Covid-19 scientific publications from Turkey

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ABDURRAHMAN TUFAN
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Covid-19 scientific publications from Turkey

Rafiye ÇİFTÇİLER1*, İbrahim C. HAZNEDAROĞLU2*, Abdurrahman TUFAN3*, Mehmet Akif ÖZTÜRK3

1Department of Hematology, Faculty of Medicine, Aksaray University Training and Research Hospital, Aksaray, Turkey
2Department of Hematology, Faculty of Medicine, Hacettepe University, Ankara, Turkey
3Department of Rheumatology, Faculty of Medicine, Gazi University, Ankara, Turkey

Abstract: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) outbreak poses a major global threat to the public health worldwide. The infectious disease caused by the virus that affected the entire world was named as the Coronavirus disease-2019 (COVID-19). The knowledge regarding the wide clinico-biological aspects of the COVID-19 continues to evolve very rapidly, given the growing data from all over the world. During this complicated process, healthcare professionals have benefited from each other's experiences in combatting against the COVID-19 syndrome. COVID-19 related studies have been performed by a wide variety of research groups in Turkey as well as the rest of the world. The aim of this paper is to outline Turkish COVID-19 research indexed in the LitCovid system. LitCovid is a curated literature hub for tracking up-to-date scientific data about the SARS-CoV-2. COVID-19's first case was detected in Turkey, on March 11th, 2020. Six months after the first case was observed, the total number of COVID-19 patients was reported to be as 286,455, and the total number of deaths due to SARS-CoV-2 was 6895. The genetic sequence of the novel coronavirus showed significant identity to SARS-CoV and MERS-CoV. Numerous drugs including lopinavir/ritonavir, favipiravir, remdesivir, umifenovir, azithromycin, and chloroquine have been suggested for the management of COVID-19 although the exact treatment is yet to be determined.

Key words: Covid-19, Turkish COVID 19 publications, literature, pathobiology, diagnosis, treatment

1. Introduction and COVID-19
On December 31st, 2019, the presence of patients with pneumonia of unknown etiology in Wuhan, China, was reported to the World Health Organization by the national authorities. This virus was officially identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The acute respiratory disease outbreak associated with SARS-CoV-2 was later named as the coronavirus disease-2019 (COVID-19). The first COVID-19 case had been observed in Turkey on March 11th, 2020 [1]. Six months after the first case was seen, the total number of COVID-19 patients was reported to be as 286,455 and the total number of deaths due to SARS-CoV-2 was 6895. The COVID-19 pandemic continues to be the focus of all people around the world. Most people infected with COVID-19 will be able to experience mild to moderate respiratory illness. However, patients with diabetes, chronic respiratory disease, and malignancies are more likely to develop more serious illnesses [2]. Elderly patients, the presence of comorbidities, higher d-dimer and C-reactive protein and lower lymphocyte levels are associated with higher mortality. In the light of the data obtained from the COVID-19 pandemic, the importance of intensive care units in the follow-up of these critical patients has been revealed [3]. The aim of this paper is to outline Turkish COVID-19 research indexed in LitCovid system.

2. COVID-19 and the curated literature hub, LitCovid
LitCovid is a curated literature hub for tracking up-to-date scientific data about the SARS-CoV-2. It is the most extensive resource on the COVID 19, supply a central access to 60544 (and expanding) relevant articles in PubMed. Articles at Litcovid are updated daily. It is categorized more by different research topics and geographic locations for better Access [4]. Countries mentioned in abstracts related to COVID 19 indexed in LitCovid is depicted in Figure 1. All articles added to this study have been discussed by searching from LitCovid.

3. Turkish COVID-19 publications indexed in LitCovid
COVID-19 related studies are available in a variety of groups in Turkey (Figure 2). Weekly publications in Turkey from 6th April to 11th October, 2020 is depicted in Figure 3. Articles are grouped under 8 headings;
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, hypertension and diabetes mellitus were the most common background diseases [62]. The clinical presentation spectrum of disease is very heterogeneous. The mean nasopharyngeal swab viral load of severe COVID-19 patients were 60-fold higher as compared to mild cases, suggesting an association between higher viral load and adverse clinical outcomes. There are several studies done regarding typing of isolated viruses in Turkey Pavel et al. successfully isolated SARS-CoV-2 virus from a patient with confirmed COVID-19 in Turkey. The study showed that hCoV-19/Turkey/ERAGEM-001/2020 was closely clustered with
other strains primarily from Australia, Canada, England, Iran, and Kuwait [5]. Karacan et al. investigated genomes of isolated viruses form patients living in Istanbul to figure out influence of viral factors on COVID-19 disease characteristics [15].

