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Review

What We Learned about COVID-19 So Far? Notes from Underground

Fatma Tokgöz Akyıl[1], Dilek Karadoğan[2], Canan Gündüz Gürkan[3], Aycan Yüksel[4], Hüseyin Arıkan[5], Tuğba Şişmanlar Eyüboğlu[6], Nagehan Emiralioğlu[7], Tuğba Ramaslı Gürsoy[6], İrem Şerifoğlu[8], Zehra Nur Töreyin[9], Feride Marim[10], Bilge Yılmaz Kara[2], Hilal Özakıncı[11], Elif Develi[12], Selin Çakmakçı[13], Tuba Çiftçi Küsbeci[14], Oğuz Karcıoğlu[15], Pınar Yıldız Gülhan[16], Merve Erçelik[16], Berrin Er[17], Özlem Ataoğlu[16], Demet Polat[18], İlknur Kaya[19], Tuğba Aslı Önyılmaz[20], Asena Aydın[21], Deniz Kızılırmak[22], Aslıhan Banu Er[23], Mukaddes Kılınç[24], Fatma Esra Günaydın[25], Selçuk Gürz[26], Selen Karaoğlanoğlu[27], Selma Çelik[28], Dorina Esendağlı[29], Hüseyin Toptay[30], Ümran Özden Sertçelik[31], Metin Akgün[32]

[1]Department of Chest Diseases, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Turkey
[2]Department of Chest Diseases, Recep Tayyip Erdoğan University School of Medicine, Rize, Turkey
[3]Department of Chest Diseases, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Turkey
[4]Department of Chest Diseases, Ufuk University, School of Medicine, Ankara, Turkey
[5]Internal Medicine Intensive Care Unit, Yüzüncü Yıl University, Dursun Odabas Medical Center, Van, Turkey
[6]Department of Pediatric Pulmonology, Gazi University School of Medicine, Ankara, Turkey
[7]Department of Pediatric Pulmonology, Hacettepe University School of Medicine, Ankara, Turkey
[8]Department of Chest Diseases, Kırıkhan State Hospital, Hatay, Turkey
[9]Department of Occupational Health and Diseases, Adana City Research and Training Hospital, Adana, Turkey
[10]Department of Chest Diseases, Kütahya University of Health Sciences, School of Medicine, Kütahya, Turkey
[11]Department of Pathology, Ankara University School of Medicine, Ankara, Turkey
[12]Department of Physiotherapy and Rehabilitation, Yeditepe University Faculty of Health Sciences, İstanbul, Turkey
[13]Department of Chest Diseases, Dokuz Eylül University School of Medicine, İzmir, Turkey
[14]Department of Chest Diseases, Yozgat City Hospital, Yozgat, Turkey
[15]Department of Chest Diseases, Çubuk Halil Sivgin State Hospital, Ankara, Turkey
[16]Department of Chest Diseases, Düzce University School of Medicine, Düzce, Turkey
[17]Internal Medicine Intensive Care Unit, Hacettepe University School of Medicine, Ankara, Turkey
[18]Department of Chest Diseases, Mersin University School of Medicine, Mersin, Turkey
[19]Department of Chest Diseases, Ardahan State Hospital, Ardahan, Turkey
[20]Department of Chest Diseases, Konak Hospital, İzmir, Turkey
[21]Department of Chest Diseases, Kestel State Hospital, Bursa, Turkey
[22]Department of Chest Diseases, Manisa Celal Bayar University School of Medicine, Manisa, Turkey
[23]Department of Chest Diseases, Denizli State Hospital, Denizli, Turkey
[24]Intensive Care Unit, Ankara Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey
[25]Department of Allergy and Immunology, Uludağ University School of Medicine, Bursa, Turkey
[26]Department of Thoracic Surgery, Ondokuz Mayıs University School of Medicine, Samsun, Turkey
[27]Department of Chest Diseases, Ordu University School of Medicine, Ordu, Turkey
[28]Department of Nursing, Yeditepe University Faculty of Health Sciences, İstanbul, Turkey
[29]Department of Chest Diseases, Baskent University School of Medicine, Ankara, Turkey
[30]Intensive Care Unit, Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, Izmir, Turkey
[31]Department of Chest Diseases, Hacettepe University School of Medicine, Ankara, Turkey
[32]Department of Chest Diseases, Ataturk University School of Medicine, Erzurum, Turkey

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Abstract

The novel coronavirus pandemic poses a major global threat to public health. Our knowledge concerning every aspect of COVID-19 is evolving rapidly, given the increasing data from all over the world. In this narrative review, the Turkish Thoracic Society Early Career Taskforce members aimed to provide a summary on recent literature regarding epidemiology, clinical findings, diagnosis, treatment, prevention, and control of COVID-19. Studies revealed that the genetic sequence of the novel coronavirus showed significant identity to SARS-CoV and MERS-CoV. Angiotensin-converting enzyme 2 receptor is an important target of the SARS-CoV-2 while entering an organism. Smokers were more likely to develop the disease and have a higher risk for ICU admission. The mean incubation period was 6.4 days, whereas asymptomatic transmission was reported up to 25 days after infection. Fever and cough were the most common symptoms, and cardiovascular diseases and hypertension were reported to be the most common comorbidities among patients. Clinical manifestations range from asymptomatic and mild disease to severe acute respiratory distress syndrome. Several patients showed typical symptoms and radiological changes with negative RT-PCR but positive IgG and IgM antibodies. Although radiological findings may vary, bilateral, peripherally distributed, ground-glass opacities were typical of COVID-19. Poor prognosis was associated with older age, higher Sequential Organ Failure Assessment score, and high D-dimer level. Chloroquine was found to be effective in reducing viral replication in vitro. Likewise, protease inhibitors, including lopinavir/ritonavir, favipiravir, and nucleoside analogue remdesivir were proposed to be the potential drug candidates in COVID-19 management. Despite these efforts, we still have much to learn regarding the transmission, treatment, and prevention of COVID-19.

