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Crimean-Congo hemorrhagic fever in Herat province of Afghanistan, 2007-2021

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Abstract

Crimean-Congo hemorrhagic fever (CCHF) is a geographically widespread tick-borne hemorrhagic disease caused by the Crimean-Congo hemorrhagic fever virus (CCHFV). In Afghanistan, the first case of CCHF was detected in Takhar province in 1998, after which no additional cases were reported for ten years. The aim of this study is to report the analyses of the clinical and epidemiological features of confirmed CCHF cases that were recorded in Herat province between 2007 and 2021. This prospective case series study was conducted at Herat Regional Hospital between January 2007 and December 2021. Demographic and clinical data were collected for each patient; all patients were hospitalized. Biochemical and hematological laboratory examination, and the detection of CCHV IgM and viral RNA was performed for all patients. Statistical analyses were performed in IBM SPSS Statistics (version 26). A total of 252 confirmed CCHF cases including 160 (63.5%) males and 91 (36.5%) females, with a mean age of 33.37±14.1 years were included in the study. The majority of patients were in 11-50 age category, 32.9% were housewife, 38.4% were farmers, shephard, and butchers. The most prevalent clinical presentations were fever (100%), headache (98.8%), body pain (96.4%), Ecchymosis (48.0%), epistaxis (44.8%) and gum bleeding (33.3%). The majority of cases occurred between April and October. The case fatality rate of CCHF in this study was 2.8%. Considering the significant social, economic and health burden CCHF places on the community, enhanced public health measures are necessary to control CCHF in Herat province and neighboring regions.

Keywords: Crimean-Congo hemorrhagic fever, CCHF, CCHFV, Herat, Afghanistan

INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a geographically widespread tick-borne hemorrhagic disease caused by the CCHF virus (CCHFV; genus *Orthonairovirus*, family *Nairoviridae*, order *Bunyavirales*; Garrison et al., 2020; Kong et al., 2022). In humans, CCHF is associated with an average mortality rate of 5-50%, and it is therefore considered a major public health threat (Kuehnert et al., 2021). CCHFV also infects a wide range of domestic and wild animals, causing an asymptomatic viremia (Balinandi et al., 2021). The natural hosts for CCHFV are livestock and small mammals, from which the virus can be transmitted to humans by *Hyalomma* species of tick vectors, or via contact with body fluid, blood and tissue of CCHF-infected patients, as well as blood and tissue of infected livestock (Adham et al., 2021; Negredo et al., 2019). The nosocomial transmission of CCHFV from hospitalized patients to healthcare workers has also been frequently documented (Niazi et al., 2019; Parlak et al., 2015; Yadav et al., 2016).

Clinical and hemorrhagic manifestations as well as epidemiological data play a vital role in recognition of the disease. However, diagnosis must be confirmed by the detection of viral nucleic acid via reverse transcription polymerase chain reaction (RT-PCR), by serological assays demonstrating CCHFV-specific antibody response or by virus isolation (Balinandi et al., 2021; Tezer & Polat, 2015).

There are four main phases of CCHFV infection: incubation period, pre-hemorrhagic, hemorrhagic and convalescent. The incubation period lasts between 3-7 days, after which the pre-hemorrhagic phase starts, accompanied by headache, abdominal pain, high fever, hypotension and myalgia (Balinandi et al., 2021; Ergonul 2006; Gürbüz et a., 2021). The hemorrhagic phase of the disease is characterized by various hemorrhagic manifestations including petechiae,

epistaxis, ecchymosis, hematemesis, and bleeding from gums, gastrointestinal and urogenital systems (Bakir et al., 2005; Ergonul et al., 2004; Niazi et al., 2019). Cardiovascular and neuropsychiatric changes, diarrhea and nausea may also occur (Whitehouse 2004). If left untreated, the patient may succumb to CCHFV infection due to a multi-organ failure. In those who survive, the convalescent phase begins 10-20 days after illness. It can take up to one year for survivors to fully recover from CCHF (Appannanavar & Mishra, 2011).

CCHF cases were first reported in Afghanistan in 1998, although epidemics have been reported in neighboring Tajikistan, Pakistan and Iran since the 1970's (Begum et al., 1970; Saidi et al., 1975; Tishkova et al., 2012). No additional CCHF cases were reported in Afghanistan until 2007. The purpose of this study is to report analyses of the clinical and epidemiological features of CCHF cases that were recorded in Herat province, between 2007 and 2021.

MATERIAL AND METHODS

Study design and patients: A prospective case series study was conducted at Herat Regional Hospital (HRH) between January 2007 and December 2021. A specially designed CCHF form was filled out for each patient who matched the standard confirmed CCHF case definition based on that of the World Health Organization (WHO) and as described elsewhere (Mofleh et al., 2012). Age, gender, address, occupation, date of admission, date of onset of symptoms, existing symptoms, epidemiological history, history of tick bite, contact with infected livestock, laboratory findings and treatment with ribavirin and supportive therapy were recorded. All patients were hospitalized.

