



Crimean-Congo hemorrhagic fever represents a zoonotic infection: A review

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ABSTRACT

One of the public health challenges is the control of Crimean-Congo hemorrhagic fever (CCHF), as this viral zoonotic disease infected both animals and humans, sometimes leading to death. Re-emergence of this endemic in some regions, such as our country, to the need for more documented information and facts about it, Iraq, has led transmitted, infected, and prevent it. Therefore, this review aimed to summarize main information about this infection. The causative virus consists of a globular RNA genome particle with a segmented negative sense encapsulated in a lipid structure containing or direct contact with infected viral glycoproteins. Infection usually occurs by ticks human or animal tissue or blood. The causative virus has a high ability to transmit in Infection in areas with mammals, whether large or small, such as rabbits and cattle. animals is asymptomatic, while in peoples it is manifested by high fever and ends with hemorrhagic syndrome. It is recommended to implement preventive measures to control tick vectors in endemic countries, and to encourage collaboration between clinical veterinary, physicians and ecologists' researchers

Keywords:

Zoonotic infection, hemorrhagic fever, tick borne.

Introduction

A zoonosis defined simply as an infectious disease caused by pathogens transmitted between animal species and humans [1-3]. It represents a public health challenge recently, especially after the emergence of the last pandemic (Covid-19), which has led to harm millions of peoples around the world, in addition to economic losses. Therefore, there remain fears of the emergence of other epidemics that may be out of control, especially viral ones [4-6]. One of the zoonotic diseases affecting humans is Crimean-Congo hemorrhagic fever (CCHF), the pathogen of which is a virus belonging to the *Nairoviridae* family, and characterized by symptoms pre-hemorrhagic syndrome [7], such as high fever with myalgia and gastrointestinal symptoms, and it may develop into hemorrhagic

manifestations from various organs, with a mortality rate of up to 30%. This hemorrhagic disease is usually transmitted to humans by ticks or contact with body fluids of infected animals or individuals [8,9]. On the other hand, it is in wild and domestic animals without clinical symptoms, but the virus multiplies and is an effective source of disease for ticks and humans, especially during the infection, which usually not exceeding 15 days [10].

In 1944-1945 it was confirmed for the first time in Russian soldiers and peasants in the Crimea and in 1956 in the Congo, exposed to ticks. Ticks, especially of the genus *Hyalomma*, are natural vectors and reservoirs of this causative virus, as they maintain this virus for long periods of months or even years [11]. It is worth noting that cattle are a common home host for the adult stage of this genus [12]. In

2016 prevalence rates were between 20 and 30% in Iraq, Iran and Turkey in cattle, camels and sheep. CCHF has been identified as potentially endemic throughout Africa, Asia and the Middle East. It should be noted that global warming induces a change in the distribution of vectors, which may lead to an increased risk of this viral agent appearing in new geographical regions. Turkey and Iran, two of Iraq's neighbors, are endemic to CCHF and have confirmed reports of recent outbreaks and rising cases. Depending on the statements of the Iraqi Ministry of Health, there

has been a rise in the number of cases over the past two years [13,14]. A current review discusses taxonomy and structure of causative virus, mode of transmission, clinical forms, and possible prevention of infection.

Taxonomy & Structure of CCHF Virus

In general, Nairoviridae is a family of Bunyavirales order, and this family includes three main genera, including Orthonairovirus, which contains CCHF virus along with other fourteen viral species [15], as display in Figure (1).