KEYWORDS: Hydroxychloroquine, SARS-CoV-2, Real-Time PCR.

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Address for Correspondence: Dilek Karadoğan, Department of Chest Diseases, Recep Tayyip Erdoğan University School of Medicine, Rize, Turkey
E-mail: cakmakcidilek@yahoo.com

INTRODUCTION

In December 2019, Wuhan in the Hubei province of China became the epicenter of a pneumonia outbreak with an unknown cause and garnered global attention. On January 7, 2020, Chinese scientists reported a novel coronavirus as the cause of pneumonia in patients in Wuhan, which was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) later on. Coronavirus disease (COVID-19) was the official name of the 2019 novel coronavirus as announced by the World Health Organization (WHO) [1]. Following the increasing number of cases and the widening geographical spread of the disease worldwide, COVID-19 spread to many countries by January 2020 [2, 3]. Consequently, on March 12, 2020, WHO announced COVID-19 outbreak a pandemic [4]. By April 3, 2020, there were 1,000,249 cases of infection and 51.515 deaths in 207 countries, and COVID-19 pandemic continues to be a global threat [5]. Since the first COVID-19 case reported on March 11, 2020, Turkey has also been confronting the challenges of COVID-19 similar to other countries worldwide [6].

Early reports from China and other countries regarding transmission dynamics; clinical, laboratory, and radiological manifestations; diagnosis; and treatment have guided the scientists in the struggle with COVID-19. Patients with comorbidities and those older than 60 years were classified as being at risk for severe disease as well as high mortality [7]. The use of real time-PCR along with computed tomography of the chest has been recommended for diagnosis [8, 9]. Certain immunomodulatory, anti-inflammatory, and antiviral agents such as hydroxychloroquine (HCQ), oseltamivir, azithromycin, and favipiravir have been used in the treatment of COVID-19 thus far [10]. Precautions to protect healthcare professionals and workers from COVID-19 infection are critical [11].

The outbreak dynamics strongly indicated sustained human-to-human transmission and emphasized the importance of personal hygiene, social isolation, and quarantine of the contacts of infected patients [12]. Despite nonspecific clinical and radiological findings of patients with COVID-19, scientists from all over the world tried to build algorithms out of common findings for facilitating and accelerating the diagnosis and treatment initiation [13, 14]. However, the increasing number of positive cases has thrown up atypical presentations as well as difficulties in diagnosis and treatment [15-17]. Thus, dedicated healthcare professionals sharing their experiences aside from the overwhelming clinical routine have enlightened their colleagues working at different levels of healthcare institutions [18]. Being at the forefront of the struggle against COVID-19, specialists of pulmonary diseases, infectious diseases, emergency medicine, critical care, and radiology, as well as the associated professional societies, have an important role to play in contributing to the ever-evolving knowledge on the current literature on COVID-19 pandemic.

Members of the Turkish Thoracic Society Early Career Taskforce have been screening and sharing the most recent and relevant data on COVID-19 with their colleagues since the outbreak in Turkey [19]. In the current review, we aimed to summarize the scientific articles regarding the novel coronavirus in terms of epidemiology, clinical findings, diagnosis, treatment, prevention, and control. This review can provide meaningful contribution for further research as well as daily practice of clinicians.

A comprehensive literature search was conducted, mainly using PubMed and Embase. The search was limited to publications written in English and published between January and April 2020. The following search terms were used: "COVID-19," "coronavirus disease," "severe acute respiratory syndrome coronavirus 2," and "SARS-CoV-2." An initial screening process resulted in the exclusion of duplicate articles. A final selection of 49 articles was made, including observational studies, systematic reviews, guidelines, and case series.

MAIN POINTS

- Turkish Thoracic Society Early Career Taskforce members aimed to provide a summary of literature regarding epidemiology, clinical findings, diagnosis, treatment, prevention, and control of COVID-19 at the beginning of pandemic, end of March 2020. Angiotensin-converting enzyme 2 receptor is an important target of the SARS-CoV-2 while entering an organism.
- Clinical manifestations range from asymptomatic and mild disease to severe acute respiratory distress syndrome. Several patients showed typical symptoms and radiological changes with negative RT-PCR but positive IgG and IgM antibodies.
- Although radiological findings may vary, bilateral, peripherally distributed, ground-glass opacities were typical of COVID-19. Chloroquine, protease inhibitors, including lopinavir/ritonavir, favipiravir, and nucleoside analogue remdesivir were proposed to be the potential drug candidates in COVID-19 management.

CLINICAL and RESEARCH CONSEQUENCES

Epidemiology and Transmission of the Disease

COVID-19 is caused by SARS-CoV-2 and represents a major public health concern [20]. In Wuhan, Hubei Province, China, a cluster of patients was diagnosed with pneumonia of an unknown etiology in late December 2019. These patients were epidemiologically linked to a single local fish and wild animal market. The genetic sequence of the COVID-19 showed more than 80% identity to SARS-CoV and 50% to MERS-CoV [21]. On March 11, 2020, WHO announced COVID-19 a pandemic. Person-to-person transmission occurs through direct contact or through droplets spread by coughing or sneezing from an infected individual [20]. In a small study conducted on pregnant women in their third trimester infected with COVID-19, there was no transmission from mother to child. However, all the pregnant mothers underwent cesarean sections; hence, it remains unclear whether transmission can occur during vaginal birth. Entry of SARS-CoV-2 into the host cells is most likely via the angiotensin-converting enzyme 2 (ACE2) receptor. The clinical spectrum of the disease can be very heterogeneous. In a

