovascular disease are common in most of the patients who die of COVID-19. ARDS was found the common cause of death in autopsy series [36,37].

Smokers were more likely to have severe symptoms of COVID-19 and they also more likely to die according to the non-smokers. approximately 2.4 times more likely to require intensive care or die compared to non-smokers. Mortality rate is lower in patients younger than 50 years compared to patients older than 70 years [36,38].

### Prevention

The WHO has stipulated strict recommendations to reduce and prevent the spread of the disease. Wearing of a mask is convenient for persons who have symptoms of COVID-19. Health caregivers and other health workers should also wear mask when they faced with suspected covid 19 patients [39]. The cleaning of hands frequently with an alcohol-based hand rub, and wash with soap for at least 20 seconds. Avoid touching eyes, nose and mouth. Objects and surfaces should be kept clean and disinfected in the environment. At least 1 meter distance between the persons should be maintained. Finally, it is very important to stay at home during pandemia [10,40].

### Conclusion

COVID-19 is the current pandemia caused

by a new coronavirus today. The previous coronaviruses and the last one have a genetic relationship but they cause different diseases with different levels of severities. The virus spread to more than 200 countries with Turkey in a short time. The numbers of infected cases and death associated with the disease increased daily. Although, fever, headaches, myalgia, and coughing are common symptoms of the disease the infection can presented with different clinical spectrum vary from mild flu-like symptoms to acute respiratory distress syndrome. Diagnosis of COVID-19 has to be based on detailed understanding of clinical features, radiographic features, and laboratory detection. There is no any effective approved vaccine or anti-viral therapeutic agents to treat COVID-19 today. Many type of medications are being evaluated for the treatment including remdesivir, favipiravir, chloroquine, hydroxychloroquine etc. The current approach to disease management focuses on supportive care. Both developed and developing countries should work for the advance and update of their health systems. Cooperation between these countries is important for disease prevention [41]. There are many ways for admission of the disease. It should not be forgotten that to reduce and/or prevent the spread of the disease is the most significant way of protection now [42].

