Infection and Drug Resistance

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Clinical and Epidemiological Characteristics of 30 Fatal Cases of Crimean-Congo Hemorrhagic Fever in Kabul, Afghanistan: A Retrospective Observational Study

Ahmad Shekaib Rasikh[1], Mohammad Maroof Aram[2], Abdul Tawab Noory[1]

[1]Department of Infectious Diseases, Ali Abad Teaching Hospital, Kabul University of Medical Sciences, Kabul, Afghanistan; [2]Department of Internal Medicine, Ali Abad Teaching Hospital, Kabul University of Medical Sciences, Kabul, Afghanistan

Correspondence: Ahmad Shekaib Rasikh, Tel +93 791906514, Email shekaib.rasikh@gmail.com

Objective: Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic disease associated with a high fatality rate. CCHF is endemic in Afghanistan, and its morbidity and mortality have increased recently but there is limited data about the characteristics of fatal cases. We aimed to report the clinical and epidemiological features of fatal CCHF cases who were admitted to Kabul Referral Infectious Diseases (Antani) Hospital.

Methods: This is a retrospective cross-sectional study. The demographic and presenting clinical and laboratory features of 30 fatal CCHF cases diagnosed by reverse transcription polymerase chain reaction (RT-PCR) or enzyme-linked immunosorbent assay (ELISA) tests were collected from the patients' records between March 2021 and March 2023.

Results: During the study period, a total of 118 laboratory-confirmed CCHF patients were admitted to Kabul Antani Hospital of whom 30 patients (25 males, 5 females) consequently died, indicating a 25.4% case fatality rate (CFR). The age of the fatal cases ranged from 15 to 62 years and their mean age was 36.6 ± 11.7 years. Concerning occupation, the patients were butchers (23.3%), animal dealers (20%), shepherds (16.6%), housewives (16.6%), farmers (10%), student (3.3%), and others (10%). The clinical symptoms of the patients on admission were fever (100%), generalized body pain (100%), fatigue (90%), bleeding (any type) (86.6%), headache (80%), nausea/vomiting (73.3%), and diarrhea (70%). The initial abnormal laboratory findings were leukopenia (80%), leukocytosis (6.6%), anemia (73.3%), and thrombocytopenia (100%), raised hepatic enzymes (ALT & AST) (96.6%) and prolonged prothrombin time/international normalized ratio (PT/INR) (100%).

Conclusion: The hemorrhagic manifestations associated with low platelet and raised PT/INR levels are linked with fatal outcomes. A high index of clinical suspicion is required to recognize the disease at an early stage and to begin the treatment promptly for reducing mortality.

Keywords: Afghanistan, Crimean-Congo hemorrhagic fever, fatal, thrombocytopenia

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is an acute tick-borne zoonotic illness caused by infection with the CCHF virus (CCHFV) belonging to the genus Orthonairovirus in the family Nairoviridae and the order Bunyavirales. The disease was first characterized with a viral etiology in the Crimea region in 1944 and named Crimean hemorrhagic fever; later, in 1956, its causative agent was discovered in Congo and was given its current name.[1–4]

CCHF is usually transmitted to humans through the bite of infected Hyalomma ticks as well as by direct contact with the blood and tissues of infected domestic animals. It is rarely transmitted from person to person via contact with blood, and other body fluids of infected patients. The occupational groups at risk of acquiring the infection are butchers, shepherds, farmers, animal dealers, and health-care workers dealing with the patients.[5–7]

Received: 1 April 2023
Accepted: 30 May 2023
Published: 2 June 2023

The clinical features of the disease vary from sub-clinical infection to severe and fatal disease. The average incubation period of the disease is 3–7 days. Its initial clinical symptoms are non-specific and include fever, fatigue, severe muscle/joint pain, headache, abdominal pain, nausea, vomiting, and diarrhea. In severe cases, hepatosplenomegaly and hemorrhage develop. Hemorrhagic manifestations develop in late-stage disease. Complications of the disease that might result in death are hemorrhage, shock, disseminated intravascular coagulation (DIC), and multi-organ failure involving the liver, kidney, and lungs.[8–11]