study reporting the viral RNA shedding patterns observed in patients with mild and severe COVID-19, the mean nasopharyngeal swab viral load of severe cases was 60 times higher than that of mild cases, suggesting that higher viral loads are associated with severe clinical outcomes [22]. Mild cases were found to have an early viral clearance, with 90% of these patients repeatedly testing negative by RT-PCR on day 10 after onset. By contrast, all severe cases still tested positive at or beyond day 10 [22]. Aerosol and surface stability of SARS-CoV-2 are similar to those of SARS-CoV-1. SARS-CoV-2 remained viable in aerosols for 3 hours, with a reduction during these 3 hours in the infectious titer [23]. SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces, although the virus titer was greatly reduced [23]. No viable SARS-CoV-2 was measured after 4 hours on copper and after 24 hours on cardboard [23]. Aerosol and fomite transmission of SARS-CoV-2 are plausible because the virus can remain viable and infectious in aerosols for hours and on surfaces for days (depending on the inoculum shed). Seasonal variation in COVID-19 incidence could affect the trajectory of the pandemic. Higher temperatures were shown to have a protective effect against the transmission of SARS in 2002-2003, possibly because of the decreased survival of the SARS-CoV on surfaces at higher temperatures. Average temperature was strongly associated with the count of local COVID-19 cases, and higher average temperature was strongly associated with lower COVID-19 incidences for temperatures of 1°C and higher [24]. For example, at mean values for the other variables, an increase in the average temperature from 1°C to 9°C and from 10°C to 19°C was associated with a decrease in the number of predicted cases per day from 24 to 19 and from 18 to 7, respectively [24]. However, temperature explained a relatively modest amount of the total variation in the incidence of COVID-19. The country-by-country difference in COVID-19 morbidity and mortality can be partially explained by the national policies on Bacillus Calmette-Guérin (BCG) vaccination. Middle high- and high-income countries that have a current universal BCG policy (55 countries) had 0.78±0.40 deaths per million people. In contrast, middle high- and high-income countries that never had a universal BCG policy (Italy, Netherlands, Belgium, USA, Lebanon) had a higher mortality rate, with 16.39±7.33 deaths per million people [25]. The earlier that a country established a BCG vaccination policy, the stronger was the reduction in their number of deaths per million inhabitants [25], consistent with the idea that protecting the elderly population might be crucial in reducing mortality. However, there is still no proof that BCG inoculation at an older age would boost defenses in the elderly.

Role of Smoking and Blood Groups in COVID-19

Smoking, to date, has been assumed to be possibly associated with adverse disease prognosis and is detrimental to the immune system and its responsiveness to infections, making smokers more vulnerable to infectious diseases. Previous studies have shown that smokers are twice more likely than non-smokers to contract influenza and have more severe symptoms, and smokers were also noted to have higher mortality in the previous MERS-CoV outbreak. A recent review revealed that smokers were 1.4 times more likely (RR=1.4, 95% CI: 0.98-2.00) to have severe symptoms of COVID-19 and approximately 2.4 times more likely to be admitted to an ICU, need mechanical ventilation, or die than non-smokers (RR=2.4, 95% CI: 1.43-4.04) [26]. A study showed that blood group A was associated with a higher risk for COVID-19 and disease mortality, whereas blood group O was associated with a lower risk [27].

ACE2 and RAAS Mechanism on the Disease

ACE2 functions as a receptor for both the SARS viruses and is expressed broadly, including in the heart and kidneys as well as on the lung alveolar epithelial cells, which are the principal target cells for SARS-CoV-2 and the site of dominant injury. The interaction between the SARS viruses and ACE2 has been proposed as a potential factor in their infectivity, and there are concerns about the use of renin-angiotensin-aldosterone system (RAAS) inhibitors that may alter ACE2 and whether variation in ACE2 expression may be in part responsible for the disease virulence in the ongoing COVID-19 pandemic. Data are lacking regarding the effects of RAAS inhibitors on lung-specific expression of ACE2. Furthermore, even if RAAS inhibitors modify ACE2 levels or activity in the target tissue, clinical data are lacking to indicate whether this would facilitate a greater engagement and entry of SARS-CoV-2 spike protein. Many viruses are cardiotropic, and subclinical viral myocarditis is common in viremia. Markers of myocardial injury have been shown to be elevated during the disease course of COVID-19 and to increase rapidly with clinical deterioration and preceding death. Trials of losartan as a treatment for COVID-19 are being conducted among patients who have not previously received treatment with a RAAS inhibitor (NCT04312009 and NCT04311177). There is a clear potential for harm related to the withdrawal of RAAS inhibitors in patients with an otherwise stable condition. COVID-19 is particularly severe in patients with underlying cardiovascular diseases. RAAS inhibitors have established benefits in protecting the kidney and myocardium, and their withdrawal may risk the clinical decompensation in high-risk patients. Switching from a RAAS inhibitor to another antihypertensive therapy in a stable ambulatory patient may require careful follow-up to avoid rebound increases in the blood pressure, and selection of dose-equivalent antihypertensive therapies may be challenging in practice. On the basis of the available evidence, multiple specialty societies support that RAAS inhibitors should be continued despite the theoretical concerns and uncertainty regarding their effect on ACE2 and the way in which these drugs might affect the propensity for or severity of COVID-19 [28].

Clinical Course

The mean incubation period for COVID-19 is 6.4 days, ranging from 2.1 days to 25 days with potential asymptomatic transmission. Cardiovascular disease and hypertension were the most common underlying diseases, followed by diabetes mellitus. Fever and cough were the most common symptoms, followed by dyspnea, myalgia, headache, sore throat, and diarrhea. Rhinorrhea was also reported with relevant clinical information. Most patients had a normal white blood cell count, but almost half of the patients had leukopenia.

