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Descriptive epidemiology of Crimean-Congo Hemorrhagic Fever (CCHF) in Afghanistan: Reported cases to National Surveillance System, 2016–2018

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ABSTRACT

Objective: This study aims to provide descriptive epidemiology of human CCHF cases in Afghanistan by demographic, geographical, and seasonal characteristics.
Methodology: This paper's findings are based on the retrospective analysis of the National Surveillance System's collected data from 2016 to 2018. Weekly cases exceeding the 90th percentile of the expected number of cases were considered to be exceptional and above normal.
Results: The National Surveillance System detected 1,284 CCHF cases from 2007 to 2018, of which 163 cases were in 2016, 245 cases in 2017 and 483 cases in 2018. A total of 891 suspected and confirmed cases were reported between 2016 and 2018, 293 (33%) of these cases were confirmed by detecting IgM antibody using ELISA and RT-PCR. Among confirmed cases, the three-year case fatality ratio (CFR) was 43.3%. Among the reported cases, 68.5% were males and 31.5% females. The frequent reported occupational groups were housewives (15%), health staff (13%), shepherds (11%), butchers (6%), students (6%), animal dealers and farmers (both 2%) respectively, 19% were unemployed, and occupation was not recorded for 26% of cases.
Conclusion: Recently, CCHF has significantly increased in Afghanistan. Despite the increased frequency of cases, the laboratory capacity to test specimens and overall knowledge of CCHF management remains limited.

Background

Crimean-Congo Hemorrhagic Fever (CCHF) is one of the most widespread tick-borne viral diseases that affects humans. The disease was first characterized in the Crimea in 1944 and given the name Crimean hemorrhagic fever. It was then recognized in 1969 as the cause of illness in the Congo, thus resulting in the current name of the disease Crimean-Congo Hemorrhagic Fever.

The causative agent is the CCHF virus classified within the Nairovirus genus of the family Bunyaviridae and transmitted by *Hyalomma* ticks and the blood or tissues from an infected animal at slaughter. Sometimes, human to human transmission may occur in the health care setting because of close contact with the blood, secretions, organs, or other body fluids of infected patients (World Health Organization (2015)). The disease is endemic in Asia, Europe, and Africa south of the 50th parallel, the northern geographical limit of the principal vector, and the case fatality ratio (CFR) range has been reported from 10–40% (Ahmed et al., 2018). In another study conducted in Turkey, the CFR was estimated to be 5–80% (Leblebicioglu et al., 2015). High-risk groups for CCHF are considered to be men and women working in agriculture, animal husbandry, slaughterhouse workers, veterinarians and also those working in health care settings (Sisman, 2013).

The onset of CCHF is sudden, with initial signs and symptoms including headache, high fever, back pain, joint pain, stomach pain, and vomiting. Red eyes, a flushed face, a red throat, and petechiae (red spots) on the palate are common. Symptoms may also include jaundice, and in severe cases, changes in mood and sensory perception. As the illness progresses, large areas of severe bruising, severe nosebleeds and uncontrolled bleeding at injection sites can be seen (Mostafavi et al., 2014). The average incubation period for CCHF virus is 3–7 days (Appannanavar and Mishra, 2011). CCHF virus is also recognized as a potential bioterrorism agent. In Iraq, it was studied as a potential biological weapon, and the virus has also

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been shown to be potentially disseminated via aerosolization (Dowall et al., 2016).

Crimean-congo hemorrhagic fever is included among the priority zoonotic diseases, along with rabies, anthrax, brucellosis, and avian influenza in Afghanistan. The country is located within the ecological range of Hyalomma ticks and experiences CCHF cases annually. The first cases of CCHF were recorded in Takhar province in March 1998 (19 cases, 12 deaths, CFR = 63.2%), and later in 2000 in the Gulran district of Hirat province (25 cases, 15 death, CFR = 60%). Active surveillance for CCHF in Afghanistan started in 2007, with 1,284 laboratory-confirmed and clinically-diagnosed cases reported until 2018, ranging from 4 cases in 2007 to 483 cases in 2018, which shows significant increase in Afghanistan (MoPH, 2018).