Diagnosis of the disease is laboratory confirmed by the detection of the virus ribonucleic acid (RNA) by reverse transcription polymerase chain reaction (RT-PCR) or detection of IgM antibody by enzyme-linked immunosorbent assay (ELISA) test in the blood. Other laboratory findings include thrombocytopenia, leukopenia, elevated hepatic enzymes (ALT and AST), and prolonged prothrombin time/international normalized ratio (PT/INR).[10,12]

CCHF is a fatal disease and most deaths occur within 2 weeks of the onset of the disease. Its case fatality rate (CFR) is reported from 3% up to as high as 50% in different regions. The difference in mortality rate is attributed to early diagnosis and supportive treatment of disease and its fatal complications.[5,6,13]

CCHF is a public health problem in the Middle East, Eastern Europe, Africa, and Asia where its vector the Hyalomma ticks exist.[5,14–17] Afghanistan is an endemic area for the CCHF. The first case in this country was reported in 1998 from Takhar (a province in the northeast of the country). Since then, several outbreaks of the disease have been reported. Active CCHF surveillance in Afghanistan was started in 2007 and by 2018 a total of 1284 clinical and laboratory-diagnosed cases were reported, ranging from 4 cases in 2007 to 483 cases in 2018.[6,18] According to the National Disease Surveillance and Response (NDSR) reports by the Ministry of Public Health of Afghanistan, a total of 87 and 426 CCHF cases were reported in 2021 and 2022, respectively, indicating an increasing trend. The majority of cases were reported from Kabul and Herat cities.[19,20]

According to the World Health Organization in 2022 Afghanistan was among the countries with the highest number of CCHF cases (50 and more cases reported per year).[21] The number of confirmed cases has been increasing in Afghanistan recently but the capacity for laboratory testing and management of the cases remains limited.[6,22,23]

The number of CCHF cases in Afghanistan particularly increases around the Eid-ul-Adha (Muslim festival of sacrifice) in which Muslims around the world sacrifice animals such as cattle, sheep, goats, or camels.[6,24] According to personal observations, each year the days and weeks around Eid-ul-Adha an increased number of suspected CCHF patients are brought to Kabul Antani Hospital and this has been increasing annually.

Several studies have been carried out on CCHF in Afghanistan but information about the clinical characteristics of fatal cases is scarce, hence this study was undertaken to report the demographic, clinical, and laboratory characteristics of CCHF cases with fatal outcomes that contribute to early identification of the cases that lead to death.

Methods

A retrospective cross-sectional study was carried out in Kabul Referral Infectious Diseases (Antani) Hospital. From March 2021 to March 2023 a total of 30 fatal CCHF cases whose diagnosis was confirmed by either RT-PCR or ELISA tests were enrolled in the study. Their demographic, presenting clinical and laboratory characteristics, which were written in either English or two national (Dari and Pashto) languages were reviewed using the patient's files, laboratory reports, and death certificates in the hospital's medical records department. A table was prepared for collecting the data, and the software SPSS (Version 26th) was used for statistical analysis. The continuous variables were presented as numbers (percentages) or as mean ± standard deviations.

Study Setting

Kabul Infectious Diseases (Antani) Hospital is the main referral tertiary public hospital in the capital of Afghanistan with an isolation ward for the care of CCHF patients referred there from across the country, although its capacity and facilities are limited. In recent years, blood samples from suspected and probable CCHF cases admitted to the hospital are sent to central public health laboratories for RT-PCR or ELISA test for confirmation of diagnosis.

Case Definition of CCHF

Kabul Antani Hospital adopts the standard CCHF case definition by the World Health Organization (WHO). According to WHO,

A suspected case is defined as a patient with sudden onset of illness with high-grade fever > 38.5 °C for more than 72 hours and less than 10 days, especially in CCHF-endemic areas and among those in contact with sheep or other livestock.