Patients requiring intensive care were older and more likely to have underlying diseases and dyspnea than non-ICU patients [8]. The clinical course of the 11 cases demonstrated the complexity of the COVID-19 profile, and the clinical manifestations were as follows: asymptomatic, mild symptomatic with negative chest computed tomography (CT), typical symptoms and radiological changes and negative RT-PCR but positive IgG and IgM antibodies, positive RT-PCR 2 weeks after recovery, typical pneumonia on chest CT but with only mild respiratory symptoms and normal C-reactive protein (CRP) levels, severe symptoms complicated by secondary bacterial pneumonia, pediatric COVID-19 with a history of allergic rhinitis, pediatric COVID-19 with a history of atopic dermatitis, COVID-19 patient with a history of urticaria, chronic obstructive pulmonary disease (COPD) with COVID-19 and influenza A pneumonia, and diarrhea, in addition to respiratory symptoms [29].

Co-infection with Influenza

In a paper comparing the disease severity between COVID-19 and influenza-associated pneumonia, COVID-19 patients were younger, and the overall proportion of comorbidities was much smaller in the COVID-19 case series (20%-51%) than in patients with influenza-associated pneumonia (70%-77%) [30]. Hypertension and diabetes were the most important chronic comorbidities in both the diseases; however, there were fewer patients with COPD or renal disease among COVID-19 patients than among influenza patients. Influenza pneumonia patients had a 2- to 3-fold lower ventilation rate than COVID-19 patients, and the median duration of ventilation was 9 days for noninvasive and 17 days for invasive ventilation in the COVID-19 case series. In contrast, the median ventilation duration in influenza pneumonia was only 2 days [30]. ARDS was observed in only 1% of the influenza pneumonia patients, whereas ARDS rate among COVID-19 patients was 2%-20%. The case fatality ratio of COVID-19 (4.5%) is similar to that of influenza-associated pneumonia (6%). Patients with both COVID-19 and influenza virus infection did not appear to show a more severe condition on the basis of similar clinical and laboratory findings, imaging studies, and prognosis compared with the patients with COVID-19 infection only [31]. However, the patients with co-infection may be more prone to the symptoms of nasal congestion and pharyngalgia. It is critical to pay attention to the potential co-infection with other respiratory viruses in patients with COVID-19, which effectively helps to prevent the aggravation of disease progression and even death.

Radiological Findings

Radiological findings in SARS-CoV-2 pneumonia are variable. Bilateral, peripherally distributed, ground-glass opacities (GGO) are the most common finding from chest CT [8]. CT images reveal pure GGO, GGO with reticular and/or interlobular septal thickening (crazy-paving pattern), and GGO with consolidation and pure consolidation (55%); pleural effusion is rarely seen. No discrete nodules, cavitation, or lymphadenopathy were observed on the chest CT images [8]. Moreover, 4 stages of lung CT were defined: stage 1 (0-4 days), GGO distributed subpleurally in the lower lobes unilaterally or bilaterally in 75% of the patients; stage 2 (5-8 days), increased crazy-paving pattern in 53% of the patients; stage 3 (9-13 days), consolidation in 91% of the patients with multilobar diffuse involvement; stage 4 (≥14 days), gradual resolution of consolidation in 75% of the patients with a decreased involvement, without crazy-paving [32]. Lung abnormalities on chest CT showed greatest severity approximately 10 days after the initial onset of symptoms. Absorption stage (stage 4) began 14 days after the onset of the initial symptoms. A study reported that the sensitivity of chest CT in diagnosing COVID-19 was 97% on the basis of the positive RT-PCR results (9), with 3% of the patients who had positive RT-PCR results showing no lesions on initial chest CT and 75% (n=308) with negative RT-PCR results having positive chest CT findings. Analyzing the serial RT-PCR assays, the subsequent RT-PCR results were detected positive in 258 (83.7%) of those patients. The mean interval time between the initial negative to positive RT-PCR results was 5.1±1.5 days, and that between the initial positive to subsequent negative RT-PCR result was 6.9±2.3 days. In the subgroup of negative to positive RT-PCR results, 67% patients showed initial positive chest CT imaging before the initial negative RT-PCR results, and 93% showed that the initial chest CT had typical imaging features consistent with COVID-19 before (or parallel to) the initial positive RT-PCR results, with a median time-interval of 8 days. Furthermore, 42% of the patients showed improvement in follow-up chest CT scans before the RT-PCR results turning negative, and only 3.5% of the patients showed disease progression on the follow-up CT scans after the RT-PCR results turning negative. As lung abnormalities may develop before clinical manifestations and nucleic acid detection, experts have recommended early CT for screening suspected patients. The high contagiousness of SARS-CoV-2 and the risk of transporting unstable patients with hypoxemia and hemodynamic failure make chest CT a limited option for patients with suspected or established COVID-19. Lung ultrasonography gives results that are similar to chest CT and superior to standard chest radiography for the evaluation of pneumonia and/or ARDS with the added advantage of ease of use at point of care, repeatability, absence of radiation exposure, and low cost. Characteristic findings of lung ultrasonography for COVID-19 included the following: thickening of the pleural line with pleural line irregularity; B lines in a variety of patterns, including focal, multifocal, and confluent; consolidations in a variety of patterns, including multifocal small, non-translobar, and translobar with occasional mobile air bronchograms; and appearance of A lines during the recovery phase; pleural effusions were uncommon. In summary, focal B lines are the main feature in the early stage and in mild infection; alveolar interstitial syndrome is the main feature in the progressive stage and in critically ill patients; A lines can be found during convalescence; and pleural line thickening with uneven B lines can be seen in patients with pulmonary fibrosis [33].

