Crimean-Congo Hemorrhagic Fever (CCHF) in Turkey: A Zoonosis Which Can Cause Nosocomial Infection: Invited Commentary

Türkiye'de Kırım Kongo Kanamalı Ateşi: Hastane Enfeksiyonuna Yol Açabilen Bir Zoonoz

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Crimean-Congo Hemorrhagic Fever (CCHF) is a fatal viral infection described in Africa, Asia, Eastern Europe, and the Middle East. The CCHF virus (CCHFV) belongs to *Nairovirus* and causes severe disease in humans, with a reported case-fatality rate of 5-30% depending on different strains and their epidemiological diversity. Humans become infected through the bites of ticks but also by contact with blood or fluids from a patient with acute CCHF.[1] Therefore, it cannot be considered only as a zoonotic tick-borne disease, but also a nosocomial infection, with high inter-personal transmission rates. CCHF is characterized by a sudden onset of high fever, chills, severe headache, dizziness, back and abdominal pains. Additional symptoms can include nausea, vomiting, diarrhea, neuropsychiatric, and cardiovascular changes. In severe cases, hemorrhagic manifestations, such as petechiae and/or ecchymosis, can develop.

There has been a significant increase in the number of published articles on CCHFV during the past 6 years. CCHFV geographical distribution is expanding to new foci of outbreaks in Turkey and the Balkan countries. CCHF epidemics sustained by a virulent serotype of the virus have already been documented in Anatolia between 2002 and 2008, with more than 2500 confirmed cases (5% fatality rate). In 2008, almost 1000 people were diagnosed as CCHF infection and 8 health care workers were infected. In the Balkan region of Turkey, in Balkan countries and in Greece a less virulent CCHFV is circulating. Since 2000, new outbreaks have been reported in Albania, former-Yugoslavia, Bulgaria. In Greece, the first human case was reported in 2008. In other countries, including Portugal, Hungary, and France only serologic evidence of CCHFV infection has been reported.[2] CCHFV isolated in Kosovo and Bulgaria is phylogenetically closely related to the Anatolian strain.[3]

CCHFV circulates in nature as a zoonosis, following a tick-vertebrate-tick cycle, and there is no evidence that the virus causes disease in animals other than humans and newborn mice. CCHFV infection is more common

among smaller wildlife species such as hares and hedgehogs that act as hosts for the immature stages of the tick vectors. On the other hand, antibodies against CCHFV have been detected in the sera of horses, donkeys, goats, cattle, sheep, and pigs in several regions of Europe, Asia, and Africa. The potential role of migratory birds and the movement of livestock carrying ticks in the spread of the virus over distant geographical areas have been described, therefore suggesting the need for implementing a European surveillance program. Climate changes might facilitate the reproduction of ticks (as well as other arthropod vectors), and consequently, increase the overall incidence of tick-borne diseases. In the northern hemisphere, *H. m. marginatum* is usually activated by the increasing temperature in the spring (usually the beginning of April), and the immature stages are active in summer between May to September.[2] Although the climate change to date is not necessarily the cause of the marked increased incidence of a variety of tick-borne diseases in Europe, the increase in temperature is associated with earlier outbreaks. The role of the climate change on the recent CCHF outbreak was discussed elsewhere.[4]

The spatial distribution of CCHF case reporting rates in Turkey was studied. A predictive model to map the habitat suitability for the vector tick was developed from satellite-based climate data covering the whole country. It was found that areas of higher risk (higher CCHF reporting) were correlated ($p< 0.05$) with zones of high climate suitability for the tick together with a high rate of fragmentation of agricultural land interspersed between forest and shrub-type vegetation.[5]

