

REVIEW

Epidemiology and Control of Congo Fever in Sacrificial Animals of Pakistan

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ARTICLE INFO

Article history

Received: 29 October 2019

Accepted: 18 November 2019

Published Online: 30 November 2019

Keywords:

Congo fever

Transmission

Eid-ul-Azha

Epidemiology

Control

ABSTRACT

The cases and deaths due to Crimean-Congo haemorrhagic fever (CCHF) virus commonly known as Congo virus (fatality rate 15%) have been reported throughout Pakistan from the last few years especially during religious occasion, Eid-ul-Azha. The annual increase in death rates due to CCHF demonstrate the importance of awareness of Congo fever at academia as well as public level. The symptoms of Congo fever which appear one to nine days after tick bite, include sudden high fever, muscle aches, abdominal pain, headache, dizziness, sore eyes, jaundice, mood swings, confusion, aggression, and sensitivity to light. The other signs include sore throat, joint pain, vomiting, diarrhea, hemorrhages, and bleeding from skin and large intestine. The infection has been reported in many species of wild as well as domestic animals including hares, cattle, sheep, goats, dogs, mice and hedgehogs. At least 31 species of *Hyalomma*, *Boophilus*, *Rhipicephalus*, *Dermacentor* (Ixodidae: hard ticks) act as vector of CCHF in which transovarial, transstadial and venereal transmission occurs. The virus attacks the immune system of the host and influences the immune cells. The Congo fever virus can be isolated from blood, plasma and many body tissues (kidneys, liver, spleen, lungs, brain and bone marrow). Mice inoculation, enzyme-linked immunosorbent assay (ELISA), reverse transcription polymerase chain reaction (RT-PCR) can be used for detection of the infection. Furthermore, IgM and IgG antibodies against CCHFV can also be detected and quantified. Education of general public, tick control with acaricides, use of anti-CCHFV immunoglobulin, usage of approved repellents to prevent tick bites, wearing neutral-coloured garments, application of a permethrin spray to the clothing, avoiding tall grasses and shrubs, applying sunscreen, avoiding direct contact with the blood or tissues of animals are the factors for successful prevention of the infection.

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1. Introduction

Crimson Congo hemorrhagic fever (CCHF), one of the tick borne, zoonotic viral infections, is significantly fatal, causing casualties in different areas of the world; particularly in developing countries. The CCHF is caused by Nairovirus which belongs to the family Bunyaviridae. Pakistan, being developing country faces many challenges due to communicable and non-communicable diseases over the period of time. In Pakistan, hasty climate change triggered by occupational and industrial activities to upkeep the human population has been measured the most paying basis for emergence or re-emergence of CCHF. The CCHF is mainly prevalent in southeastern Europe, Africa, Middle East and Asia. In general, the vectors of Congo fever are hard ticks of Ixodidae family, including *Hyalomma (H.)* (particularly *H. marginatum*), *Boophilus*, *Rhipicephalus* and *Dermacentor*. The ixodid ticks are also notorious as the main reservoir for CCHF. Almost 30 Ixodid species have been found positive for CCHF through screening^[21]. Congo fever can be transmitted to the human through vector bite, direct contact with tissues, blood of infected livestock and body fluids of infected patients. The nosocomial transmission, contact with viremic livestock and/or human blood and sporadic outbreaks due to tick bite have been reported frequently in Pakistan.

The farmers and health care workers are at high risk of CCHF. Clinical symptoms related with CCHF are haemorrhage, fever and sometimes nonspecific prodromal symptoms may occur. Differential diagnosis of CCHFV is somewhat difficult from viral haemorrhagic fevers (VHFs) and undifferentiated febrile. It is epidemic with high case fatality ratio (3-30%) due to hindrances in prevention and treatment. The case fatality rate of CCHF up to 5-80% has also been reported^[27].

The prevalence of CCHF has been reported from different areas of the world including South Africa, Tajikistan, India, United Arab Emirates, Iran, Turkey and Pakistan^[4,6,12,33,34,45,47,48]. Pakistan is at 4th position after Turkey, Russia and Iran in infected cases and 2nd after Turkey in fatal CCHF cases, respectively according to The Program for Monitoring Emerging Diseases (Pro MED) during 1998-2013^[23].

The domestic and wild animals including goats, cattle, birds and rodents act as amplifying host for CCHF virus (WHO, 2013). It is considered as emerging arboviral infection due to climate change resulting in increased vector bionomics. Till now, there is no availability of commercial vaccine and specific treatment against this virus^[3]. The climatic conditions present in Pakistan are found to be

suitable for vector growth and replication so chances of CCHF spread has increased many folds^[26]. In Pakistan, first case of Congo fever was reported in 1976 in General Hospital, Rawalpindi^[6] and later on, it becomes endemic in year 2000^[51]. In Pakistan, public health sector has been facing challenges by many epidemics of Congo fever and still it is going on. At present polio, dengue epidemics and CCHF emerged as important fatal infection from public health point of view.