Prognosis

In a retrospective cohort study from China with 191 patients of whom 137 were discharged and 54 died in hospital, in univariable analysis, odds of in-hospital death was higher in patients with diabetes or coronary heart disease [34]. Age, lymphopenia, leucocytosis, and elevated levels ALT, lactate dehydrogenase, high-sensitivity cardiac troponin I, creatine

kinase, D-dimer, serum ferritin, IL-6, prothrombin time, creatinine, and procalcitonin were also associated with death. Multivariable regression showed increasing odds of in-hospital death associated with older age, higher Sequential Organ Failure Assessment score, and D-dimer greater than 1 µg/mL on admission. Median duration of viral shedding was 20.0 days in survivors, but SARS-CoV-2 was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days. A report regarding COVID-19 patients dying in Italy revealed that mean age of those patients was 78.5 years, and most (70.6%) of them were men [35]. Overall, 1.2% of the deceased patients presented with no comorbidities, 23.5% with a single comorbidity, 26.6% with 2, and 48.6% with 3 or more. ARDS was observed in the majority of patients (96.5%), followed by acute renal failure (29.2%), acute cardiac injury (10.4%), and superinfection (8.5%). The median time from the onset of symptoms to death was 8 days, from the onset of symptoms to hospitalization was 4 days, and from hospitalization to death was 4 days. Only 1.1% of COVID-19 positive patients under the age of 50 died and had comorbidities such as cardiovascular, renal, psychiatric pathologies, diabetes, and obesity.

What Do We Have to Treat COVID-19?

So far, there has been no effective treatment for COVID-19. Several potential drug candidates, including lopinavir/ritonavir, favipiravir, neuraminidase inhibitors, remdesivir, umifenovir (Arbidol), azithromycin, and chloroquine (CQ) have been proposed. In a systematic review regarding CQ for the treatment of COVID-19, it was reported that CQ was highly effective in reducing viral replication *in vitro* using Vero E6 cells, with standard dosing, because of its favorable penetration in tissues, including in the lung [36]. Studies revealed that it shows potential broad-spectrum antiviral activity by increasing the endosomal pH required for virus/cell fusion as well as interfering with the glycosylation of cellular receptors of SARS-CoV [37]. CQ is an established antimalarial agent that has been tested in clinical trials for its anticancer activity. The favorable effect of CQ appears to be due to its ability to sensitize the cancerous cells to chemotherapy and radiation therapy and induce apoptosis. Previous reports showed that free zinc ions and CQ combination inhibits lysosome function and induces apoptosis in ovarian tumor cells [38]. Thus, CQ is a zinc ionophore, and this property that may contribute to its anticancer and antiviral activity. CQ and HCQ have demonstrated a marked efficacy in clinical and radiological regression, negative conversion, shortening of the disease period, and acceptable safety in treating COVID-19 associated pneumonia in multicenter clinical trials conducted in China (36). French researchers underlined their potentially favorable risk-benefit balance, high safety, and low cost [36]. The multicenter collaboration group of the Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province recommended several precautions because of the development of QT interval prolongation or bradycardia and appearance of visual and/or mental disturbance/deterioration. HCQ, which exhibits an antiviral effect highly similar to that of CQ, could serve as a better therapeutic approach and is likely to attenuate the severe progression of COVID-19, inhibiting the cytokine storm by suppressing T cell activation [39].

Several drugs such as interferon α (IFN-α), CQ, Arbidol, remdesivir, and favipiravir are currently undergoing clinical studies to test their efficacy and safety in the treatment of COVID-19. IFN-α is a broad-spectrum antiviral drug that is usually used to treat hepatitis, although it is reported to inhibit SARS-CoV reproduction *in vitro* [10]. Favipiravir is a new type of RNA-dependent RNA polymerase inhibitor. In addition to its anti-influenza virus activity, favipiravir is capable of blocking the replication of flavi-, alpha-, filo-, bunya-, arena-, noro-, and other RNA viruses; therefore, favipiravir may have potential antiviral action on SARS-CoV-2, which is an RNA virus. It was shown that favipiravir had more potent antiviral action than lopinavir/ritonavir, and it had significantly fewer adverse effects than the lopinavir/ritonavir group [10]. Remdesivir is a nucleoside analogue and a broad-spectrum antiviral drug. Animal experiments indicated that remdesivir could effectively reduce the viral load in the lung tissue of mice infected with MERS-CoV, improve lung function, and alleviate pathological damage to the lung tissue. In order to evaluate the efficacy and safety of the drug in patients with COVID-19, a phase III clinical trial was launched in China, and the trial is expected to conclude by the end of April 2020 [10]. Darunavir (a second-generation human immunodeficiency virus [HIV]-1 protease inhibitor), type II transmembrane serine protease inhibitors, and BCR-ABL kinase inhibitor imatinib may have potential efficacy in treating COVID-19 [10]. Indinavir, saquinavir, lopinavir, carfilzomib, ritonavir, remdesivir, atazanavir, darunavir, tipranavir, fosamprenavir, enzaplatovir, presatovir, abacavir, bortezomib, elvitegravir, maribavir, raltegravir, montelukast, deoxyrhapontin, polydatin, chalcone, disulfiram, carmofur, shikonin, ebselen, tideglusib, PX-12, TDZD-8, cyclosporin A, and cinanserin are other agents with potential antiviral activity against SARS-CoV-2 [10].