The high transmission rates of CCHFV and its ability to produce severe human disease with high fatality rates has resulted in classification of this organism as a category C bioterrorism agent.[2] Epidemiologically, CCHF cases are distributed mainly among those who work outdoors and are exposed to ticks. Most of affected persons work in agriculture and/or husbandry. Health care workers (HCW) represent the second most commonly affected group. HCW are under serious risk of infection, particular those who directly care for CCHF patients with frank hemorrhaging. Early diagnosis is critical for the patients and potential nosocomial infections, and for the prevention of transmission in the community. Suspected cases should be evaluated to plan the management, which includes supportive care, particularly hematological support.[2] Supportive therapy is an essential part of the case management for CCHF patients. It includes the administration of thrombocytes, fresh frozen plasma, and erythrocyte preparations. The antiviral drug, ribavirin, has been found to be effective against CCHFV in laboratory studies, although its exact mechanism of action against the virus is unclear. Despite this, its clinical use in CCHF is controversial, but it is the only antiviral drug we can use. Without an effective vaccine against CCHF and few treatment options, prevention against infection is the key.

The ESCMID conference on "Viral Haemorrhagic Fevers" was organized by European Society of Clinical Microbiology and Infectious Diseases, Turkish Society of Clinical Microbiology and Infectious Diseases, and Italian Virologic Society in 27-28 June 2008 in İstanbul. The faculty members were from Argentina, USA, UK, Germany, Italy, Switzerland, Sweden, France, Greece, South Africa, Spain, Slovenia, Iran, and Belgium. The scientific program of the meeting combined a variety of scientific disciplines. WHO representatives, ministry of health authorities, media members, and leading scientists on VHFs had participated to the meeting. Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK) summarized the results of the meeting as follows:[6]

1. Viral Hemorrhagic Fevers are seen in different geographies with different names. Recently, There is an outbreak of CCHF in Turkey. Sharing of the knowledge on different experiences has a great importance to combat against these life threatening infections.

2. CCHF should be defined as one of the leading public health threats in Europe and should be prioritized by the policy makers.

3. International and national funding bodies should support the research on CCHF and other emerging infections.

4. The participants were agree on the use of ribavirin particularly in the early phase of the disease course. Consequently the participants were not agree on running a randomized controlled clinical study to assess the effectivity of ribavirin on CCHF. Because not to give ribavirin to some of the patients wouldn't be ethical.

5. The patients should be diagnosed and treated on the site of infection and the rate of patient transfer should be reduced. The capacity of laboratory diagnosis and treatment on the local level should be increased.

6. The efficacy of the education efforts targeted to prevent tick bite should be evaluated and should be re-considered in terms of effectivity.

We should accept that CCHF outbreak in Turkey is an outstanding, but also very interesting one with its various aspects. I believe that, the struggle against such a multisectoral infection will improve our capacity to combat against many other infections in the future.

REFERENCES

1. Ergonul O. Crimean-Congo haemorrhagic fever. Lancet Infect Dis 2006; 6:203-14.
2. Ergonul O, Whitehouse CA. Introduction. In: Ergonul O, Whitehouse CA, eds. Crimean Congo Hemorrhagic Fever: A Global Perspective. Dordrecht: Springer; 2007. p.3-11.
3. Midilli K, Gargili A, Ergonul O, Sengoz G, Ozturk R, Bakar M, et al. Imported Crimean-Congo hemorrhagic fever cases in Istanbul. BMC Infect Dis 2007;7: 54.
4. Randolph S, Ergonul O. Crimean-Congo Hemorrhagic Fever: exceptional epidemic of viral hemorrhagic fever in Turkey. Future Virol 2008 3: 303-6.
5. Estrada-Peña A, Zatansever Z, Gargili A, Aktas M, Uzun R, Ergonul O, et al. Modeling the Spatial Distribution of Crimean-Congo Hemorrhagic Fever Outbreaks in Turkey. Vector Borne Zoonotic Dis 2007; 7:667-78.
6. Conference proceedings, "Viral Haemorrhagic Fevers", European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK), Italian Virologic Society, 27-28 June 2008, Istanbul.