A probable case is defined as a suspected case with an acute history of febrile illness ≤10 days AND Thrombocytopenia < 50000/mm3 with any 2 of the following: petechial or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in stools, ecchymosis, gum bleeding, other hemorrhagic symptom AND unknown predisposing host factors for hemorrhagic manifestations.

A confirmed case is defined as a probable case with confirmation of the presence of IgM or IgG antibodies to the CCHF virus in serum by ELISA and/or detection of viral nucleic acid in the specimen by RT-PCR.[21,25]

Ethics Statement

The proposal for this study was approved by the research committee of the Kabul University of Medical Sciences. The requirement of informed consent was waived due to its retrospective and anonymous characteristics. The consent of the Kabul Antani Hospital authority was obtained for collecting the data, and the confidentiality of the collected data is maintained. All aspects of this study comply with the ethical standards of the relevant institutional committees on studies involving human contacts and the Declaration of Helsinki adopted in 1975 and subsequent revisions.

Results

From March 2021 to March 2023 a total of 234 suspected and probable CCHF patients were admitted to Kabul Referral Infectious Diseases (Antani) Hospital. 118 (50.4%) of these cases were confirmed by the ELISA and/or RT-PCR test. These 118 confirmed cases were comprised of 28 (23.7%) females and 90 (76.3%) males. Among the confirmed cases, 30 patients (comprised of 25 males and 5 females) consequently died, indicating an overall 25.4% CFR. The CFR was 17.8% and 27.8% among females and males, respectively. These data indicate a male preponderance overall and also in fatal cases. Among the fatal cases, the diagnosis of 11 patients was confirmed by RT-PCR, while 19 cases were confirmed by the detection of IgM antibody using the ELISA test. The dead patients' age ranged from 15 to 62 years and their mean age was 36.6 ± 11.7 years, and 83.3% of patients were between 20 and 50 years old. The most frequent occupational groups affected were butchers/slaughterhouse workers, animal dealers, shepherds, housewives, farmers, students, and others, respectively. The majority of cases (53.3%) were residents of rural areas, as shown in Table 1.

The mean duration from onset of symptoms to hospital admission was 5.3 ± 1.9 days ranging from 2 to 10 days and from onset of symptoms to death was 7 ± 2.1 days ranging from 4 to 12 days. The most common clinical manifestations of patients on admission were fever, generalized body pain, fatigue, hemorrhage (any type), headache, nausea/vomiting, and diarrhea, respectively. The sites of hemorrhage were epistaxes, skin (petechiae/ecchymosis), gingival bleeding, melena, hematemesis, hematuria, and vaginal bleeding, respectively (Table 2).

At the time of admission, all of the patients had thrombocytopenia and prolonged prothrombin time/international normalized ratio (PT/INR). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were elevated in 29 (96.6%) patients. Twenty-four (80%) had leukopenia, 2 (6.6%) had leukocytosis, and 22 (73.3%) had anemia as shown in Table 3.

Concerning treatment, all of the patients have received oral ribavirin (started at the time of admission). The mean time from the onset of symptoms to the start of ribavirin was 5.3 ± 1.9 days. In addition, all of the patients received platelet mass, fresh frozen plasma (FFP), and antibiotics. Based on data from the patients' death certificates, the complications of the disease that led to the death of the patients were recorded as shock (93.3%), multi-organ failure (76.6%), and disseminated intravascular coagulation (DIC) (66.6%).

Table 1 Demographic Characteristics of Fatal CCHF Cases

	n (%) or Mean ± Standard Deviation
Overall	30 (100)
Gender	
Male	25 (83.3)
Female	5 (16.6)
Age (years)	36.6 ± 11.7
< 20	2 (6.6)
20–30	9 (30.0)
31–40	8 (26.6)
41–50	8 (26.6)
51–60	2 (6.6)
> 60	1 (3.3)
Occupation	
Butcher	7 (23.3)
Animal dealer	6 (20.0)
Shepherd	5 (16.6)
Housewives	5 (16.6)
Farmer	3 (10.0)
Student	1 (3.3)
Other	3 (10.0)
Residence	
City	14 (46.7)
Rural	16 (53.3)