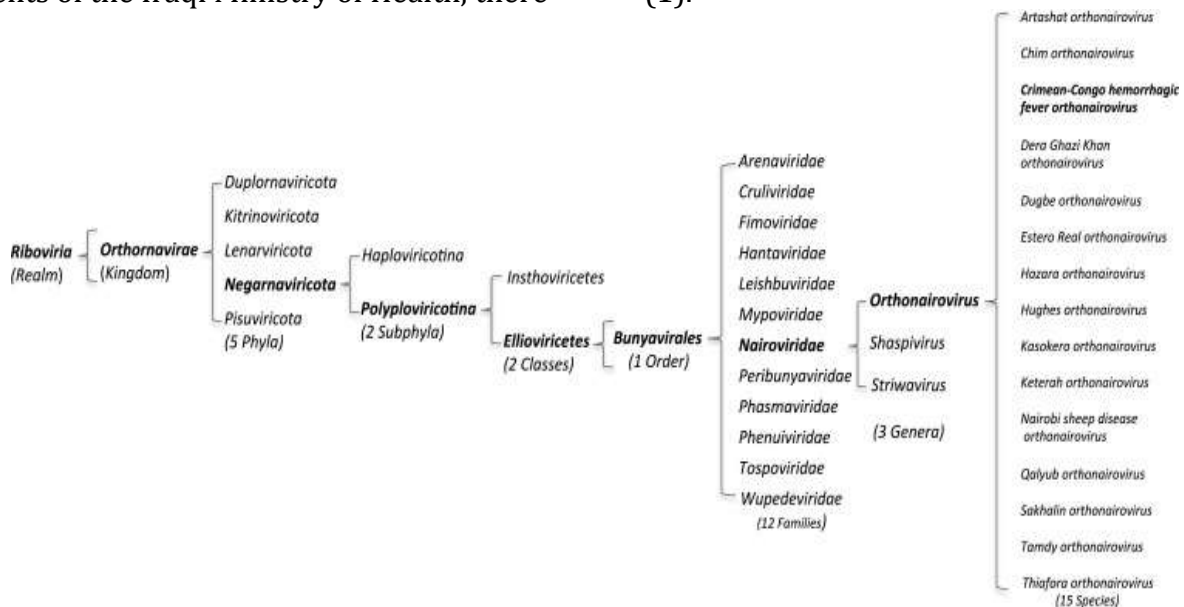


Figure 1: Taxonomy of CCHFV in Bunyavirales order [16].

This virus like a spherical particle and has a single-stranded RNA genome with a segmented negative sense with diameter ranges approximately from 80 to 120 nm. It consists of (3) clear segments: small, medium, and large

(S, M, and L respectively). The genome is enveloped by a lipid structure that contains the viral glycoproteins (G1 and G2)[17], as illustrate in figure (2) .

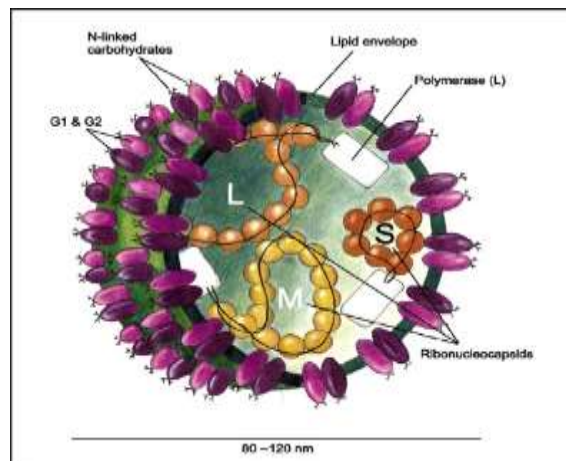


Figure 2: Structure of CCHF virus [18].

Transmission

Ticks especially of *Hyalomma* genus serve as competent vectors and primary reservoirs for CCHFV. The infection is transmitted to humans usually through the bites or crushing of infected ticks with bare hands, or contact with tissues or blood of infected animals or even people [19], as shown in Figure (3). So that, people in contact with animal blood, medical staff, and laboratory workers are more likely to be infected. This disease can be transmitted from one person to another through contacts or hospital acquired infections. Moreover, severe infant–maternal transmission of CCHF may lead to infant and fetal mortality [20]. The infection rate is high during the spring and summer seasons when ticks multiply, and there is a significant correlation between the ability

of ticks to transmit this virus and the ecosystem in which they grow. It should be noted that the causative virus has a high ability to transmit in areas that have mammals, whether large or small, such as cattle, sheep, and rabbits [21]. The virus overcomes the salivary glands and even the intestinal barriers inside the tick, and the efficiency of the tick vector by inducing the transmitted infection depends on avoiding the innate immune response to the tick. The minimum virus titer required to infect ticks varies among tick species. After intracellular virus inoculation, virus titer positively correlates with blood feed. Viral infection in ticks is not completely silent and may affect tick survival, behavior, and gene expression [22,23].