Biochemical and hematological laboratory examination: Patients' venous blood samples were collected, stored in optimal conditions and sent to HRH central laboratory for examination. of leukocytes and thrombocytes.

IgM ELISA and RT-PCR: Patients' blood samples were sent to the Central Public Health Laboratory (CPHL) of the Afghanistan Public Health Institute, Kabul for laboratory diagnosis of CCHF, by the detection of CCHFV IgM (VectoCrimea-CHF-IgM ELISA, Vector- Best, https: //www.vector-best.ru) or viral RNA (RealStar CCHFV RT-PCR Kit, Altona Diagnostics, https://www. altona-diagnostics.com).

Statistical analysis: Statistical analyses were performed using IBM SPSS Statistics (version 26.0) software. Descriptive statistics are presented as mean, standard deviation (SD), and ranges for quantitative variables, and as numbers and percentages for categorical variables.

Ethical consideration: The study protocol was approved by the Human Ethics Committee of Herat University (HU-HEC; approval number # 0317). Privacy and confidentiality of data were maintained throughout the study.

RESULTS

A total of 252 confirmed CCHF cases including 160 (63.5%) males and 91 (36.5%) females were recorded at HRH, between 2007 and 2021, and included in this study. The Mean age of patients was 33.37±14.1 (range 10-75 years). The majority of patients (29.8%) were in 11-50 age category, and one-third (32.9%) were housewives. Table 1 displays sociodemographic characteristics of patients under study.

Table 1: Sociodemographic characteristics of study participants

Characteristics	N0 (%)
Sex	
Male	160 (63.5)
Female	91 (36.5)
Age	
0-10	1 (0.4)
11-20	57 (22.6)
21-30	75 (29.8)
31-40	44 (17.5)
41-50	48 (19.0)
51-60	20 (7.9)
>60	7 (2.8)
Occupation	
Housewife	83 (32.9)
Farmer	63 (25.0)
Shepherd	17 (6.7)
Butcher	17 (6.7)
Self-employed	12 (4.8)
Worker	5 (2.0)
Student	4 (1.6)
Security guard	1 (0.4)
Collegian	1 (0.4)
Jobless	2 (0.8)
Other	47 (18.7)

The most common clinical manifestations were fever (100%) and headache (98.8%), while the most prevalent hemorrhagic manifestations were ecchymosis (48.0%) and epistaxis (44.8%). The case fatality rate of CCHF in this study was 2.8% (seven people); the CFR for men was (1.9%) and for women (4.3%). The mean time between onset of clinical manifestations and patients' admission to hospital was 5.49±2.48 days (range 1-19 days). Table 2 shows the frequency of clinical and hemorrhagic manifestations of study participants.

The majority of cases (92.9%) occurred between the months of May and September. Figure 1 displays the number of cases included in this study, according to the months of the year.

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Table 2: Clinical and hemorrhagic manifestation of study participants

Items	No (%)
Clinical manifestations	
Fever	252 (100)
Headache	249 (98.8)
Body pain	243 (96.4)
Malaise	25 (9.9)
Extreme fatigue	11 (4.4)
Nausea	2 (0.8)
Hemorrhagic manifestations	
Ecchymosis	121 (48.0)
Epistaxis	113 (44.8)
Gum bleeding	84 (33.3)
Petechiae	50 (19.8)
Purpura	30 (11.9)
Hematemesis	21 (8.3)
Hemoptysis	17 (6.7)
Injection spot	17 (6.7)
Vaginal bleeding	11 (4.4)
Hematochezia	2 (0.8)

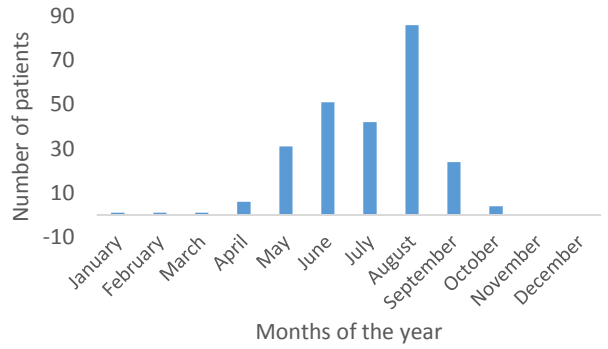

Figure 1. Distribution of cases included in this study according to the months of the year

DISCUSSION

There have been many reports regarding the occurrence of CCHF in Herat (Mofleh et al., 2012; Mustafa et al., 2011; Niazi et al., 2019). In Afghanistan, the first CCHF case was reported in 1998 in Takhar province, after which no CCHF cases were detected for ten years (Mustafa et al., 2011). Since 2007, the number of CCHF cases has gradually increased in the country. No systematic analysis regarding the epidemiology and clinical symptomatology of CCHF has been reported for outbreaks in Herat. Therefore, we undertook a detailed analysis of the CCHF cases, to better understand the disease's epidemiology and demographic characteristics, clinical manifestations and case-fatality rate in Herat, since its appearance in 2007. This work builds on public health measures previously implemented in Herat for surveillance, prevention and management of this fatal disease.