Table 2 The Clinical Features of Fatal CCHF Cases on Admission

	n (%) or Mean ± Standard Deviation
Overall	30 (100)
Days from onset of symptoms to hospital admission	5.3 ± 1.9
Days from onset of symptoms to death	7 ± 2.1
Clinical symptoms	
Fever	30 (100)
General body pain	30 (100)
Fatigue	27 (90)
Bleeding (any site)	26 (86.6)
Headache	24 (80.0)
Nausea/vomiting	22 (73.3)
Diarrhea	21 (70.0)
Bleeding type/site (n =26)	
Epistaxis	19 (73.0)
Skin (Petechiae/Ecchymosis)	16 (61.5)
Gingival	15 (57.6)
Melena	13 (50.0)
Hematemesis	8 (30.7)
Hematuria	7 (26.9)
Vaginal	1 (3.8)
Days from onset of symptoms to start of Ribavirin	5.3 ± 1.9

Table 3 The Initial Laboratory Results of Fatal CCHF Cases

	n (%) or Mean ± Standard Deviation
Overall	30 (100)
White Blood Cell count, $\times 10^9$/L; normal range, 4.5–11	4.0 ± 2.3
Normal	4 (13.3)
Leukocytosis	2 (6.6)
Leukopenia	24 (80.0)
Hemoglobin, g/dl; normal range, 12–17	10.8 ± 2.1
Normal	8 (26.6)
Decreased (Anemia)	22 (73.3)
Thrombocytes (Platelets), $\times 10^9$/L; normal range, 150–450	34.4 ± 24.1
Normal	0 (0.0)
Decreased	30 (100)
Alanine Transaminase (ALT), U/L; normal range, 7–55	980.1 ± 989.9
Normal	1 (3.3)
Increased	29 (96.6)
Aspartate Transaminase (AST), U/L; normal range, 8–48	1195.9 ± 1318.3
Normal	1 (3.3)
Increased	29 (96.6)
Prothrombin time (PT), seconds; normal range, 11–16	31.5 ± 7.5
Normal	0 (0.0)
Prolonged	30 (100)
International Normalized Ratio (INR); normal, 0.9–1.1	2.52 ± 0.75
Normal	0 (0.0)
Prolonged	30 (100)

Discussion

The findings of this paper are based on retrospective analysis of epidemiologic and presenting clinical and laboratory features of fatal CCHF cases admitted to Kabul Referral Infectious Diseases (Antani) Hospital. It is hoped that these findings will help clinicians of CCHF endemic areas in the early identification of fatal cases by being aware of some of the striking clinical and laboratory characteristics presented by the patients, and also help guide appropriate and effective management for future patients.

Kabul Antani Hospital is the only referral tertiary public hospital in the capital of Afghanistan with an isolation ward for the care of CCHF patients; hence, the cases enrolled in this study could potentially be representative of the country.

The data by the WHO and NDSR indicate that the number of CCHF cases and their fatalities in Afghanistan have been increasing in recent years.[19–21] Two other studies have also been conducted on CCHF in Kabul Antani Hospital almost 5 years ago. According to the study by Shohra Qaderi et al carried out in this hospital, among the suspected CCHF cases admitted from March 2017 to December 2018, the number of laboratory-confirmed cases was 51 (22%) while in this study we found 118 (50.4%) indicating a significant increase in tests positivity among the suspected and probable cases. The CFR in their study was 21.56%. In another study by Hossein Hatami et al in this hospital, the CFR was reported 15% while in the current study we found 25.4%. This indicates a proportional increase in CFR with the rise in the number of cases.[22,23] The CFR observed among the subjects of our study is consistent with CFR reported by the WHO (10–40%); however, it is higher than the CFR found in a systematic review and meta-analysis conducted in 2021 by Jean Thierry Ebogo Belobo et al. The latter study reported an overall 11.7% CFR with higher CFR in low-income countries.[26,27] In addition, the higher CFR among males compared to females in our study is in agreement with the study by Mofleh et al.[25]