Some steps have already been taken in response to the disease in the country. The national strategy for prevention and control of zoonotic diseases in Afghanistan (2017–2021) is developed and implementation has started. Also, the national taskforce committee for zoonoses is being established which leads the implementation of the national strategy for the prevention and control of zoonoses including joint outbreak investigation and response to outbreaks of zoonotic diseases, and collaboration in the development of common response strategies. The Memoranda of Understanding (MoU) between relevant stakeholders, including the Ministry of Public Health (MoPH), World Health Organization (WHO), Ministry of Agriculture, Irrigation and Livestock (MAIL), municipalities and other relevant stakeholders, has been signed to strengthen joint collaboration with related sectors for on-time outbreak detection, investigation, and response.

It is worth mentioning that despite the above accomplishments, there are some areas needing improvement which were identified by an assessment of capacities required for CCHF prevention and control in Afghanistan conducted in 2018, with technical support from WHO and the Pasteur Institute of Iran. During the assessment, a number of shortfalls were noted, including a lack of specific preventive and control strategies at country level; insufficient resources for the management of CCHF; limited space for isolation wards in hospitals; insufficient stock availability of antivirals (ribavirin) at the country and hospital level; low awareness in health personnel about the diagnosis, treatment, and prevention of disease; and a low awareness of community at risk about disease prevention. To decrease the CCHF cases and deaths, the national response plan for the prevention and control of CCHF has been recently developed by MoPH, WHO, MAIL, municipalities, and other relevant stakeholders based on the assessment findings.

A Joint External Evaluation (JEE) of International Health Regulations (IHR-2005) core capacities conducted in December 2016 also recommended that the joint response mechanism and multi-sectoral cooperation should be improved, and more active surveillance and electronic information sharing should be initiated for zoonotic disease both by animal and human health (JEE, 2017).

This paper aims to document and describe the epidemiology of CCHF during 2016–2018 by retrospective analyses of CCHF data from the National Disease Surveillance and Response (NDSR) department of MoPH.

Methods

Study design

This paper's findings are based on retrospective analysis of National Disease Surveillance and Response (NDSR) system's collected data from January 2016 to December 2018. This study aims to provide descriptive epidemiology of human CCHF cases in Afghanistan by demographic, geographical, seasonal, and occupational characteristics.

Study participants

All suspected and confirmed cases (of both sexes and all ages) reported to the surveillance system from January 2016 to 30 December 2018 were included in the study. A total of 891 suspected and confirmed cases were reported during this period, for all of whom the surveillance line list was filled and laboratory confirmation result was obtained.

Case definition of CCHF

The NDSR defines a *suspected CCHF* case as a patient with sudden onset of illness with a high-grade fever over 38.5 °C for more than 72 h and less than 10 days, especially in a CCHF endemic area and among those in contact with sheep or other livestock (shepherds, butchers, and animal handlers). Fever is usually associated with headache and muscle pains. A *probable case* is defined as a **s**uspected case with an acute history of febrile illness of 10 days or less having any two of the following symptoms: thrombocytopenia less than 50,000 /mm^3, petechial or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in stools, ecchymosis, gum bleeding, other hemorrhagic symptom and no known predisposing host factors for hemorrhagic manifestations. A *confirmed case* is defined as any suspected case with serological confirmation using enzyme-linked immunosorbent assay (ELISA) to detect IgM against the CCHF virus or detection of viral nucleic acid by real-time reverse transcription-polymerase chain reaction (RT-PCR). The Central Public Health Laboratory (CPHL) in Kabul started testing for CCHF using RT-PCR tests in 2018 and remains the only laboratory with this capacity.