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#### REFERENCES

1. Tyrrell DA, Fielder M. *Cold Wars: The Fight Against the Common Cold*. Oxford University Press. ISBN 978-0-19-263285-2. ; 2002. p. 96.
2. Almeida JD, Berry DM, Cunningham CH, Hamre D, Hofstad MS, Mallucci L et al. "Virology: Coronaviruses". *Nature*. 1968; 220 (5168): 650. doi:10.1038/220650b0
3. Groot RJ, Baker SC, Baric R, Enjuanes L, Gorbalenya AE, Holmes KV et al. "Family Coronaviridae". In King AM, Lefkowitz E, Adams MJ, Carstens EB, International Committee on Taxonomy of Viruses, International Union of Microbiological Societies. *Virology Division (eds.)*. Ninth Report of the International Committee on Taxonomy of Viruses. Oxford: Elsevier, 2011. pp. 806–28. doi:10.1016/B978-0-12-384684-6.00068-9.
4. Lai Chih-Cheng, Shih Tzu-Ping, Ko Wen-Chien, Tang Hung-Jen, Hsueh Po-Ren. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Coronavirus Disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents*. 2020; 55(3): 105924. doi: 10.1016/j.ijantimicag.2020.105924
5. Phan T. Novel coronavirus: From Discovery to Clinical Diagnostics. *Infect Genet Evol*. 2020;79:1-2. doi: 10.1016/j.meegid.2020.104211.
6. Hasöksüz M, Kılıç S, Saraç F. Coronaviruses and SARS-CoV-2. *Turk J Med Sci*. 2020; 50: 549-56.
7. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C. Cardiac and arrhythmic complications in patients with COVID-19. *J Cardiovasc Electrophysiol*. 2020; 31(5): 1003-1008. doi:10.1111/jce.14479
8. Xu L, Liu J, Lu M, Yang D, Zheng X. "Liver injury during highly pathogenic human coronavirus infections". *Liver International*. 2020; 40 (5): 998–1004. doi:10.1111/liv.14435
9. Carod-Artal FJ. Neurological complications of coronavirus and COVID-19. *Complicaciones neurológicas por coronavirus y COVID-19*. *Rev Neurol*. 2020; 70(9):311-22. doi:10.33588/rn.7009.2020179
10. World Health Organization (WHO). *Coronavirus*. Geneva: WHO; 2020 [Accessed 08 June 2020]. Available from: <https://www.who.int/health-topics/coronavirus>
11. Zhu Na, Zhang Dingyu, Wang Wenling, Li Xingwang, Yang Bo, Song Jingdong et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Eng J Med*. 2020; 382(8):727-33. doi: 10.1056/NEJMoa2001017
12. Rothan Hussin A, Byrareddy Siddappa N. The Epidemiology and Pathogenesis of Coronavirus Disease (COVID-19) Outbreak. *J.Autoimmun*. 2020 Feb 26. [Epub ahead of print] doi: 10.1016/j.jaut.2020.102433
13. Coronavirus Update (Live):<https://www.worldometers.info/coronavirus>. Access date: 25.05.2020.
14. Adams ML, Katz DL, Grandpre J. Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States. *Emerg Infect Dis*. 2020; 26(8): 10.3201/eid2608.200679. doi:10.3201/eid2608.200679
15. Wenham C, Smith J, Morgan R. Gender and COVID-19 Working Group. COVID-19: the gendered impacts of the outbreak. *Lancet*. 2020; 395(10227): 846-48. doi:10.1016/S0140-6736(20)30526-2
16. Woo PC, Huang Y, Lau SK, Yuen KY. "Coronavirus genomics and bioinformatics analysis". *Viruses*. 2010; 2 (8): 1804–20. doi:10.3390/v2081803.
17. Liu Jia, Zheng Xin, Tong Qiaoxia Tong, Li Wie, Wang Baoju, Sutter Kathrin et al. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERS-CoV, and 2019-nCoV. *J Med Virol*. 2020; 92(5):491-4. doi: 10.1002/jmv.25709.
18. Malik YA. Properties of Coronavirus and SARS-CoV-2. *Malays J Pathol*. 2020; 42(1): 3-11. PMID: 32342926
19. Yixuan W, Yuyi W, Yan C, Qingsong Q. Unique Epidemiological and Clinical Features of the Emerging 2019 Novel Coronavirus Pneumonia (COVID-19) implicate special control measures. *J Med Virol*. 2020. 2020 Mar 5. [Epub ahead of print] doi: 10.1002/jmv.25748
20. Yan-Rong G, Qing-Dong C, Zhong-Si H, Yuan-Yang T, Shou-Deng C, Hong-Jun J et al. The Origin, Transmission and Clinical Therapies on Coronavirus Disease 2019 (COVID-19) Outbreak – an Update on the Status. *Mil Med Res*. 2020; 7(1): 11. doi: 10.1186/s40779-020-00240-0
21. "Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)". Centers for Disease Control and Prevention (CDC). Access Date: 6 April 2020.
22. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) (PDF) (Report). World Health Organization (WHO). Date: 16–24 February 2020.
23. Lai CC, Liu YH, Wang CY, Wang YH, Hsueh MY SC, Yen MY et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths [published online ahead of print, 2020 Mar 4]. *J Microbiol Immunol Infect*. 2020; doi:10.1016/j.jmii.2020.02.012
24. Goh KJ, Choong MC, Cheong EH, Kalimuddin S, Wen SD, Phua GC et al. Rapid Progression to Acute Respiratory Distress Syndrome: Review of Current Understanding of Critical Illness from COVID-19 Infection. *Ann Acad Med Singapore*. 2020; 49(3):108-118. PMID: 32200400
25. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [published correction appears in *Lancet*. 2020 Jan 30.]. *Lancet*. 2020; 395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
26. Fu F, Lou J, Xi D, Bai Y, Ma G, Zhao B. Chest computed tomography findings of coronavirus disease 2019 (COVID-19) pneumonia. *Eur Radiol*. 2020;1-10. doi: 10.1007/s00330-020-06920-8.
27. Li G, De Clercq E. "Therapeutic options for the 2019 novel coronavirus (2019-nCoV)". *Nature Reviews. Drug Discovery*. 2020; 19 (3): 149–150. doi:10.1038/d41573-020-00016-0
28. Sun D. Remdesivir for Treatment of COVID-19: Combination of Pulmonary and IV Administration May Offer Additional Benefit. *AAPS J*. 2020; 22(4):77. Published 2020 May 26. doi:10.1208/s12248-020-00459-8
29. Dong L, Hu S, Gao J. Discovering drugs to treat coronavirus disease 2019 (COVID-19). *Drug Discov Ther*. 2020; 14(1), 58-60. doi: 10.5582/ddt.2020.01012
30. Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virol J*. 2005; 2:69. Published 2005 Aug 22. doi:10.1186/1743-422X-2-69
31. Zhang Q, Wang Y, Qi C, Shen L, Li J. Clinical trial analysis of 2019-nCoV therapy registered in China [published online ahead of print, 2020 Feb 28]. *J Med Virol*. 2020;10.1002/jmv.25733. doi:10.1002/jmv.25733
32. Dhama K, Sharun K, Tiwari R, Dadar M, Malik YS, Singh KP et al. COVID-19, an emerging coronavirus infection: advances and prospects in designing and developing vaccines, immunotherapeutics, and therapeutics [published online ahead of print, 2020 Mar 18]. *Hum Vaccin Immunother*. 2020;1-7. doi:10.1080/21645515.2020.1735227
33. Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). *Biosci Trends*. 2020;14(1):69-71. doi:10.5582/bst.2020.01020
34. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020; 30:269–71. doi: 10.1038/s41422-020-0282-0
35. Casadevall A, Pirofski LA. The convalescent sera option for containing COVID-19. *J Clin Invest*. 2020;130(4):1545-1548. doi:10.1172/JCI138003

36. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Access date: 21 March 2020
37. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy [published online ahead of print, 2020 Mar 23]. *JAMA*. 2020;10.1001/jama.2020.4683. doi:10.1001/jama.2020.4683
38. Vardavas CI, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. *Tob Induc Dis*. 2020;18:20. Published 2020 Mar 20. doi:10.18332/tid/119324
39. Beyazadam D, Alimoglu O. Healthcare Workers Are Losing Their Lives in the Battle of Covid-19 All Over the Globe. *Anadolu Klinigi Tıp Bilimleri Dergisi*.2020; 25(1):183-184.
40. Türkiye Cumhuriyeti Sağlık Bakanlığı COVID 19 Rehberi (14.04.2020) Access:https://covid19bilgi.saglik.gov.tr/depo/rehberler/COVID-19\_Rehberi.pdf?-type=file
41. Lee Andrew. Wuhan novel coronavirus (COVID-19): why global control is challenging? *Public Health*.2020;179:A1-A2 doi: 10.1016/j.puhe.2020.02.001.
42. Demirbilek Y, Pehlivanürk G, Özgüler ZO, Meşe EA. COVID-19 outbreak control, example of ministry of health of Turkey. *Turk J Med Sci*. 2020;50: 489-94.