Angiotensin-converting enzyme 2 (ACE2), a major component of the renin angiotensin system (RAS), is the principal receptor of the SARS-CoV-2 [7]. COVID-19 disease begins with the binding of the virus to ACE2 receptors expressed in wide variety of tissues. Many clinical characteristics of severe patients are unique to COVID-19. Most of the patients exert a self-limiting viral respiratory disease which ends with the development of neutralizing anti-viral T cell and antibody immunity. The exaggerated immune response against virus is primary factor for development of severe disease [11]. Tastan et al. showed that T cells and NKT cells can be stimulated with the virus and can be assessed significantly in an in-vitro setup. Additionally, a decrease in B cell population in higher concentrations of the

Figure 3. Weekly publications in Turkey from 6th April to 22nd October, 2020.

Table 1. Selected "general subgroup" of Turkish COVID-19 publications indexed in LitCovid.

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<td>Halach et al.</td>
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inoculums was seen; probably activated and proliferated T cells interfered with B cell proliferation [13]. Severe lymphopenia and eosinopenia, extensive pneumonia and lung tissue damage, a cytokine storm leading to acute respiratory distress syndrome and multiorgan failure are seen in severe patients with COVID-19. Lymphopenia causes a defect in antiviral and immune regulation. The cytokine storm begins with extensive activation of cytokine-secreting cells with innate and adaptive immune mechanisms of both which contribute to poor prognosis [17].

5. Diagnosis of COVID-19
Due to its strong infectious potential, it is essential to diagnose COVID-19 rapidly and accurately to reduce the risk of transmission and as a future goal to treat cases promptly for reducing mortality. The most important mode of transmission of the virus is through respiratory droplets
from person to person, contact with infected people and rarely through fecal-oral transmission. Studies have shown that cases often have a history of traveling to the outbreak area or contact with infected people. The gold standard for diagnosis is real-time reverse transcriptase polymerase chain reaction (rRT-PCR) testing. However, rRT-PCR test results usually require many hours to be produced. It has also been reported that rRT-PCR tests show false negative diagnoses in the early stages of the disease. Thoracic CT provides rapid results and has demonstrated diagnostic value when rRT-PCR test is negative in the early stages of the disease. Aslan et al. evaluated the diagnostic performance of low-dose chest computed tomography in patients under investigation for COVID-19. They suggest isolating patients with typical CT findings, but negative rRT-PCR results, and repeating rRT-PCR to avoid misdiagnosis [46]. When we looked at the clinical findings, fever, shortness of breath, cough and travel to endemic districts were questioned as major screening parameters at the early stages of the epidemic. However, in the later stages of the epidemic, different symptomatologies such as headache, sore throat, nasal congestion, rhinorrhea, fatigue, tonsillar swelling and conjunctivitis were reported. Among these, frequent chemosensor dysfunctions involving olfaction and taste were reported. Sayın et al. identified the taste and smell impairment in COVID-19 patients. The study reported that COVID-19–positive subjects are strongly exhibited smell/taste impairment [44]. Solak et al. reported that of the 18% of 382 patients diagnosed with COVID-19 exhibited dermatological symptoms. The most common complaints shown in the study were rash, bruising and sores [47]. It has been reported that approximately 6-10% of symptomatic
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<td>Sayin et al.</td>
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<td>Ozturk et al.</td>
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<td>Aksu et al.</td>
<td>Factors determining COVID-19 pneumonia severity in a country with routine BCG vaccination (51)</td>
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<td>Tuberculosis and COVID-19: an overlapping situation during pandemic (52)</td>
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<td>Tanacan et al.</td>
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<td>A pandemic center's experience of managing pregnant women with COVID-19 infection in Turkey: a prospective cohort study (59)</td>
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<td>Demir et al.</td>
<td>COVID-19 in kidney transplant recipients: a multicenter experience in Istanbul (36)</td>
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<td>Ozger et al.</td>
<td>The factors predicting pneumonia in COVID-19 patients: preliminary results of a university hospital in Turkey (60)</td>
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<td>Korkmaz et al.</td>
<td>The epidemiological and clinical characteristics of 81 children with COVID-19 in a pandemic hospital in Turkey: an observational cohort study (61)</td>
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COVID-19 patients had headache. Significant features of headache presentation in symptomatic COVID-19 patients are presented as new onset, moderate-severe, bilateral headache in the temporoparietal, forehead or periorbital regions with pulse or pressure quality [8]. As the whole world, there are articles from Turkey related to COVID-19 infection characteristics in children. Approximately 1 - 5% of cases diagnosed with COVID-19 are children. Overall, COVID-19 appears to cause less severe disease in children than adults. Approximately 90% of pediatric patients are grouped into asymptomatic, mild or moderate disease. However, 6.7% of cases were severe ones. Severe disease has been reported to occur generally in patients younger than 1 year of age and those children with an underlying disease [43].