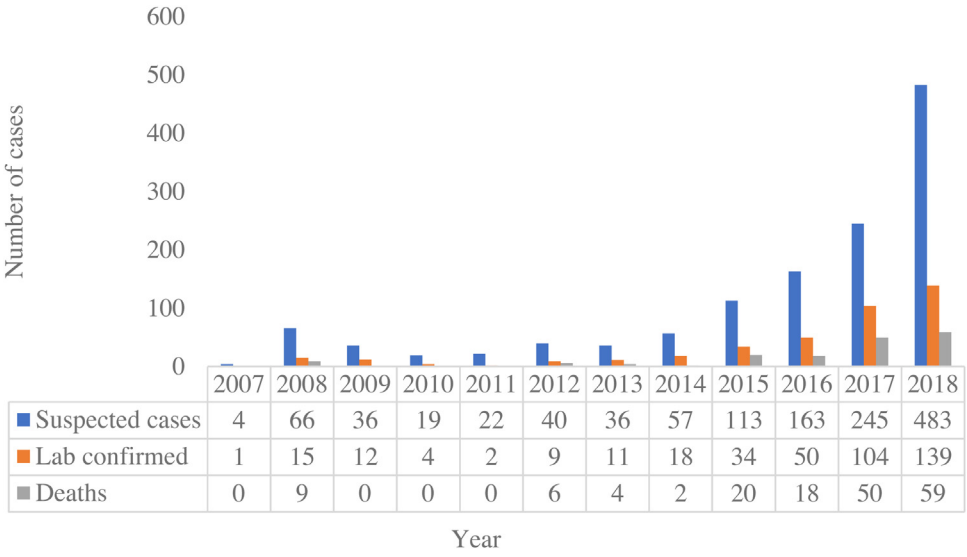
Data collection and report to NDSR

After receiving an alert from the health facility or community, the provincial rapid response teams (RRTs) investigated the case (s), provided an initial response, and collected specimens from the suspected case(s) of CCHF. The RRT members include public health surveillance officer, communicable disease control officer, emergency preparedness and response officer and animal health representative. The surveillance officers collected the data from the cases during the investigation, filled the CCHF line list for all cases and reported to the national surveillance unit. The collected samples are shipped to the CPHL in Kabul for all of which results were sent back to the surveillance unit and entered in the national database. The samples are tested by ELISA to detect IgM against the CCHF virus or detection of viral nucleic acid by real-time RT-PCR. The negative samples were not tested further for other viral hemorrhagic fever (VHF). Animals have not been tested during the outbreak of CCHFV either.

Statistical data analysis

Categorical variables were summarized in the form of proportions and frequency tables. Means, medians and interquartile range were calculated for continuous numerical variables. The variables collected from the cases included demographic characteristics (e.g. sex, age, and occupations), geographical location, date of onset, symptoms, received treatment, exposure, and outcome.

For setting the threshold, for each week, the number of cases in the period 2 weeks before and 2 weeks after, in 2014, 2015, 2016 and 2017 were used to calculate a weekly "expected value" using the WHO threshold setting method. Next, for each week in 2018, the observed numbers of cases were compared against the 90th and 75th percentiles of the expected number of cases calculated previously. Weekly cases exceeding the 90th percentile of expected number of cases were considered to be exceptional and above



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Suspected cases	4	66	36	19	22	40	36	57	113	163	245	483
Lab confirmed	1	15	12	4	2	9	11	18	34	50	104	139
Deaths	0	9	0	0	0	6	4	2	20	18	50	59

Figure 1. It shows number of suspected and confirmed CCHF cases and death in Afghanistan, 2007–2018. The blue color stands for number of suspected cases, orange for lab confirmed cases and gray color stands for number of deaths due to CCHF. The horizontal axis year (from 2007 to 2018) and vertical axis shows the number of CCHF cases.