Afghanistan has a male dominant society and almost all occupational groups at risk of CCHF such as butchers/slaughterhouse workers, shepherds, farmers, and animal dealers are men. This could explain the greater propensity of CCHF cases in our study towards males and also the higher CFR among them compared to females. Previous studies in this hospital also showed lower CFR among females compared to males.[22] Similarly, the gender and occupation-wise

distribution of patients in our study is consistent with studies by Sharifi-Mood et al, Babak Farzinnia et al in Iran, and the study by Mustafa Cevik et al in Turkey.[15,28,29] All of the female patients in our study were housewives, which indicates that the women might have contracted the virus through contact with contaminated meat during cooking as women in Afghanistan are mainly involved in household chores. In addition, women also might have predisposed to CCHF while caretaking their male family members who are infected. Thus, control and prevention interventions should be targeted towards these at-risk groups.

The majority of fatal cases in this study were aged 20 to 50 years and their mean age (36.6 ± 11.7 years) was lower than the fatal cases in the study of Cevik et al (53.5 ± 17.4 years). Although the mean age of the fatal cases in their study was higher compared to non-fatal cases, the difference was not statistically significant.[15]

The study by Kavak et al revealed that among CCHF patients, hemorrhage was the main factor associated with mortality.[30] The frequency of hemorrhagic symptoms was higher among fatal cases in our study (86.6%) compared to the study by Shohra Qaderi et al (81%) and also the study by Cevik et al (81.5%). All types of hemorrhage were consistently more frequent among fatal cases compared to survived cases in their studies.[15,22]

According to a study by Ergonul et al in Turkey who reported an overall 7.4% CFR, the most frequently observed hemorrhagic manifestations among the fatal cases were hematemesis and melena, while in our study these symptoms were found only in 30.7% and 50% of the patients, respectively; the most common bleeding sites in our study were epistaxis, petechiae/ecchymosis, and gum bleeding.[31] Among the female patients in the current study, only one patient developed vaginal bleeding, which is rare and a sign of serious disease in women. A similar case was reported by Shohra Qaderi et al.[32]

Moreover, CCHF patients may present with non-specific symptoms.[9] Previous studies have revealed that non-specific symptoms like myalgia, nausea/vomiting, and diarrhea were more prevalent in fatal cases compared to survivors. The presence of these non-specific and atypical symptoms as the presenting complaints of the patients requires the clinicians in CCHF endemic areas to have a high index of suspicion, particularly among at-risk occupational groups like those dealing with livestock.[15,22]

According to the study by Shohra Qaderi et al, the mean time from onset of symptoms and admission to the hospital among the fatal cases was 4.7 days, while in the current study we found it 5.3 ± 1.9 days.[22] A study by Kavak et al revealed that delay in hospital admission was associated with a higher mortality rate among CCHF patients.[30]

The most common hematological changes in this study were thrombocytopenia (100%), prolonged PT/INR (100%), and elevated liver enzymes (96.6%) which were shown to be significantly associated with mortality in a study carried out by Hamidreza Kouhpayeh.[10] In addition, according to the study of Kavak et al, the INR, AST, and ALT levels were significantly higher, and platelet count was significantly lower in fatal cases compared to survivors.[30] Likewise, compared to non-fatal cases, the proportion of thrombocytopenia, prolonged PT/INR and raised hepatic enzymes were more frequently observed among fatal cases in the study by Cevik et al.[15]

A study by Niazi et al in the Herat City of Afghanistan in 2017 revealed that CFR among CCHF patients was significantly associated with longer PT; this was observed in 100% of the fatal cases in our study.[33] Similarly, a positive association of death with longer PT has been previously described by Bastug et al.[34]