Lopinavir, an HIV type 1 aspartate protease inhibitor, showed *in vitro* inhibitory activity against SARS-CoV and MERS-CoV. Ritonavir is combined with lopinavir to increase its plasma half-life through the inhibition of cytochrome P450. A trial was conducted to evaluate the efficacy of lopinavir-ritonavir combination in adult patients hospitalized with COVID-19 with an oxygen saturation (Sao2) of 94% or Pao2/Fio2 of less than 300 mm Hg [40]. Patients were randomly assigned in a 1:1 ratio to receive either lopinavir-ritonavir in addition to standard care or standard care alone. Treatment with lopinavir-ritonavir was not associated with a difference from standard care in the time to clinical improvement and mortality rate [40]. Gastrointestinal adverse events were more common in the lopinavir-ritonavir group, but serious adverse events (hepatitis, pancreatitis, serious skin lesions, QT prolongation) were more common in the standard care group. Lopinavir-ritonavir treatment was stopped early in 13 patients (13.8%) because of adverse events [40]. Teicoplanin could be administered for the treatment of SARS-CoV-2 infection. Spike glycoprotein (S protein) is the leading mediator of viral entry, followed by further cleavage of S protein in endocytic vesicles mediated by cathepsin L. Teicoplanin blocks virus entry by specifically inhibiting the activity of cathepsin L. In a study, it was demonstrated that teicoplanin could inhibit the entry of HIV-1-2019-nCoV-S pseudoviruses [41]. The routinely used dose (400 mg/day) could be considered for patients with COVID-19. If the effect is not significant, dose

could be optimized because of its low toxicity. Doses such as 800 mg/day or 1.200 mg/day could be considered to improve drug efficiency. Given that the principle of antiviral therapy is to prevent virus infection and amplification at a stage as early as possible, the use of teicoplanin is recommended in the early stage [41].

Bronchoscopy for COVID-19 Infected Patients

American Association for Bronchology and Interventional Pulmonology published a statement on the Use of Bronchoscopy and Respiratory Specimen Collection in Patients with Suspected or Confirmed COVID-19 Infection [42] induced sputum is not recommended, bronchoscopy should only be considered in intubated patients if upper respiratory samples are negative and other diagnosis is considered that would significantly change the clinical management. Alternative respiratory specimen collection in the intubated patient is tracheal aspirate. If bronchoscopy is being performed, it must be performed in negative pressure room isolation, and all personnel should wear N95 masks and standard personal protective equipment, which includes gown, gloves, respiratory protection, and eye protection, and must follow standard high-level disinfection for reusable bronchoscopes. Bronchoscopy for urgent/emergent reasons should be considered only if a lifesaving bronchoscopic intervention is deemed necessary. Indications include massive hemoptysis, benign or malignant severe airway stenosis, or suspicion of an alternative or secondary infectious etiology or malignant condition with resultant significant endobronchial obstruction.

Much to Learn for COVID-19

Despite the whole world's efforts to understand COVID-19, many aspects about this disease remain unclear: first, whether SARS-CoV-2 can be transmitted through the fecal-oral route; second, the epidemiological and clinical characteristics of asymptomatic carriers; third, whether COVID-19 has neurological manifestations; and finally, the temporal features of the SARS-CoV-2-induced inflammatory response in relation to the timing of therapeutic interventions. Finally the role of systemic steroids and immunomodulatory agents on the treatment of coronavirus-related infections remain unclear. Once the pre-diagnosis or diagnosis is made, isolation is urgently needed. Patients with mild disease may be managed at home, ensuring home isolation and informing about the alarming symptoms of the disease. Adequate hydration, nutrition, and symptom control are necessary. In case of hypoxia, oxygen supply should be maintained, and if needed, noninvasive or invasive ventilation and extra corporeal membrane oxygen support may be used. When co-infection is suspected, antibiotics and antifungals should be added. To decrease the damage associated with COVID-19, public health and infection control measures are urgently required to limit the spread of the virus. It is essential to limit human-to-human transmission in order to reduce infections among close contacts and healthcare workers. Enhanced standard infection prevention and control practices are recommended in healthcare facilities, especially in emergency departments. The internet also has the potential for the development and spread of misinformation or fake news. Governments should be responsible for providing accurate knowledge and clarifying misinformation to help the public face this novel infection [8].

COVID-19 in Pediatric Population

Sensitivity to SARS-CoV-2 is varied in different age groups. Similar to adults, COVID-19 is common in children. However, the course of the disease is milder, and less mortality has been reported. Although the reasons for this are not fully understood, some theories have been proposed. One of them is that children are more protected and have fewer outdoor activities, which leads to less contact with viruses. Similar to polio or rubella, several infectious diseases may be less severe in children. Moreover, children have very few underlying medical conditions, and immune system responses are not as vigorous as in adults. Lower ACE2 receptor expression is thought to be another reason for less severe infection; however, there is no proven information on this subject [43].

Previous data showed that children carry the virus mostly in the upper respiratory tract, including nasopharyngeal carriage. Although an important mode of transmission of SARS-CoV-2 is through infected droplets, it is also transmitted by direct contact, aerosols, and fecal-oral route [44]. Due to fecal spread of the virus for a few weeks after the diagnosis, the transmission is possible through fecal-oral route, especially in infants and children who have not finished toilet training. Nasal secretions and prolonged fecal viral spread in children also play an important role in the social transmission of the virus at school, home, and nursing homes. Prolonged spread of the virus in symptomatic children and virus excretion in asymptomatic children render public health measures to reduce viral transmission less effective [45]. COVID-19 can lead to different clinical presentations in children and infants, varying from asymptomatic infection to severe respiratory distress. Although children have less severe clinical course than adults, children with underlying disease are at a higher risk of serious illness. Young age, underlying lung disease, and immunodeficiency are associated with more serious clinical outcomes in children [45]. The most common clinical symptoms of the disease are fever, weakness, dry cough, nasal congestion, runny nose, and sore throat. In addition, abdominal pain, vomiting, diarrhea, and abdominal tenderness have been reported in some children. Difficulty in breathing, vomiting, cough, and fever are other common symptoms reported in infants. Vertical transmission from mother to baby during pregnancy is also not proven yet [44]. There are a few reports about the evaluation of infants born from infected mothers; there were no viruses detected in amniotic fluid, cord blood, throat swab sample of the infants, and breast milk [46]. Co-infection with other viruses has also been reported in two-third of children with coronavirus infection. This situation is thought to be similar for COVID-19 [45].