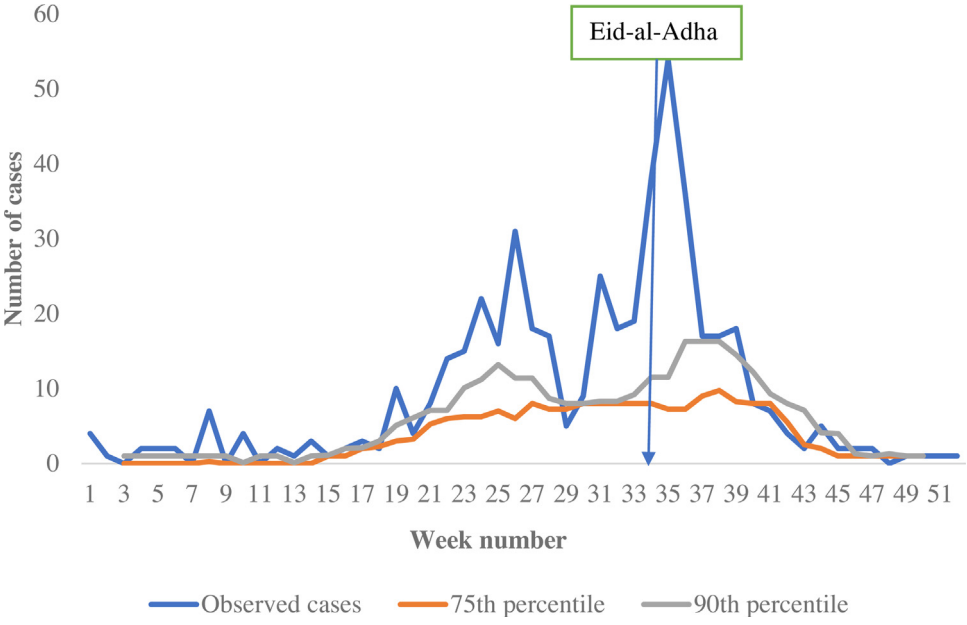


Figure 2. The Figure 2 shows number of observed CCHF cases in 2018 versus 75th and 90th percentile threshold. Eid-al-Adha happened on week 34 which is marked due to increasing trend of CCHF during the Eid celebration. The horizontal axis shows epidemiological week number from week 1 to 52 and vertical axis shows the number of CCHF cases.

normal. Both 75th percentile and 90th percentile were used to observe the changes in thresholds. The SPSS software (version 20) was used for calculating descriptive statistics and final analysis.

Results

The National surveillance system detected 1,284 CCHF cases from 2007 to 2018, of which 163 cases were in 2016, 245 cases in 2017 and 483 cases in 2018. A total of 891 suspected and confirmed cases were reported between 2016 and 2018, 293 (33%) of these cases were confirmed by detecting IgM antibody using ELISA and RT-PCR (Figure 1).

Most of the cases are usually reported during the summer and start rising in May and declining in October. Based on the 75th and 90th percentile, cases of CCHF exceeded the threshold on week 19 of 2018 and declined on week 37th. The CCHF cases in 2018 started to increase on week 34 which coincides with Eid-al-Adha and reached a peak on week 35 (Figure 2).

Among confirmed cases, the three-year case fatality ratio (CFR) was 43.3% (36% in 2016, 48% in 2017 and 42.2% in 2018). The CFR among suspected cases was 14.3% (11% in 2016, 20% in 2017 and 12% in 2018) during the same period. The data show a significant increasing trend of CCHF cases and deaths in Afghanistan.

Geographically, cases have been reported from 33 out of 34 provinces during the recent three years, with the greatest proportions of cases reported from Hirat and Kabul provinces (Figure 3).

The data about demographic characteristics are shown in Table1. Among the reported cases, 68.5% were males and 31.5% females.