In addition to supportive treatments, all of the fatal cases in our study received oral ribavirin. The absence of a control group in this study was a limitation; hence, we were not able to compare the efficacy of ribavirin between fatal and survived cases. Ribavirin is recommended for the treatment of CCHF; however, there are contradictory data regarding its efficacy among researchers. A study by Koksal et al showed that the use of ribavirin makes no significant contribution to the prognosis of CCHF.[35] The study by Ergonul et al in Turkey suggested using ribavirin to be beneficial in treating CCHF.[31] In addition, a systematic review and meta-analysis by Bafrani et al revealed that ribavirin was effective in reducing mortality, especially if started in the early phase of the disease (within 4 days of onset of symptoms).[36] The average duration from the onset of symptoms to the start of ribavirin in our study was 5.3 days. Lateness in hospital admission and subsequent delay in start of ribavirin and supportive treatments might have affected mortality in patients.

As the majority of CCHF patients ultimately need intensive care, the lack of a well-equipped intensive care unit in the CCHF ward of Kabul Antani Hospital might also have contributed to the fatalities among our patients. Because of its retrospective design, our paper could not study other variables such as the history of past travel, tick contact, viral load,

etc. Moreover, the physical examination of the patients was poorly recorded, and the reports of other laboratory parameters or imaging investigations were lacking.

Conclusion

The number of CCHF cases and their fatalities in Afghanistan has increased recently. Most of the fatal cases in this study were males, aged 20–50 years and were involved with occupations dealing with livestock. All cases had a fever and general body pain. Majority of patients presented with hemorrhagic symptoms; moreover, the frequency of non-specific symptoms like fatigue, headache, nausea/vomiting, and diarrhea were also common. Therefore, physicians in CCHF endemic areas should have knowledge about various symptoms of the disease for early clinical diagnosis. Thrombocytopenia and prolonged PT/INR, which are linked with hemorrhage and fatality, were present in all patients. In addition, most cases had elevated hepatic enzymes, leukopenia, and anemia. The main complications that led to the death of the patients were shock, multi-organ failure, and DIC. Prompt laboratory diagnosis and early start of treatments are crucial to reducing mortality.

Acknowledgments

The authors would like to thank the authorities and staff of the Kabul Infectious Diseases (Antani) Hospital for their cooperation in the data collection for this study.

Disclosure

The authors declare no conflicts of interest in this work.