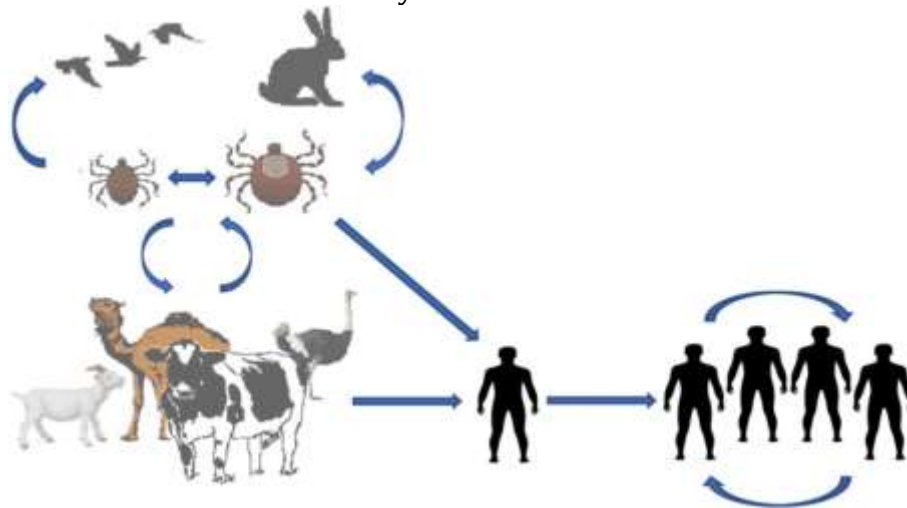


Figure 3: Transmission of CCHF infection [24].

Clinical symptoms in Animals & Humans

In general, infection in animals, especially wild and domesticated mammals, is characterized by the absence of clinical symptoms. However, viremia can persist in mammals for up to 14 days. Animals play an important role in the life cycle of this infection, and the causative virus amplified before being transmitted to peoples by ticks [25]. In humans, this disease characterize by suddenly high fever, chills, and

dizziness in addition to gastrointestinal disturbances such as vomiting and diarrhea. It is called the pre-hemorrhagic period and usually ends after three days. The incubation period of the disease extends to a week. The hemorrhagic phase is shorter as the patient suffers from blood loss in the digestive, respiratory and urinary tracts in addition to blood loss from the skin that ranges from petechiae to bruises [26,27].



Figure 4: Patient infected with CCHF [28].

Prevention and Control

The key measure to achieving prevention for this infection is avoiding tick bites by applying acaricides in livestock production farms. It is known that controlling this infection in the animal host is not easy because it is asymptomatic. Acaricides are particularly useful when used prior to the slaughter of animals, with a 14-day pre-mortem quarantine period in endemic areas. Animal movements across borders, especially to endemic countries, must also be controlled and protecting humans from transmission of infection through the application of protection measures, especially in individuals at risk [29,30]. Unfortunately, there is no confirmed and safe vaccine available. People in contact with animals, and those living in affected countryside, must wear long, light-colored protective clothing for quick identification of ticks [31]. However, when a tick gets stuck, it must be lifted with quickly fine-tipped tweezers, and the bites areas should be cleaned

and hands sanitized as much as possible. Care must be taken when touching carcasses and body fluids of dead animals, and not to handle without gloves [32]. Not to dispose of animal waste and blood in the waterways, as well as sanitary burial directly, but the correct methods must be followed [33]. Also, prevent the practices of slaughtering animals outside designated slaughterhouses [34]. During Eid Al-Adha, the procedures for examining animals for tick infection, as well as disinfection of animals using insecticides, must be intensified with strict regulation of animal movement supported by a monitoring program because of increased rates of animal movements [35,36]. In order to complete the application of controlling any zoonotic infection, especially viral ones, one health strategies must be implemented [37]. The role of environmental health comes in preventing pests such as rodents, insects, birds and pets from reaching the slaughter area and disposing of solid and liquid waste [38].