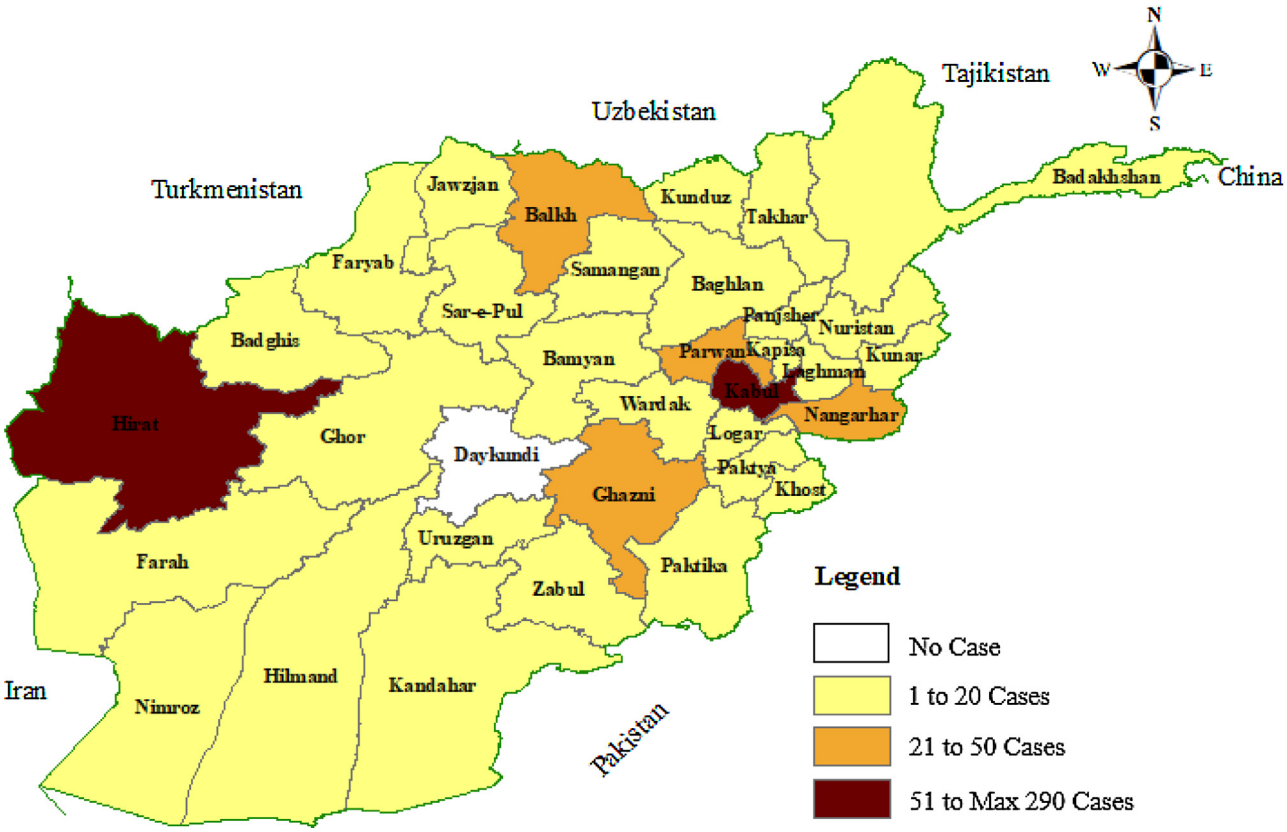


Figure 3. It shows geographical distribution of reported CCHF cases in Afghanistan from January 2016 to December 2018. The provinces are divided into four categories. Provinces with no CCHF cases, 1–20 cases, 21–50 cases and more than 51 cases which are colored.

Table 1
Demographic characteristics of CCHF cases.