Of the 252 patients included in this study, 63.5% were male and 36.5% were female. This is in accordance with other CCHF studies conducted in Turkey, Iran and Afghanisan (Aktas et al., 2016; Niazi et al., 2019 Sharififard et al., 2016). The higher occurrence of CCHF in males is due to more frequent exposure of men to CCHF risk factors such as farming and animal handling (Greiner et al., 2016; Aslam et al., 2016). Overall, 88.9% of CCHF cases in this study were aged between 11 to 50 years. This is probably because this age group is the working-age in Afghanistan and more people were exposed to CCHF risk factors in these age groups than in younger or older categories. The mean age of CCHF cases in this study was 33.3 years, which is similar to the findings of CCHF studies conducted in Afghanistan (39.7 years), Iran (31.4 years), Pakistan (30.3 years), and Turkey (30.1 years) (Aslani et al., 2017; Ertugrul et al., 2009; Khurshid et al., 2015; Niazi et al., 2019;) However, two studies conducted in Turkey and Georgia have indicated the average age of CCHF patients to be in mid-50s (Aktas et al., 2019; Greiner et al., 2016). The discrepancy between these studies is likely due to different study designs and/or differences in population demographics between these countries.

All CCHF cases in this study occurred during April to October, with a peak between June to August. This period is considered the warm season in Herat province, with average temperatures ranging from 30ºC to 42ºC. Other studies have also reported more CCHF cases during April to October in Afghanistan, Pakistan and Turkey (Niazi et al., 2019; Bakir et al., 2005; Mofleh et al., 2012; Ertugrul et al., 2009; Haider et al., 2016). The higher incidence of CCHF in spring and summer months is because larvae and nymphs of *Hyalomma* ticks develop into adults during these warm seasons.

Many studies indicated that farming, animal handling and slaughtering are the main sources of CCHFV infection (Adham et al., 2021; Sharififard et al., 2016; Ayatollahi et al., 2015). In this study, 38.4% of CCHF cases identified as either butcher, farmer or shepherd in occupation. This is in accordance with a similar study in Herat stating that 38.1% of CCHF cases were in this occupational category (Niazi et al., 2019). Of concern was the finding that one-third (32.9%) of CCHF cases were housewives. Niazi and colleagues (2019) and Sharififard and colleagues (2016) also found that a large proportion (36.5% and 26.2%; respectively) of CCHF patients in Afghanisan and Iran were housewives. In our study, all housewives were exposed to infected meat. Therefore, it is of critical importance for housewives and domestic workers to be aware of the risks of CCHFV transmission, especially during the peak CCHF season.

The most common clinical features of CCHF in this study were fever, headache, body pain, and fatigue.

Ecchymosis, epistaxis, and gum bleeding were the most abundant types of bleeding in patients under study. These clinical manifestations have been frequently reported in several CCHF clinical studies. For example, in investigations conducted in Afghanistan, Iran and Turkey, fever, myalgia, headache, ecchymosis and epistaxis were among the most common types of clinical features in patients (Klinic et al., 2016; Niazi et al., 2019; Sharififard et al., 2016).

Different mortality rates of CCHF have been reported, with estimates between 5% to 83% (Leblebicioglu et al., 2016; Yadav et al., 2013) and the smallest outbreaks showing the largest fatality rates (Bente et al., 2013). In Afghanistan, the mortality rate ranged from 3.3% in 2014 to 30.0% in 2008 (DEWS 2015). In this study, the overall case fatality rate was 2.8% (1.9% for men and 4.3% for women). The difference between the mortality rates of CCHF in different studies may be due to several factors, including different circulating CCHFV genotypes or pathotypes, study designs (i.e. inclusion of sub-clinical and non-clinical but seropositive cases) and the quality of care for the patients.

This study is important for people in Afghanistan, especially in Herat province, because it identifies the most at-risk target demographics (age and occupation). Considering the findings of this study, public health authorities should design and implement CCHF control strategies to better manage future outbreaks. This study is also important for people travelling to the Herat province. Herat is one of the most historical places in Afghanistan, and borders Turkmenistan and Iran. It attracts a large number of tourists each year. Although to date, no CCHF cases have been reported from tourists travelling to Herat, cases in a worker and tourist returning to their home countries from Senegal and northwest Afghanistan (Samangan province) have been described (Jauréguiberry et al., 2005; Chamberlain et al., 2013). It is therefore strongly advised that tourists travelling to this province should be made aware of the symptoms of CCHF and risk factors for infection. When suspected symptoms appear, CCHF should be considered in the differential diagnosis.

CONCLUSION

The present study demonstrates that male gender, those who work with animals or animal tissues and housewifes are more vulnerable to CCHF. The control and mitigation measures currently implemented for CCHF in Herat province to date have shown no or very little success in containing or preventing this fatal disease. Considering the significant social, economic and health burden CCHF places on the community, alternative or enhanced public health measures appear to be necessary to control CCHF in Herat province and neighboring regions.

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