6. Treatment of COVID-19

Until now, there has been no effective treatment for COVID-19. Several potential drug candidates, including lopinavir/ritonavir, favipiravir, neuraminidase inhibitors, remdesivir, umifenovir (Arbidol), azithromycin, and hydroxychloroquine (HCQ)/ chloroquine (CQ) have been suggested [62]. Results of studies are conflicting or insufficient to make clear recommendations. Many in vitro studies demonstrated efficacy of anti-viral agents for viral replication including; protease inhibitors including lopinavir/ ritonavir, favipiravir, and the nucleoside analogue remdesivir [62]. The optimum method of controlling an outbreak with a rapidly spreading respiratory pathogen is the isolation of the patients at healthcare facilities under appropriate respiratory precautions. However, this might result in shortage in hospital beds for patients who need respiratory support, hence Turkish Ministry of Health released a guideline for COVID-19 patients who can self-isolate themselves at home [34]. Convalescent plasma is suggested as an adjunct treatment to anti-viral therapy in COVID-19 patients. It has been proposed that protective effect of convalescent plasma would continue for weeks upon administration. For this treatment, donor is carefully evaluated and 200-600 mL plasma is collected with apheresis devices [73]. Hacibekiroglu et al. reported observations on effect of convalescent plasma according to blood groups in the management of critically ill patients diagnosed with COVID-19. They reported that duration in intensive care stay, the rates of mechanical ventilator and vasopressor support, the case fatality rate and discharge rate were lower in patients who received convalescent plasma containing anti-A Ab than not containing anti-A Ab [78]. Thrombotic complications due to inflammation, cytokine-mediated microvascular damage and pulmonary thromboinflammation occur as an important problem in patients infected with COVID-19. They reported that duration in intensive care stay, the rates of mechanical ventilator and vasopressor support, the case fatality rate and discharge rate were lower in patients who received convalescent plasma containing anti-A Ab than not containing anti-A Ab [78]. There are different studies conducted on pediatric patients in the treatment group. Yayla et al. evaluated 220 pediatric patients with COVID-19, of which 48.2% were male, with a median age of 10 years, and 9.5% had underlying diseases. Extracorporeal membrane oxygenation was needed for 2 patients (0.9%) and mechanic ventilation was needed for 3 patients (1.4%). Available therapies were
Table 6. Selected “treatment subgroup” of Turkish COVID-19 publications indexed in LitCovid.

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<td>Convalescent plasma therapy in patients with COVID-19 (73)</td>
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used in 6 patients (2.7%), with hydroxychloroquine being
the most commonly used drug either alone (1 patient) or
in combination with favipiravir (5 patients). Two patients
(0.9%) had died and 9 (4.1%) were still hospitalized
during the study period. Although the disease course of
COVID-19 seems to be mild in children, critical illness
is important, and the treatment method primarily should
consist of supportive care [50]. Sahin et al. reported a study
related with 100 pregnant women who were suspected
diagnosis of SARS-CoV-2 infection. Twenty-nine of the
patients had the diagnosis confirmed by RT-PCR. Eight
of the remaining 71 cases had clinical findings highly
suggestive for COVID-19. Ten (34.5%) of the confirmed
cases had co-morbidities. COVID-19 therapy was given
to 10 (34.5%) patients. There were no intensive care unit
admission among patients. Pregnancy complications were
seen in 7 (24.1%) patients. Half of the births (5/10) were
cesarean deliveries. None of the neonates were positive for
SARS-CoV-2. Samples of breastmilk were also negative for
the virus. Three newborns needed neonatal intensive care
admission for insults other than COVID-19 [59].

7. Conclusion
Human being is tackling with dual threat, pandemic and
its’ socioeconomic consequences. Efforts are ongoing
globally to find a definitive cure for the SARS-CoV-2
infection. There is significant contribution of Turkish researchers to current scientific knowledge on COVID-19, mainly on transmission, passive prevention, disease features, diagnosis and partly treatment approaches which constitutes initial, characterization step for a new disease.

Advanced steps involve molecular characterization, active prevention and development of effective treatments against virus which need to be done more coordinated and with international collaboration.

References


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