	CCHF cases (n)	CCHF cases (%)
Overall	839	100
Gender		
Male	615	69
Female	285	32
Age (Years)		
1–15	69	8
16–30	402	45
31–45	224	25
46–60	148	17
60+	51	5
Occupation		
Animal dealer	15	1.7
Butcher	54	6
Farmer	20	2.3
Health staff	118	13
Housewife	136	15
Shepherd	101	11
Student	50	6
Unemployed	166	19
Others	231	26

The reported cases age ranged from 2 to 90 years, with a mean of 34 years old and a median of 30 (IQR 24 years, data skewed). Almost half of the cases (45%) were reported among 16–30 years old. More than two-thirds (68%) of cases were reported among 16–44 years old, which is the most economically active age group. For the occupation, most of those reported were housewives (15%), health staff (13%), shepherds (11%), butchers (6%), students (6%), animal dealers and farmers (both 2%) respectively, 19% were unemployed, and occupation was not recorded for 26% of cases.

Regarding exposures, 12% of reported cases were bitten by a tick, 4% did not know, and the remaining 83% were not bitten by a tick. Moreover, 4% of cases had secondary exposure being in contact with similar patients. Among those who had contact with similar patients, all were their close family members.

The leading symptoms were fever over 38.5 °C (85%), headache (80%), and muscle pain (75%). The type of hemorrhage varied among cases. All cases had a petechial purpuric rash, 98% had epistaxis, 99% had hematemesis and 93% had hemoptysis. Thrombocytopenia less than 50000/mm3 was recorded among 55% of cases. Supportive treatment therapy including intravenous fluids, analgesia, and platelet and/or blood transfusions was provided for all (100%) cases, and (91%) received antiviral therapy (Ribavarin).

Discussion

The CCHF cases and deaths show an annual increasing trend. Based on the surveillance data, the cases ranged from 4 cases in 2007 to 163 cases in 2016, 245 cases in 2017 and 483 cases in 2018. The anecdotal evidence by program experts suggests that one of the reasons for increase in number of CCHF cases could be that the provinces in West and North (with high percentage of CCHF infected animals) have been affected by drought, causing migration of livestock and people to parts of the country with better grazing, potentially mixing with other herds of livestock and increasing exposure to infected ticks by otherwise susceptible herds. It means more people and wider geographical areas are exposed to the CCHF infection which results in more human cases and deaths. Poor living condition/living closely with animals, internally displaced persons (IDPs), lack of vector control and inadequate management of infected patients could be other causes

of an increased number of cases (World Health Organization, 2017). Another reason might be the improved Surveillance system, more than 250 staff members, both human health and animal health sectors, have been trained on managing CCHF cases since 2015. Additionally, public awareness programs about CCHF have been conducted through mass media campaigns, brochures, and leaflets in recent years. About 400 religious scholars were oriented on CCHF to raise awareness to the public through their preaching. Still, the epidemiological studies have not been conducted to determine the cause of increased cases.

Hirat province has a border with Iran, which is also an endemic area for CCHF where the animal movements across borders occur. In 2017, 33 cases of CCHFV were reported in Iran notably from governorates bordering Hirat (Aghamali and Kafil, 2017). Similarly, an increased number of CCHF cases have been reported in Eastern Mediterranean Region (EMR) recently (Al-Abri et al., 2017). Despite increased cases in Pakistan, the provinces bordering with Pakistan had fewer cases of CCHFV. The studies suggest that most of CCHFV isolates in Afghanistan, Iran and Pakistan belong to the same Asia 1 genogroup (Khurshid et al., 2015).

The 2018 outbreak in Afghanistan with 483 cases has been the largest in Afghanistan. Based on the 90th percentile epidemic threshold set for CCHF, the outbreak started on week 19 of 2018 and ended on week 37. The seasonal trend of CCHF shows a rising trend in May and a declining trend in October in Afghanistan. The peak month is during Eid-al-Adha, the Muslim Festival of Sacrifice. During this festival, Muslims around the world sacrifice animals such as cattle, sheep, goats, or camels. The same increasing trend during this festival is seen in other Middle Eastern countries. In the past, Eid-al-Adha has occurred in the autumn or winter months, but in the next 10–15 years, the festival will occur in the summer months when animals are more likely to be viraemic and infectious for CCHF virus, since ticks are more likely to be or to have recently been feeding on these animals. This may lead to an increase in the number of CCHFV infections as a result of careless practices during the slaughtering of animals, inadequate knowledge of the disease, and the dissemination of CCHFV through uncontrolled animal movement in and between countries (Leblebicioglu et al., 2015). Our results also show that 12% of reported cases were bitten by a tick, and 4% of cases had secondary exposure being in contact with similar patients. Among those who had contact with similar patients, all were their close family members.