References

1. World Health Organization. Introduction to Crimean-Congo haemorrhagic fever; 2018. Available from: https://cdn.who.int/media/docs/default-source/documents/health-topics/crimean-congo-haemorrhaigc-fever/introduction-to-crimean-congo-haemorrhagic-fever.pdf?sfvrsn=14c8c199_2&download=true. Accessed May 31, 2023.
2. CDC. Crimean-Congo hemorrhagic fever; 2018. Available from: https://www.cdc.gov/vhf/crimean-congo/pdf/factsheet.pdf. Accessed May 31, 2023.
3. Aslam S, Latif MS, Daud M, et al. Crimean-Congo hemorrhagic fever: risk factors and control measures for the infection abatement (Review). *Biomed Rep*. 2016;4:15–20. doi:10.3892/br.2015.545
4. Garrison AR, Alkhovsky V, Avšič-županc T, et al. ICTV virus taxonomy profile: nairoviridae. *J Gen Virol*. 2020;101(8):798–799. doi:10.1099/jgv.0.001485
5. Mostafavi E, Pourhossein B, Chinikar S. Clinical symptoms and laboratory findings supporting early diagnosis of Crimean-Congo Hemorrhagic fever in Iran. *J Med Virol*. 2014;86(7):1188–1192. doi:10.1002/jmv.23922
6. Sahak MN, Arifi F, Sayedzai SA. Descriptive epidemiology of Crimean-Congo Hemorrhagic Fever (CCHF) in Afghanistan: reported cases to National Surveillance System, 2016 –2018. *Int J Infect Dis*. 2019;88:135–140. doi:10.1016/j.ijid.2019.08.016
7. Ince Y, Yasa C, Metin M, et al. Crimean-Congo hemorrhagic fever infections reported by ProMED. *Int J Infect Dis*. 2014;26:44–46. doi:10.1016/j.ijid.2014.04.005
8. Karakecili F, Cikman A, Aydin M, Binay UD, Kesik OA, Ozcicek F. Evaluation of epidemiological, clinical, and laboratory characteristics and mortality rate of patients with Crimean-Congo hemorrhagic fever in the northeast region of Turkey. *J Vector Borne Dis*. 2019;55(September):215–221. doi:10.4103/0972-9062.249479
9. Gönen İ. Clinical and laboratory findings of patients with Crimean-Congo hemorrhagic fever in the emergency department at hospital admission. *J Microbiol Infect Dis*. 2011;1(1):1–4. doi:10.5799/ahinjs.02.2011.01.0001
10. Kouhpayeh H. An overview of complications and mortality of Crimean-Congo hemorrhagic fever. *Int J Infect*. 2019;6(2):6–10. doi:10.5812/iji.91707
11. Farooq H, Beveridge N, Fletcher T, et al. A systematic review on the incidence and mortality of Crimean-Congo Haemorrhagic Fever (CCHF) in Pakistan. *Int J Infect Dis*. 2021;101:250. doi:10.1016/j.ijid.2020.11.088
12. Kilinc C, Gückan R, Capraz M, et al. Examination of the specific clinical symptoms and laboratory findings of Crimean-Congo hemorrhagic fever. *J Vector Borne Dis*. 2016;53(June):162–167.
13. Bakir M, Engin A, Gozel MG, Elaldi N, Kilickap S, Cinar Z. A new perspective to determine the severity of cases with Crimean-Congo hemorrhagic fever. *J Vector Borne Dis*. 2012;49(June):105–110.
14. Kuehnert PA, Stefan CP, Badger CV, Ricks KM. Crimean-Congo Hemorrhagic Fever Virus (CCHFV): a silent but widespread threat. *Curr Trop Med Rep*. 2021;8:141–147. doi:10.1007/s40475-021-00235-4
15. Cevik MA, Erbay A, Bodur H, et al. Clinical and laboratory features of Crimean-Congo hemorrhagic fever: predictors of fatality. *Int J Infect Dis*. 2008;12:374–379. doi:10.1016/j.ijid.2007.09.010
16. Ahmed A, Tanveer M, Saqlain M, Khan GM. Knowledge, perception and attitude about Crimean Congo Hemorrhagic Fever (CCHF) among medical and pharmacy students of Pakistan. *BMC Infect Dis*. 2018;18:1–10. doi:10.1186/s12879-017-2892-9
17. Shahhosseini N, Wong G, Babuadze G, et al. Crimean-Congo Hemorrhagic fever virus in Asia, Africa and Europe. *Microorganisms*. 2021;9(1907):1–24. doi:10.3390/microorganisms9091907