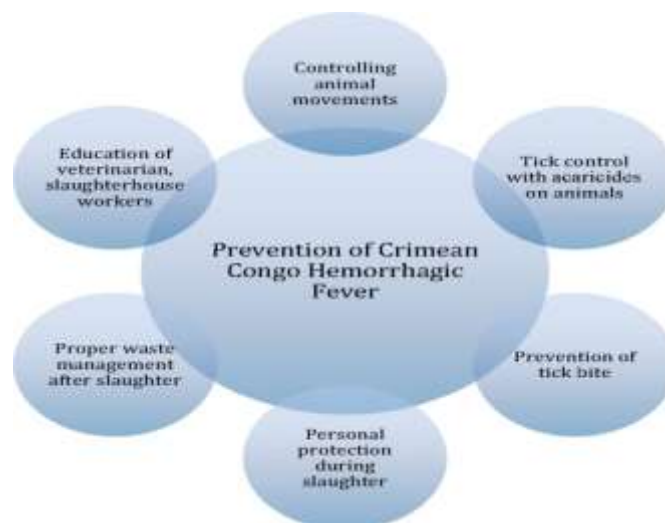


Figure 5: Key factors for prevention of CCHF [39].

Conclusions

This review confirms the possibility of transmission of CCHF infection during slaughter practices, which plays an important role in infection with the causative virus. Therefore, it must be reminded of the inevitability of managing zoonotic diseases, especially in endemic countries. Local authorities in endemic countries should implement effective measures to control tick vectors. Collaboration between clinical veterinary, physicians and environmental scientists should also be encouraged.

References

- 1- Ghareeb OA, Ali QA. Waterborne Zoonotic Bacterial Pathogens. *Texas Journal of Medical Science*. 2023 Jun; 21:63-69.
- 2- Ghareeb OA, Sultan AI. Nipah-An Emerging Viral Zoonotic Disease: A Review. *Annals of the Romanian Society for Cell Biology*. 2021 Apr 7:456-465.
- 3- Ghareeb OA. Ebola-A fatal Emerging Zoonotic Disease: A Review. *Annals of the Romanian Society for Cell Biology*. 2021;25(6):8748-8754.
- 4- Kzar AJ, Faiq TN, Ghareeb OA. Recent infection with black fungus associated with COVID-19: a review. *Pakistan Journal of Medical and Health Sciences*. 2021; 15 (5) : 1771-1773.
- 5- Al-Haidari KA, Faiq TN, Ghareeb OA. Preventive value of black seed in people at risk of infection with COVID-19. *Pakistan Journal of Medical and Health Sciences*. 2021 Jan 1; 15 (1):384-387.
- 6- Ciloglu A, Ibis O, Yildirim A, Aktas M, Duzlu O, Onder Z, Simsek E, Yetismis G, Ellis VA, Inci A. Complete mitochondrial genome characterization and phylogenetic analyses of the main vector of Crimean-Congo haemorrhagic fever virus: *Hyalomma marginatum* Koch, 1844. *Ticks and Tick-Borne Diseases*. 2021 Sep 1;12(5):101736.
- 7- Aslam M, Abbas RZ, Alsayeqh A. Hemorrhagic Fever in Asia and the Middle East. *Frontiers in Public Health*. 2023 Jan 26;11:1093817.
- 8- Telford C, Nyakarahuka L, Waller L, Kitron U, Shoemaker T. Spatial prediction of Crimean Congo hemorrhagic fever virus seroprevalence among livestock in Uganda. *One Health*. 2023 Jun 12:100576.
- 9- Klucher J, Gonzalez A, Shishido AA. Crimean-Congo Hemorrhagic Fever: A Refresher and Update for the SOF Provider. *Journal of Special Operations Medicine: a Peer Reviewed Journal for SOF Medical Professionals*. 2023 Feb 8:UZTO-DWEP.
- 10-Matthews J, Secka A, McVey DS, Dodd KA, Faburay B. Serological Prevalence of Crimean-Congo Hemorrhagic Fever Virus Infection in Small Ruminants and Cattle in The Gambia. *Pathogens*. 2023 May 23;12(6):749.
- 11-Sankhe S, Talla C, Thiam MS, Faye M, Barry MA, Diarra M, Dia M, Ndiaye O, Sembene PM, Diop B, Fall G. Seroprevalence of Crimean-Congo Hemorrhagic Fever Virus and Rift Valley Fever Virus in human population in Senegal from October to November 2020. *IJID regions*. 2023 Jun 1;7:216-21.
- 12-Badji A, Ndiaye M, Gaye A, Dieng I, Ndiaye EH, Dolgova AS, Mhamadi M, Diouf B, Dia I, Dedkov VG, Faye O. Detection of Crimean-Congo Haemorrhagic Fever Virus from Livestock Ticks in Northern, Central and Southern Senegal in 2021. *Tropical Medicine and Infectious Disease*. 2023 Jun 12;8(6):317.
- 13-Jafar U, Usman M, Ehsan M, Naveed A, Ayyan M, Cheema HA. The outbreak of Crimean-Congo hemorrhagic fever in Iraq-Challenges and way forward. *Annals of Medicine and Surgery*. 2022 Sep 1;81:104382.
- 14-Alhilfi RA, Khaleel HA, Raheem BM, Mahdi SG, Tabche C, Rawaf S. Large Outbreak of Crimean-Congo