Dong et al. [47] from China reported that 13% of pediatric cases had asymptomatic infection although they had virus positivity. Severe clinical conditions characterized by dyspnea or hypoxemia have been reported in 5% of children, and 0.6% of this group progressed to ARDS or respiratory failure. Progression to shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute

kidney injury can be seen in some critically ill pediatric patients. They also concluded that the risk of serious clinical findings is higher in preschool children and infants than in older children [47].

Laboratory findings in children did not show a consistent pattern like that in adults and previous infections with other coronaviruses like SARS-CoV and MERS-CoV. Leukocyte and lymphocyte changes are prominent in adults; however, very few children had been reported with leukocyte and lymphocyte count abnormalities. The inflammatory markers CRP and procalcitonin (PCT) were elevated in very few pediatric patients, unlike in adults [48]. Lymphopenia, leukocyte, and CRP abnormalities are recommended as predictors of severe infection.

COVID-19 pneumonia in children is mainly mild, and the chest X-ray may be normal. Chest CT can present characteristic changes of subpleural GGOs, and consolidations with surrounding halo and patchy GGOs might be considered as typical signs. These kind of changes can also be seen in other viral infections such as influenza, adenovirus, and respiratory syncytial virus. Moreover, it should be kept in mind that co-infection with these viruses is common in children. The diagnosis of COVID-19 pneumonia by CT imaging alone may not be sufficient, especially in children with co-infection with other pathogens [49].

Treatment usually depends on adult clinical experiences. Treatment in children should be decided discretely for each patient and well planned in the possible severe cases. Supportive treatment with symptom management, oxygen treatment, and liquid electrolyte support should be administered if needed. Caution should be exercised because of the possibility of pulmonary edema in fluid-electrolyte supportive treatment [44]. According to the Turkish Ministry of Health Management and Treatment Guidelines in Children, oseltamivir, hydroxychloroquine, azithromycin, and protease inhibitors such as lopinavir/ritonavir combination are the recommended drugs, depending on the patient. Ribavirin may be used in children on the basis of the clinical condition and severity of the disease [50]. Treatment with a nucleoside analogue, remdesivir, showed improvement in adult patients, although there are no data for its use on children. IFN α2b nebulization administered in MERS-CoV and SARS-CoV may be considered in COVID-19. Additionally, there are ongoing investigations about the serum obtained from patients who have recovered from COVID-19 to verify if they are beneficial for patients with COVID-19 [44].

In conclusion, since the flu pandemic in 1918, mankind has become more vulnerable to pandemics. COVID-19 pandemic has been a global threat since January 2020. The management of COVID-19 has been challenging for healthcare professionals, emphasizing the importance of individual risk factors as well as personalized treatment regimen. During this process, healthcare professionals have benefited from each other's experiences in confronting COVID-19. The present review of essential scientific articles regarding COVID-19 may also contribute to the knowledge of healthcare professionals and researchers seeking important data on this topic.

As stated by the famous writer, Noah Harari, "history indicates that real protection comes from the sharing of reliable scientific information, and from global solidarity."

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REFERENCES

1. WHO | Novel Coronavirus - China [Internet]. [cited 2020 Apr 3].Available from: URL: https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/.
2. Report on the epidemiological features of coronavirus disease 2019 (covid-19) outbreak in the republic of korea from january 19 to March 2, 2020. J Korean Med Sci 2020;35. [Crossref]
3. Bernard Stoecklin S, Rolland P, Silue Y, et al. First cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020. Euro Surveill NLM (Medline) 2020;25. [Crossref]
4. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed 2020;91:157160.
5. COVID-19 European Centre for Disease Prevention and Control [Internet]. [cited 2020 Apr 4].Available from: URL: https://www.ecdc.europa.eu/en/covid-19-pandemic.
6. World Health Organization. Novel Coronavirus (2019- nCoV) Situation Report-51. [Internet]. 2020. Available from: URL: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.
7. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med 2020;1199-207.
8. Lai CC, Shih TP, Ko WC, et al. 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 Mar;55:105924. [Crossref]
9. Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology 2020. [Crossref]