18. Mustafa ML, Ayazi E, Mohareb E, et al. Crimean-Congo hemorrhagic fever, Afghanistan, 2009. *Emerg Infect Dis*. 2011;17(10):3–4. doi:10.3201/eid1710.110061
19. Ministry of Public Health A. National Disease Surveillance & Response (NDSR) weekly epidemiological report; 2022. Available from: https://moph.gov.af/sites/default/files/2022-01/NDSRWER52-2021.pdf. Accessed May 31, 2023.
20. Ministry of Public Health A. National Disease Surveillance & Response (NDSR) weekly epidemiological report; 2023. Available from: https://moph.gov.af/sites/default/files/2022-12/NDSRWER47-2022.pdf. Accessed May 31, 2023.
21. World Health Organization. Crimean-Congo Haemorrhagic Fever (CCHF) outbreak toolbox; 2022. Available from: https://cdn.who.int/media/docs/default-source/outbreak-toolkit/final_cchf-outbreak-toolbox_20221011.pdf?sfvrsn=757e0181_1. Accessed May 31, 2023.
22. Qaderi S, Mardani M, Shah A, Shah J, Bazgir N. Crimean-Congo Hemorrhagic Fever (CCHF) in Afghanistan: a retrospective single center study. *Int J Infect Dis*. 2021;103:323–328. doi:10.1016/j.ijid.2020.11.208
23. Hatami H, Qaderi S, Omid AM, González AD, de Andrade SM. Investigation of Crimean-Congo hemorrhagic fever in patients admitted in Antani Hospital, Kabul, Afghanistan, 2017–2018. *Int J Prev Med*. 2019;10(117):1–5. doi:10.4103/ijpvm.IJPVM_40_18
24. Al-abri SS, Hewson R, Al-kindi H, et al. Clinical and molecular epidemiology of Crimean-Congo hemorrhagic fever in Oman. *PLoS Negl Trop Dis*. 2019;19(April):1–15.
25. Mofleh J, Ahmad AZ. Crimean–Congo haemorrhagic fever outbreak investigation in the Western Region of Afghanistan in; 2012. Available from: https://www.emro.who.int/emhj-volume-18-2012/issue-5/article-17.html. Accessed May 31, 2023.
26. World Health Organization. Crimean-Congo haemorrhagic fever; 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/crimean-congo-haemorrhagic-fever. Accessed May 31, 2023.
27. Thierry J, Belobo E, Kenmoe S, et al. Worldwide epidemiology of Crimean-Congo hemorrhagic fever virus in humans, ticks and other animal species, a systematic review and meta-analysis. *PLoS Negl Trop Dis*. 2021;(April):1–19.
28. Sharifi-mood B, Metanat M, Alavi-naini R. Prevalence of Crimean-Congo hemorrhagic fever among high risk human groups. *Int J High Risk Behav Addict*. 2014;3(1):5–8. doi:10.5812/ijhrba.11520
29. Farzinnia B, Saghafipour A, Telmadarraiy Z. Study of the epidemiological status of Crimean-Congo hemorrhagic fever disease in Qom Province, 2011, Iran. *Qom Univ Med Sci J*. 2013;7(4):2013.
30. Kavak N, Gürbüz Y. Factors affecting mortality in Crimean-Congo hemorrhagic fever. *J Surg Med*. 2019;3(6):428–432.
31. Ergonul O, Celikbas A, Baykam N, Eren S, Dokuzoguz B. Analysis of risk-factors among patients with Crimean-Congo haemorrhagic fever virus infection: severity criteria revisited. *Eur Soc Clin Infect Dis*. 2006;12(6):551–554.
32. Qaderi S, Hatami H, Omid AM, Sayad J. Vaginal bleeding as a sign of Crimean-Congo hemorrhagic fever infection: a case report. *J Med Case Rep*. 2022;16:1–4. doi:10.1186/s13256-021-03218-1
33. Niazi A-R, Jawad MJ, Amirnajad A, Durr PA, Williams DT. Crimean-Congo Hemorrhagic fever, Herat province, Afghanistan, 2017. *Emerg Infect Dis*. 2019;25(8):1596–1598. doi:10.3201/eid2508.181491
34. Bastug A, Kayaaslan B, Kazancioglu S, Aslaner H, But A. Crimean-Congo Hemorrhagic fever: prognostic factors and the association of Leukocyte counts with mortality. *Jpn J Infect Dis*. 2016;69(5):51–55. doi:10.7883/yoken.JJID.2014.566
35. Koksal I, Yilmaz G, Aksoy F, et al. The efficacy of ribavirin in the treatment of Crimean-Congo hemorrhagic fever in Eastern Black Sea region in Turkey. *J Clin Virol*. 2010;47(1):65–68. doi:10.1016/j.jcv.2009.11.007
36. Arab-bafrani Z, Jabbari A, Hashemi MM, Arabzadeh AM, Gilanipour A, Mousavi E. Identification of the crucial parameters regarding the efficacy of ribavirin therapy in Crimean–Congo haemorrhagic fever (CCHF) patients: a systematic review and meta-analysis. *J Antimicrobial Chemother*. 2019;74(August):3432–3439. doi:10.1093/jac/dkz328