

Letter to the Editor

Association between Crimean–Congo hemorrhagic fever (CCHF) and coronavirus disease 2019 (COVID-19): A systematic review

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To the Editor—We read the paper of Mehmood et al¹ with great interest. Their letter was based on a newspaper report of novel coronavirus (COVID-19) and Crimean–Congo hemorrhagic fever (CCHF) coinfection, and its scientific basis is questionable.

As cited by Mehmood et al, we previously described the management scheme of CCHF in Turkey in detail.² In 2003, a multi-disciplinary advisory board including representatives of Ministry of Health and the Ministry of Food was established. The management of CCHF patients has been carried out in the referral hospitals determined by the Ministry of Health in every region of the country. The virologic diagnosis has been established by the National Reference Laboratory. Records of all CCHF patients are entered into the national CCHF database. Education campaigns were organized for healthcare workers and those engaged in agriculture and animal husbandry in endemic regions. The World Health Organization (WHO), the European Center for Disease Prevention and Control (ECDC), the Food and Agricultural Organization of the United Nations (FAO) and the WHO collaborating Center at Porton Down, United Kingdom, are among the collaborative institutions, and the EpiSouth project, EDENext, ARBO-ZOONET CCH fever, and PREPARE are the networking projects involved in Turkey.² As a result of these measures and studies, the case fatality rate of CCHF is much lower, 4.8%, compared to countries in which CCHF is prevalent such as Pakistan (13.9%) and Iran (17.6%).³

We agree with the authors' comment that CCHF and COVID-19 have clinical symptoms in common. However, this is universal fact and is not restricted to the cases in Turkey. We performed a search according to the PRISMA guideline, using databases of PUBMED, SCOPUS, and Web of Science, and using the keywords "Crimean Congo Hemorrhagic Fever AND COVID-19" without language and manuscript type restriction (PROSPERO registration CRD42021271507). The inclusion criteria were "patients with confirmed positive COVID-19 AND with confirmed positive CCHF. There remained 33 publications when duplications were removed. After screening titles and abstracts, 11 full-text articles were assessed for eligibility. Two case reports were included the final analysis after excluding the reports not meeting inclusion criteria.^{4,5} The analysis showed only 2 case

reports of COVID-19 and CCHF coinfection from Turkey (Table 1).^{4,5} It is a rare occurrence.

Differential diagnosis of COVID-19 includes several viral and bacterial diseases such as influenza, adenovirus, human metapneumovirus, *Mycoplasma pneumoniae*, *Legionella pneumophila*, and *Streptococcus pneumoniae*.⁶ In areas where CCHF is endemic, this viral disease is included in the differential diagnosis. CCHF may mimic multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19.⁷ Severe COVID-19 pneumonia in adults has several clinical, laboratory, and radiographic features in common with CCHF.

Two reviews have discussed that the COVID-19 pandemic may have negatively affected the diagnosis and management of other illnesses, including CCHF. An additional 2 reports from Pakistan focused on the potential threat of CCHF due to mass gatherings during the Eid al Adha holiday.^{8,9} However, there is no evidence that CCHF cases increased following Eid al Adha in Turkey. One observational study noted increased CCHF cases after the COVID-19 pandemic began in 2020 compared to previous years in eastern region of Turkey.¹⁰ On the other hand, the health infrastructure in the country allows the effective diagnosis and management of CCHF and no burden of CCHF or COVID-19 cases is overwhelming the capacity of the healthcare system in Turkey.

In conclusion, our systematic review showed that coinfecting cases of COVID-19 and CCHF are rare. However, there appeared to be no difficulty with diagnosis, hospitalization needs, and treatment of the patients with CCHF during COVID-19 pandemic in Turkey, in contrast to the comment issued by Mehmood et al.¹ The need for an evidence-based approach is clear.

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Table 1. Patients Coinfected With COVID-19 and CCHF Reported From Turkey

Author	Age, y	Sex	Signs & Symptoms	Examination	Abnormal Laboratory Findings	Tick Exposure	COVID-PCR	CCHF-PCR	Thorax CT	Treatment	Outcome
Buyuktuna SA, et al ⁴	35	Female	Fever, body pain	Body temperature 38 °C, respiratory rate 22, other examination is normal	Leukopenia, thrombocytopenia, increased levels of ALT, AST, D-dimer, CRP, prolonged INR	Yes	+	+	Cystic bronchiectatic changes in apical, posterior, and anterior segments of upper lobe of the right lung and superior and posterior segments of lower lobe of the left lung	Favipiravir	Survived
Dülger AC, et al ⁵	65	Male	Dry cough, myalgia and fever	Oxygen saturation 95% on ambient air, other examination is normal	Pancytopenia, increased levels of ALT, AST, D-dimer	Not described	+	+	Multiple bilateral peripheral ground-glass opacities	Favipiravir	Survived

Note. PCR, polymerase chain reaction; CCHF, Crimean-Congo hemorrhagic fever; CT, computed tomogram; ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; INR, international normalization ratio.

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