- Haemorrhagic Fever in Iraq, 2022. *IJID Regions*. 2023 Jan 18.
- 15-Papa A, Marklewitz M, Paraskevopoulou S, Garrison AR, Alkhovsky SV, Avšič-Županc T, Bente DA, Bergeron É, Burt F, Di Paola N, Ergünay K. History and classification of Aigai virus (formerly Crimean–Congo haemorrhagic fever virus genotype VI). *Journal of General Virology*. 2022 Apr 12;103(4):001734.
- 16-Serretiello E, Astorri R, Chianese A, Stelitano D, Zannella C, Folliero V, Santella B, Galdiero M, Franci G, Galdiero M. The emerging tick-borne Crimean-Congo haemorrhagic fever virus: A narrative review. *Travel Medicine and Infectious Disease*. 2020 Sep 1;37:101871.
- 17-Sánchez-Seco MP, Sierra MJ, Estrada-Peña A, Valcárcel F, Molina R, de Arellano ER, Olmeda AS, San Miguel LG, Jiménez M, Romero LJ, Negrodo A. Widespread detection of multiple strains of Crimean-Congo hemorrhagic fever virus in ticks, Spain. *Emerging Infectious Diseases*. 2022 Feb;28(2):394.
- 18-Ergonul O. Chapter 10—Crimean-Congo Hemorrhagic Fever. *Emerging Infectious Diseases*. 2014:135-48.
- 19-Khosti A, Sardar S, Gulsharif S. Crimean-Congo Hemorrhagic Fever (CCHF): An Emerging Disease in Afghanistan. *Integrated Journal for Research in Arts and Humanities*. 2023 Jan 15;3(1):34-40.
- 20-Kalal MN. Crimean-congo haemorrhagic fever: a global perspective. *International Journal of Research in Medical Sciences*. 2019 Dec;7(12):4812.
- 21-Sorvillo TE, Rodriguez SE, Hudson P, Carey M, Rodriguez LL, Spiropoulou CF, Bird BH, Spengler JR, Bente DA. Towards a sustainable one health approach to crimean–congo hemorrhagic fever prevention: Focus areas and gaps in knowledge. *Tropical Medicine and Infectious Disease*. 2020 Jul 7;5(3):113.
- 22-Munir F, Shakoor A, Aleem MT. Crimean-Congo hemorrhagic fever: Immuno pathogenesis and recent advances in the development of vaccines. *Microbial Pathogenesis*. 2023 Mar 5:106054.
- 23-Hamidinejad MA, Ghaleh HE, Farzanehpour M, Bolandian M, Dorostkar R. Crimean-Congo hemorrhagic fever from the immunopathogenesis, clinical, diagnostic, and therapeutic perspective: A scoping review. *Asian Pacific Journal of Tropical Medicine*. 2021;14(6):254-65.
- 24-Fillâtre P, Revest M, Tattevin P. Crimean-Congo hemorrhagic fever: An update. *Medecine et maladies infectieuses*. 2019 Nov 1;49(8):574-85.
- 25-Spengler JR, Estrada-Peña A, Garrison AR, Schmaljohn C, Spiropoulou CF, Bergeron É, Bente DA. A chronological review of experimental infection studies of the role of wild animals and livestock in the maintenance and transmission of Crimean-Congo hemorrhagic fever virus. *Antiviral research*. 2016 Nov 1;135:31-47.
- 26-Shrivastava N, Kumar JS, Yadav P, Sharma S, Shete AM, Jain R, Shrivastava A, Dash PK. Development and evaluation of indirect antibody ELISA assay for early diagnosis and surveillance of Crimean-Congo hemorrhagic fever infection in humans. *Virus Research*. 2022 May 1;313:198717.
- 27-Hawman DW, Feldmann H. Crimean–Congo haemorrhagic fever virus. *Nature Reviews Microbiology*. 2023 Mar 14:1-5.
- 28-Bente DA, Forrester NL, Watts DM, McAuley AJ, Whitehouse CA, Bray M. Crimean-Congo hemorrhagic fever: history, epidemiology, pathogenesis, clinical syndrome and genetic diversity. *Antiviral research*. 2013 Oct 1;100(1):159-89.
- 29-Al-Rubaye D, Al-Rubaye TS, Shaker M, Naif HM. Recent outbreaks of crimean–congo hemorrhagic fever (CCHF) In Iraq. *Sci Arch*. 2022;3:109-12.