10. Dong L, Hu S, Gao J. Discovering drugs to treat coronavirus disease 2019 (COVID-19). Drug Discov Ther 2020;14:58-60. [Crossref]
11. Ran L, Chen X, Wang Y, et al. Risk Factors of Healthcare Workers with Corona Virus Disease 2019: A Retrospective Cohort Study in a Designated Hospital of Wuhan in China. Clin Infect Dis 2020. [Crossref]
12. Chan JFW, Yuan S, Kok KH, et al. A risk factors of healthcare workers with Corona Virus Disease 2019: A retrospective cohort study in a designated hospital of Wuhan in China. Lancet 2020;395:514-23. [Crossref]
13. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res 2020;4.
14. Alhazzani W, Hylander Møller M, Arabi YM, et al. Surviving sepsis campaign: Guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19) 2020 Available from: URL: http://guidecanada.org/. [Crossref]
15. Guillen E, Pineiro GJ, Revuelta I, et al. Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation? Am J Transplant 2020. [Crossref]
16. Qu J, Yang R, Song L, et al. Atypical lung feature on chest CT in a lung adenocarcinoma cancer patient infected with COVID-19. Ann Oncol Off J Eur Soc Med Oncol 2020. [Crossref]
17. Chatre C, Roubille F, Vernhet H, et al. Cardiac complications attributed to Chloroquine and Hydroxychloroquine: A systematic review of the literature. Drug Saf 2018;919-31. [Crossref]
18. Moorthy V, Restrepo AMH, Preziosi MP, et al. Data sharing for novel coronavirus (COVID-19). Bull World Health Organ 2020. Available from: URL: https://www.who.int/bulletin/volumes/98/3/20-251561/en/. [Crossref]
19. Türk Toraks Derneği Erken Kariyer Görev Grubu. COVID-19 makalelerinin özetleri. Nisan 2020. (Turkish Thoracic Society Early Career Members Committee. Summaries of COVID-19 articles). Available from: URL: https://www.toraks.org.tr/userfiles/file/COVID%2019%20Literat%C3%BCrleri%2008042020%20g%C3%BCncelleme(1).pdf
20. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020:102433. [Crossref]
21. R Lu, X Zhao, J Li, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding, Lancet 2020;565-74.
22. Yang Liu, Li-Meng Yan, Lagen Wan, et al. Viral dynamics in mild and severe cases of COVID-19. Lancet Infect Dis 2020.
23. Van Doremalen, Neeltje, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. New Eng J Med 2020. [Crossref]
24. Bannister-Tyrrell M, Meyer A, Faverjon C, et al. Preliminary evidence that higher temperatures are associated with lower incidence of COVID-19, for cases reported globally up to 29th February 2020. Available From: URL: https://www.medrxiv.org/content/10.1101/2020.03.18.20036731v1. [Crossref]
25. Miller A, Reandelar MJ, Fasciglione K, et al. Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: an epidemiological study. medRxiv 2020. [Crossref]
26. Vardavas C, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. Tob Induc Dis 2020;18:20. [Crossref]
27. Zhao J, Yang Y, Huang H, et al. Relationship between the ABO Blood Group and the COVID-19 Susceptibility. Available From: URL: https://www.medrxiv.org/content/10.1101/2020.03.11.20031096v2.full.pdf.
28. Vaduganathan M, Vardeny O, Michel T, et al. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19. N Engl J Med 2020. [Crossref]
29. Dong X, Cao Y, Lu X, et al. Eleven faces of Coronavirus Disease 2019. Allergy 2020. [Crossref]
30. Tolksdorf K, Buda S, Schuler E, et al. Influenza-associated pneumonia as reference to assess seriousness of coronavirus disease (COVID-19). Euro Surveill 2020. [Crossref]
31. Ding Q, Lu P, Fan Y, et al. The clinical characteristics of pneumonia patients co-infected with 2019 novel corona virus and influenza virus in Wuhan, China. J Med Virol 2020;10.1002/jmv.25781. [Crossref]
32. Pan F, Ye T, Sun P, et al. Time Course of Lung Changes on Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology 2020;295:200370. [Crossref]
33. Qian Yi Peng, Xiao Ting Wang, Li Na Zhang and Chinese Critical Care Ultrasound Study Group (CCUSG). Findings of lung ultrasonography of novel corona virus pneumonia during the 2019-2020 epidemic. Intensive Care Med 2020;46:849-50. [Crossref]
34. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020. [Crossref]
35. Palmieri L, Andrianou X, Bella A, et al. COVID-19 Surveillance Group. Characteristics of COVID-19 patients dying in Italy Report based on available data on March 20th, 2020. Available From: URL: https://www.epicentro.iss.it/coronavirus/bollettino/Report-COVID-2019_20_marzo_eng.pdf.
36. Cortegiani A, Ingoglia G, Ippolito M, et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. J Crit Care 2020. [Crossref]
37. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. BioScience Trends 2020;14:72-73. [Crossref]
38. Xue J, Moyer A, Peng B. Chloroquine is a zinc ionophore. PLoS One 2014;9:e109180. [Crossref]
39. Dan Zhou, Sheng-Ming Dai, Qiang Tong. COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression. J Antimicrob Chemother 2020. [Crossref]
40. Cao B, Wang Y, Wen D, et al. a trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. Engl J Med 2020.
41. Zhang J, Ma X, Yu F, et al. Teicoplanin potently blocks the cell entry of 2019-nCoV. bioRxiv 2020. [Crossref]
42. Wahidi MM, Lamb C, Murgu S, et al. American Association for Bronchology and Interventional Pulmonology (AABIP) statement on the use of bronchoscopy and respiratory specimen collection in patients with suspected or confirmed COVID-19 Infection. Available From: URL: https://aabronchology.org/wp-content/uploads/2020/03/2020-AABIP-Statement-on-Bronchoscopy-COVID.GAE-updated-Version.pdf. [Crossref]
43. Lee PI, Hu YL, Chen PY, et al. Are children less susceptible to COVID-19? J Microbiol Immunol Infect 2020;S1684-1182:30039-6.
44. Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: What neonatologist need to know. J Med Virol 2020. [Crossref]
45. Cruz A, Zeichner S. COVID-19 in children: initial characterization of the pediatric disease. Pediatrics 2020;pii:e20200834. [Crossref]
46. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet 2020;395:809-15. [Crossref]
47. Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 Coronavirus Disease in China. Pediatrics 2020;pii: e20200702
48. Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. Clin Chem Lab Med 2020. [Crossref]
49. Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr Pulmonol 2020. [Crossref]
50. Sağlık Bakanlığı COVID-19 Çocuk Hasta Yönetimi ve Tedavisi Rehberi. Available From: URL: https://covid19bilgi.saglik.gov.tr/tr/