

## Investigation of Crimean-Congo hemorrhagic Fever in Patients Admitted in Antani Hospital, Kabul, Afghanistan, 2017–2018

### Abstract

**Background:** Crimean-Congo hemorrhagic fever (CCHF) is the most medically significant hemorrhagic fever. Afghanistan as an endemic region of CCHF has shown a rapidly growing incidence of the CCHF recently, but there is no data on the characteristic of the disease in this country, here we study the epidemiological, clinical, and paraclinical features of this disease in patients with CCHF, based on the collected data from the patients document records from March 2017 to January 2018 in the referral infectious diseases hospital of Afghanistan (Kabul Antani Hospital). **Methods:** A cross-sectional study in 120 patients admitted in Kabul ANTANI hospital was carried out from March 2017 to January 2018. All of the patients were included based on the standard case definitions by World Health Organization. **Results:** Among the 120 patients admitted to CCHF ward, 29 were confirmed by ELISA (18% IgM, 8% IgG+) and the reminders defined as “probable cases” according to WHO case definition. Case fatality rates were calculated as 15% and the overall mean ages were 35 years. The peak of the disease incidence occurred between August and July. Almost all patients reported fever, bleeding, and thrombocytopenia. **Conclusions:** Early detection plays an important role in patients’ outcome. Considering that the most cases of the disease are associated with some contacts around Eid-Adha and death attributable to CCHF usually occur in the first 7 days of disease onset, educating population, and especially slaughters, gloves using by housewives during contacts with meat or animal products, and early detection and immediate treatment would have essential roles in primary and secondary prevention of CCHF. Hemorrhagic manifestations and low platelet count provide a clue to early detection of disease. Vaginal bleeding can be a sign of CCHF and needs immediate action.

**Keywords:** Afghanistan, Crimean-Congo hemorrhagic fever, Mediterranean region, uterine hemorrhage

### Introduction

Crimean-Congo hemorrhagic fever (CCHF) is an acute, severe vector-borne viral hemorrhagic fever with considerable mortality in humans. The causative agent is the genus Nairovirus within the family Bunyaviridae.<sup>[1,2]</sup> The virus can be transmitted to humans through the bite of infected ticks, direct contact with fresh meat, or blood of livestock, and health care workers are considered as in high risk of mortality during outbreaks.<sup>[3-6]</sup> Human CCHF is characterized by a sudden onset of fever, headache, dizziness, nausea, weakness, irritability, and severe limb and loin pain that shows a wide range of severity, from a mild, nonspecific febrile illness to shock and death. The hemorrhagic symptoms include petechiae and/or ecchymosis spreading over the chest, abdomen, and

rest of the body; sometimes large purpuric areas are reported. In severe cases, bleeding from the gums, nose, lung, uterus, and intestine are reported and can progress to multiorgan failure.<sup>[7,8]</sup> Thrombocytopenia is a common laboratory finding parameter, other findings are leukopenia with a marked lymphopenia, coagulopathy, and elevated liver enzymes.<sup>[9]</sup> The case fatality rate is about 30% overall.<sup>[10]</sup> But, ranges of 2%–70% have been reported.<sup>[11]</sup> Currently, no approved vaccine is available against CCHF virus, supportive therapy is the cornerstone of treatment. The only ways for effective prevention of CCHF virus infection are avoiding tick bites, safe slaughtering of livestock, and universal health care precaution.<sup>[9,12,13]</sup> The disease is endemic in >30 countries in the world. In recent years, the incidence of CCHF has increased rapidly in the countries of the World Health Organization Eastern