Epidemiological profile of CCHF is reported from different areas of the world^[44,46], but unfortunately in Pakistan, no data is available regarding this. National Institute of Health (NIH) is the only institute in Pakistan which in collaboration with WHO monitoring CCHF on daily bases and providing instructions to the concerned health department^[20]. About 20 casualties were reported from Pakistan in 2016 due to CCHF and high prevalence was reported in Sindh^[11] due to lack of proper monitoring system for CCHF outbreak in Pakistan^[26]. Therefore, main objective of this review is to discuss the factors responsible for transmission of Congo fever due to which Pakistan is at high risk for CCHF and to check the epidemiology and control measures against CCHF.

2. Transmission of CCHF

Main vectors and reservoirs for CCHFV are hard ticks. Due to more prevalence of *Hyalomma* vector, wide range of animals can act as host for CCHFV which help in hematophagy for different tick stages. The favorable climatic and ecologic conditions, arid types of vegetation and public behavior are the potent factors which affect the establishment and maintenance of CCHF in an area. Larval and nymphal stages of *Hyalomma* genus feed on hares and small birds while adult stages feed blood on sheep, cattle and other large mammals. There are some other species which are three-host ticks and after each molting, they drop off from their host. Migration of infected animals from infected area to other area is the main factor for CCHF transmission. Transmission can occur through contact with infected animals' blood and other products, person to person contact and contact with infectious body fluids. Humans may participate in increasing in CCHFV transmission through recreational activities, change in use of land and through migration of infected animals^[30]. Due to such kind of activities, there may be increase in incidence of CCHF in future.

Main route of CCHF transmission is tick bite, other than this direct contact with infected animal blood, tissues and body fluids and skin of infected person may play important role for the transmission of the disease^[16,40]. Mostly, disease is asymptomatic in animals^[14] and

is considered a threat for population including farmers, veterinarians and health care workers dealing with CCHF infected persons. There is another type of viral transmission occurred in which requirement of viremic animal is not compulsory and direct transmission takes place during feeding of infected ticks to the others. During this, feeding viral substances present in the tick saliva increases the viral transmission. Due to inefficient managerial practices and biosafety policies, chances of CCHF epidemics increased [51].

In Pakistan, majority of people are interrelated with agriculture sector, especially in rural areas and are engaged with livestock management. Numerous vectors acting as the main source of pathogen transmission are more prevalent in agricultural areas of Pakistan, so, community are at high risk for vector-borne diseases especially CCHF. Across boundaries, livestock movement also play important role in transmission of CCHF [22]. In Pakistan, Khan et al. [25] reported that about 37%, 45% and 18% cases of CCHF transmitted by person to person, animal contact and unknown ways, respectively. There are some risk factors which play important role in transmission of CCHFV i.e. crushing and rubbing of infected ticks on skin and slaughtering of infected animals and nosocomial infection. Factors responsible for the transmission of CCHF in animals and humans are given in figure 1.

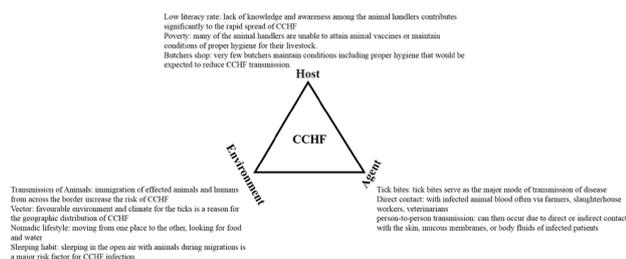


Figure 1. Factors responsible for the transmission of CCHF in animals and humans

Humans can get infection through tick bite or bare skin contact with tick, per mucosal and percutaneous route. Aerosol transmission is also considered a possible route in some territories of Russia but there is no sure report [40]. There is a single report regarding sexual transmission [28] but it is necessary to confirm the presence of CCHFV in body fluids of livestock workers and slaughterhouse workers as they are at high risk of sudden exposure to the virus [3]. Transmission of CCHF is also reported through human to human interaction and 15-20% mortality rate reported in health care workers due to direct contact with body secretions of infected patient [5,13,41]. Due to lack of early diagnosis facilities, chances of nosocomial transmission increased many folds and along this needle prick injuries and splash also reported due to lack of personal protective

equipment supply [15].

3. Epidemiology of CCHF

People working with animals i.e. livestock workers, slaughterhouse workers and animal herd workers and travelers in endemic areas are at high risk for CCHF. It is also reported that health care workers are at risk through contact with infected body fluids and blood.

The CCHF first described by a Tajikistan physician in 1100 AD in a patient showing haemorrhagic symptoms [31,43]. Disease was first identified during an outbreak in 1944 in Crimea and later in 1965 identified and isolated in Congo and so the name Crimean-Congo haemorrhagic fever (CCHF) was given. Disease is endemic in many areas of the world i.e. Middle East, Africa, Asia and Eastern Europe (Messina et al., 2015). Among tick-borne diseases, CCHF covers a large geographical area and virus has been isolated from 30 countries covering four regions Asia (Tajikistan, China, Afghanistan, Pakistan, Kazakhstan, India, Uzbekistan), Middle East (Iraq, United Arab Emirates (UAE), Iran, Oman Kuwait, Saudi Arabia), Africa (Mauritania, Democratic Republic of Congo, South Africa, Uganda, Sudan, Nigeria, Senegal) and Europe (Kosovo, Russia, Turkey, Bulgaria, Spain, Greece) (WHO, 2016). Due to its widespread distribution, it must be considered as global health threat. Distribution of CCHF is related with prevalence of ixodid ticks especially *Hyalomma* genus. In Europe, main vector for CCHF is *H. marginatum* while in Asia, *H. asiaticum*. In 2006, *H. marginatum* was first time detected in southern Germany and Netherland [24,32]. In January 2011, first case of CCHF was reported in India and main vector involved in transmission was *H. anatolicum* [35].