- 30-Leblebicioglu H, Sunbul M, Memish ZA, Al-Tawfiq JA, Bodur H, Ozkul A, Gucukoglu A, Chinikar S, Hasan Z. Consensus report: preventive measures for Crimean-Congo hemorrhagic fever during Eid-al-Adha festival. *International Journal of Infectious Diseases*. 2015 Sep 1;38:9-15.
- 31-Mohammed TA, Mostafa AH, Ahmad JQ, Yahya NB, Tayib GA. The Trojan horse feature of SARS-CoV-2 behind the re-emergence of the Crimean-Congo hemorrhagic fever in Iraq. *Human Vaccines & Immunotherapeutics*. 2022 Nov 30;18(6):2128610.
- 32-Norouzi M, Dayer MS, Ghaffarifar F. Molecular detection and characterisation of *Theileria* in hard ticks of small ruminants in Zarrin Dasht County, Southern Iran. *Veterinary Medicine and Science*. 2023 Jan;9(1):372-9.
- 33-Sahito AM, Mir SL, Waseem M, Awan MA, Shaikh S, Essar MY. The possibility of the emergence of Crimean-Congo virus cases during Eid ul Adha: A troubling situation during a blessed festival. *Annals of Medicine and Surgery*. 2022 Sep 1;81:104379.
- 34-Nasirian H. New aspects about Crimean-Congo hemorrhagic fever (CCHF) cases and associated fatality trends: A global systematic review and meta-analysis. *Comparative immunology, microbiology and infectious diseases*. 2020 Apr 1;69:101429.
- 35-Meurens F, Dunoyer C, Fourichon C, Gerds V, Haddad N, Kortekaas J, Lewandowska M, Monchatre-Leroy E, Summerfield A, Schreur PJ, van der Poel WH. Animal board invited review: Risks of zoonotic disease emergence at the interface of wildlife and livestock systems. *Animal*. 2021 Jun 1;15(6):100241.
- 36-Ghasemian A, Al-Alo KZ, Falsafi S, Mostafavi SK. The worldwide spread of Crimean Congo hemorrhagic fever orthonaviruses and Q fever: risk factors and implications for control strategies of a zoonotic disease. *Revista Brasileira de Higiene e Sanidade Animal*. 2022 Mar 31;16(1):1-3.
- 37-Ghareeb OA, Ramadhan SA. COVID-19-a novel zoonotic disease: Origin, prevention and control. *Pak. J. Med. Health Sci*. 2021 Jan 1;15: 221-223.
- 38-Sorvillo TE, Rodriguez SE, Hudson P, Carey M, Rodriguez LL, Spiropoulou CF, Bird BH, Spengler JR, Bente DA. Towards a sustainable one health approach to crimean-congo hemorrhagic fever prevention: Focus areas and gaps in knowledge. *Tropical Medicine and Infectious Disease*. 2020 Jul 7;5(3):113.
- 39-Leblebicioglu H, Sunbul M, Memish ZA, Al-Tawfiq JA, Bodur H, Ozkul A, Gucukoglu A, Chinikar S, Hasan Z. Consensus report: preventive measures for Crimean-Congo hemorrhagic fever during Eid-al-Adha festival. *International Journal of Infectious Diseases*. 2015 Sep 1;38:9-15.