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Mediterranean Region (WHO EMR), with sporadic human cases and outbreak of CCHF being reported from a number of countries in the region.<sup>[11,14]</sup> Afghanistan is located in endemic range of the Hyalomma tick and experiences the disease regularly, as an average of 5–50 human cases are reported every year in the country. The most severe outbreak of the CCHF reported in 2008, between July 10 and October 22 in Herat city: 30 human cases were reported including 9 death.<sup>[15-18]</sup> The last most severe outbreak of the disease occurred in 2016, where 156 cases including 18 death (CFR: 11.5%) were reported. According to the last report in 2017, the total number of cases reported from Afghanistan was 237 including 41 death (CFR: 17.2%); the highest number of cases was reported in Kabul and Herat provinces, two provinces border Pakistan and Iran where livestock transboundary movement is not controlled. Herat provinces has an endemic focus for CCHF, a total of 67 cases including 10 death (CFR: 14.9%) were reported from this province.<sup>[19]</sup> Unfortunately, there is no comprehensive studies on the characteristic of epidemiological, clinical, and paraclinical features of Crimean-Congo hemorrhagic fever patients in Afghanistan. Thus, this study was undertaken to investigate these features in patients admitted to Antani Hospital, Kabul, Afghanistan, in 2017 as a correlational descriptive study.

## Methods

A cross-sectional and correlational study on clinical, paraclinical, and epidemiologic features of Crimean-Congo hemorrhagic fever in 120 patients admitted in Kabul ANTANI Hospital as referral hospital of infectious disease in Afghanistan, was carried out from March 2017 to January 2018. Pertinent information was extracted from their medical records and studied. All of the patients with both suspected and confirmed CCHF were included. We used the standard case definitions based on World Health Organization resources.<sup>[20,21]</sup> A suspected patient is defined as an individual with sudden onset of illness with high-grade fever  $>38.5^{\circ}\text{C}$  for  $>72$  h and  $<10$  days, especially in CCHF endemic regions and among those in contact with livestock. A probable case defined as Suspected cases in addition, the following criteria; a history of sudden onset of fever, for  $<10$  days and thrombocytopenia  $<50,000/\text{mm}^3$  with two of the following hemorrhagic manifestations: petechial or purpuric rashes, epistaxis, hematemesis, hemoptysis, melena, ecchymosis, gum bleeding, hematuria, and other hemorrhagic symptom, in the absence of any known precipitating factor for hemorrhagic manifestations. Confirmed case is defined as a probable case with positive diagnosis of CCHF in blood sample, Presence of IgG or IgM antibodies to the CCHF virus in serum by enzyme-linked immunosorbent assay (ELISA) and/or detection of viral nucleic acid in specimen by polymerase chain reaction and/or isolation of the virus. By the aid of trilingual health professionals,

suitable data including the various epidemiological, clinical, and paraclinical parameters as describes in result were obtained from the patients' history documents that were previously written in three national languages used in Afghanistan (Farsi, Pashto, and English).

## Statistical analysis

The recorded data were analyzed with SPSS (version 16) software; continuous variables were compared between groups using the nonparametric Mann–Whitney *U*-test. Chi-square, Fisher's exact, and regression logistic tests were used to compare the variables as appropriate during analysis. *P* values  $<0.05$  were considered statistically significant.

## Results

The study group comprised of 80 males and 40 females; the overall male-to-female ratio was 2:1, and thus a male preponderance was seen in this study and significant statistically ( $P < 0.01$ ). The mean age of the studied subjects was  $35 \pm 17.13$  (range, 10–85) years. The females and males mean age was  $32.9 \pm 16.2$  and  $36 \pm 17$  years, respectively, and there is no difference between the mean age of males and females ( $P = 0.35$ ). Overall, 21 and 12 patients, out of 120 patients had occupational exposure as shepherds and butchers, respectively, but the rate of death in different occupations was not statistically significant ( $P = 0.5$ ). The majority of CCHF cases (78 cases, 65%) were recorded from June to September, around the time of the Eid-Adha (sacrifice feast in Islam) [Figure 1]. Of all cases, 74.2% lived in rural areas and 81.7% of them were referred from different hospitals of the country. Just 5 out of 116 patients had a family member with CCHF manifestation, but they had not carried to hospital due to mild symptoms. History of animal in house and past animal contact was obtained in order of 14 (11%) and 18 (15%) of patients. There were 9 (7.5%) positive case of tick contact and just 3 patients had contact with similar ones. Almost all patients were treated with oral Ribavirin and supportive care, as shown in Table 1. The mean time from onset of symptoms and admission to hospital was 6.7 (range, 3–12) days and from admission to death, 3 (range, 1–9) days. Case fatality rate in this study was calculated 15% (18 of 120). About 108 serum samples were sent to reference laboratory of country and 29 of these cases were positive for CCHF by ELISA test, 22 (18.3%) were (IgG-, IgM+), and 7 (8%) had (IgG+, IgM-). A great proportion of men died than women, but the difference was not statistically significant ( $P = 0.6$ ). Epistaxis was significantly associated with high frequency of death, as 10 out of 18 (55.5%) cases of death were presented with epistaxis. Almost all cases were presented with fever (100%) and other manifestations were myalgia (69%) and hemorrhage (59%) [Table 2]. Neurological complications were rare but noted only among fatal cases. The mean platelet counts were