The CFR was 43.3% among confirmed cases and 14.3% among suspected cases during the recent three-year period. This result is consistent with other studies such as the Ahmed et al., 2018 study in Pakistan, which found 10–40% CFR. In addition, the high-risk occupational groups were housewives (15%), health staff (13%), shepherds (11%), butchers (6%), students (6%), animal dealers and farmers (both 2%) respectively. Housewives might be at risk because of being in contact with the blood of animals while cooking and not using protection methods. A total number of 14 CCHF cases (13%) were reported among health care staff during the recent three-year period in Afghanistan; however, no nosocomial infection was reported. World Health Organization also suggests that human to human transmission may occur in health care settings because of close contact with the blood, secretions, organs, or other body fluids of patients (WHO, 2015). The reported cases among students might be because of accidental exposure to ticks or animals. According to another study in Turkey, the high-risk group for CCHF was men and women working in agriculture and animal husbandry and also those working in health care settings (Sisman, 2013). Many studies have suggested that slaughterhouse workers, butchers, and livestock handlers are high-risk groups for CCHF (Sharifi-Mood et al., 2014; Hadinia et al., 2012).

The leading symptoms were fever over 38.5 °C (85%), headache (80%), and muscle pain/myalgia (75%). Other studies have also shown similar results. One study in Pakistan showed that fever and hemorrhage were among the most frequent clinical presentation of CCHF (Sheikh et al., 2005). The type of hemorrhage varied among cases in Afghanistan. All cases had petechial purpuric rash, 98% had epistaxis, 99% had hematemesis and 93% had hemoptysis. Similarly, the Sheikh et al. (2005) study showed that petechiae and epistaxis were among the frequent hemorrhagic signs and symptoms.

Thrombocytopenia or platelets less than 50,000/mm^3 was recorded among 55% of cases. Another study found 78% of thrombocytopenia among patients (Khurshid et al., 2015). Supportive treatment therapy including intravenous fluids, analgesia and blood transfusions was provided for all (100%) cases, and (91%) received antiviral therapy (Ribavarin). The recommended treatment is intravenous ribavirin. However, oral ribavirin could be administered in its absence as well in addition to other symptomatic treatments (Sheikh et al., 2005).

Conclusion

Recently, CCHF has significantly increased in Afghanistan. Despite the increasing frequency of cases, the laboratory capacity to test specimens and overall knowledge of CCHF management remains limited. Those who are exposed to the vector (*Hyalomma* ticks), potentially infected animals, the blood and tissues of freshly slaughtered livestock are most at risk. Still, this data is descriptive and cannot provide enough information about the cause of increased cases and cannot say anything about the geographical movement of CCHF strains. Still, it provides evidence of a high case fatality ratio and remains a major public health concern, which needs enhanced coordination of animal and human health sectors to work for control and prevention of CCHF in Afghanistan. As the cases reach a peak during Eid-al-Adha, regular CCHF awareness programs are needed for health staff, animal handlers, housewives and other people at risk at the national level through various communication channels. Further research is needed to identify the causes of increased CCHF cases, and also CCHF genotype and sequencing of strains are recommended to identify pathogen genotypes and lineage, strain movement and sequence diversity of the CCHF in Afghanistan.

Conflict of interest

None of the authors had conflict of interest

Funding source

No funding was needed.

Ethical approval

This paper is based on secondary data analysis of available Surveillance data and human subjects were not directly involved for data collection of this paper. Thus, ethical approval was not required.

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