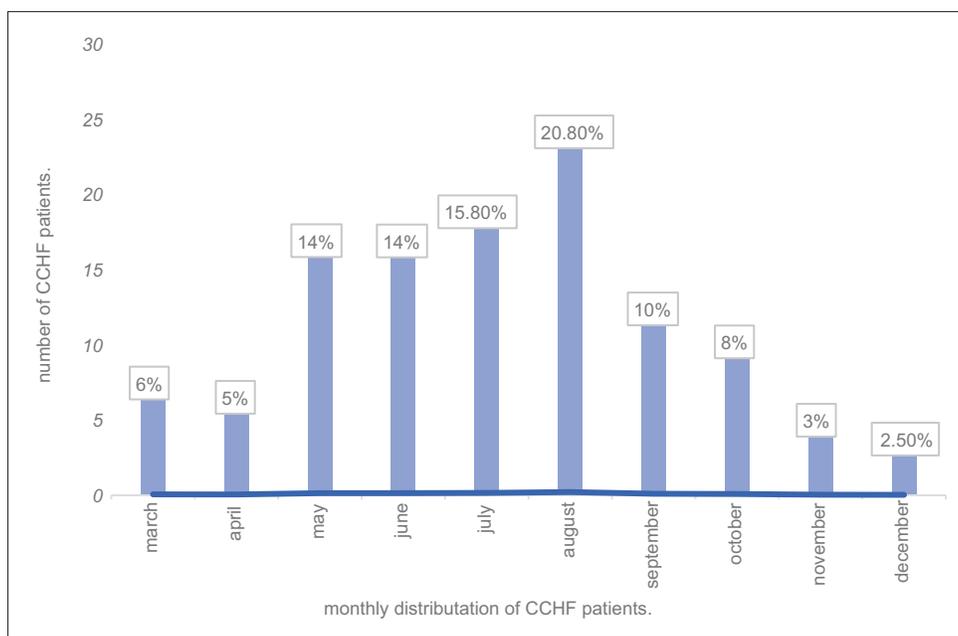


Figure 1: Monthly distribution of Crimean-Congo hemorrhagic fever among Afghan patients in 2017

**Table 1: Treatment were received by patients admitted in Crimean-Congo hemorrhagic fever ward in Antani hospital of Kabul, Afghanistan (n=118)**

Treatment	n (%)
Ribavirin	114 (96.6%)
Platelate	107 (90.6%)
Antibiotic	116 (98.3%)
Blood transfusion	22 (18.0%)

**Table 2: Clinical sign and type of hemorrhage in patients admitted in CCHF's ward in Antani hospital of Kabul, Afghanistan**

Clinical sign	Number of CCHF cases	Percentage of CCHF cases
n=119		
Fever	117	98.3
Hemorrhage	59	50
Myalgia	97	81.5
n=78		
Nonspecific clinical sign		
Nausea	28	35.9
Vomiting	24	30.7
Stomach ache	10	12.8
n=77		
Type of hemorrhage		
Epistaxis	52	67.5
Melena	16	20.7
Petechial	15	19.4
Ecchymosis	14	18.18
Gum bleeding	8	10.3
Hematemesis	9	11.6
Hematuria	6	7.7
Vaginal bleeding	2	2.6

CCHF=Crimean-Congo hemorrhagic fever

32.  $10^3/\mu\text{L} \pm 26$  (range, 19–115) and white blood cells were 4.  $10^3/\mu\text{L} \pm 36$  (range, min [ $1.10^3/\mu\text{L}$ ] to max [ $19.10^3/\mu\text{L}$ ]).

## Discussion

The case fatality ratio due to CCHF ranged from 33% in 2008 to 11.5% in 2016, in different studies from different geographical region of Afghanistan,<sup>[15,19]</sup> but in this study was 15% that shown a higher fatality ratio than 2016, despite almost all of the patients received Ribavirin and supportive therapy. Previous studies shown a higher mortality rate in butchers and housewives,<sup>[15]</sup> but the difference was not significant in this study; however, the presented insignificance could be due to insufficient number of occupations (84 from 120). There was no any under 10-year-old CCHF cases in this study; this may be due to preoccupation and housekeeping in adults. Death occurred in 13–45 years of ages in agreement with previous studies.<sup>[15]</sup> Five family members had infection and 26% of CCHF patients had animal in house or past animal contact, just nine patients reported tick contact. Most cases were recorded from June to September around Eid-Adha, due to increasing in the slaughtering of animals in this time that increases the risk of virus transmission. This time surge showed the animal and animal products contact as more important route of transmission than tick bites, in agreement with previous study in Afghanistan and Iran, versus Pakistan; hyperaired climate and extensive livestock emerge as important contributing factors to upsurge of CCHF infections in this country.<sup>[16,22,23]</sup> The mean time between disease onset and administration was 6.7 days, which showed longer time than corresponding average interval in patients from UAE (3.5 days), Iran (4 days), Pakistan (4.3 days),

and Turkey (5.5 days).<sup>[24-27]</sup> This may be due to cultural barriers or poor health literacy.<sup>[28]</sup> The mean time between onset of symptoms and death was 6.7 days, which suggest a fast deterioration of general condition with CCHF, in agreement with previous study in Iran (7 days).<sup>[24]</sup> There were no difference between IgM + and/or IgG + and death. In this study, CCHF patients commonly present with fever, headache, and myalgia. Mean platelet count was  $32.10^3/\mu\text{L}$  that confirmed thrombocytopenia as dominate hematological changes of CCHF, and low normal leukocytes (mean of WBC =  $40.10^3/\mu\text{L}$  in this study) could suggest CCHF. Epistaxis was the dominate sign but not statistically significant ( $P = 0.1$ ).

The limitations of this study included extended sample storages as the collection sites of hospital with resultant low positive detection rate. The study was based on patients documented records; thus, there was not a clear history of blood group, past animal or tick contact, type of animal or tick contact, past travel history, measures of liver function test, proteinuria, and poor physical examination. Viral load which can be independent predictor of mortality was not studied. The absence of a control groups in order to obtain the efficacy of Ribavirin was the other limitation.

## Conclusions

CCHF is a serious public health problem and endemic in Afghanistan, early detection plays an important role in patients' management and prognosis. Our epidemiologic finding suggested that most of the cases were occurred around Eid-Adha and confirmed that meat and animal products are important routes of transmission than tick bites and death attributable to CCHF usually occurred in the first 7 days of onset of disease. Hemorrhagic manifestations (melena) and low platelet count provide a clue to early detection of disease. In endemic areas of CCHF, the doctors and all of the women must not consider the vaginal bleeding as mere sign of gynecology; it can be a sign of CCHF and needs immediate action. Impaired consciousness was assumed with a fatal outcome of this study.

## Lessons learned

- Afghanistan is a hyperendemic region for CCHF and needs special preventive considerations
- CCHF is an emerging infectious disease in Afghanistan
- As the primary prevention, education is an important key to finding cases early and improving outcomes
- Safe slaughtering and educate slaughters, and gloves using by housewives during contacts with meat or animal products are essential
- More researches are needed to investigate real distribution of infected ticks and animals and then controlling the sources and vectors
- As the secondary prevention, early diagnosis, admission, and antiviral and supportive treatment are essential for the management of CCHF.

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## Conflicts of interest

There are no conflicts of interest.

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