Its name Congo, is the main source of confusion about its prevalence outside the Congo, however, it is reported from Pakistan by a senior surveillance coordinator of communicable diseases in Islamabad, Dr. Muhammad Najeeb Khan Durrani. In Pakistan, CCHF virus was isolated very first time in 1960s from ticks collected from Changa-Manga forest, Lahore [9]. Asia-1 and Asia-2 genotypes of CCHFV have been considered as the most prevalent genotypes in Pakistan. However, the first case was reported in 1976 in Central General Hospital, Rawalpindi. During this year total eleven cases were reported and one infected patient was died among them, however, one surgeon and an operation theatre attendant were also died due to direct contact with patient [12]. In 1994, cases and death due to CCHF was reported from Quetta, Baluchistan [19] and in 2000 from Khyber Pakhtunkhwa [8], in 2002 from Bagh in Azad Jammu and Kashmir [6]. Number of deaths reported in last six years from different provinces of Pakistan is given in figure 2. World Health Organization along with the Na-

tional Focal Point, Ministry of Health, Pakistan reported 26 cases in 2010, 61 cases in 2012, 16 in 2013, 25 in 2015^[37,50]. The percentage of confirmed CCHF cases reported in Pakistan during different seasons is given in figure 3.

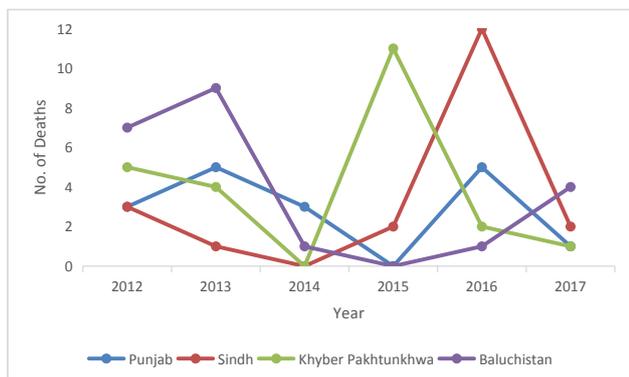


Figure 2. Number of deaths reported from different provinces of Pakistan during 2012 to 2017

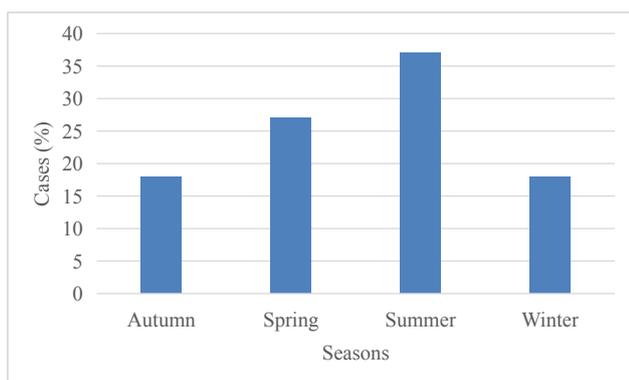


Figure 3. Percentage of confirmed CCHF cases reported in Pakistan during different seasons

Change in climatic conditions, worldwide distribution of *Hyalomma* vector and availability of range of hosts in European countries especially Mediterranean Sea areas are more prone to CCHF infection in near future. Dry climates, arid vegetation and prevalence of large and small mammals favor the *Hyalomma* growth by providing hematophagy for different life cycle stages. Human activities and ecological factors are important for establishment and maintenance of CCHF in an area. Humans can minimize the CCHF risk through modifying their recreational activities, land use and by adopting the policies for safe transportation of animals^[30].

4. Livestock and Eid-ul-Azha

Livestock play an important role in the economy of Pakistan, owned by rural community and commercial dairy farmers. In Pakistan, currently, 24.24 million sheep, 23.34 million buffalos, 22.42 million cattle and 49.14 million goats population have been reported^[1]. A large number

of community is directly linked with these animals such as veterinary care, tick removal, animal slaughtering and butchery. So, chances of CCHF transmission increase from animals to humans as reported in a study from Afghanistan^[36].

Unfortunately, in Pakistan, people of high-risk areas are in close contact with the livestock that increases the CCHF risk. Animal transportation from one region to other also help in transmission of CCHF especially at Eid-ul-Azha (a religious festival of Muslims to sacrifice cattle to give away to others). As a result, large number of CCHF cases are reported around that time^[29,42]. Eid-ul-Azha is celebrated according to the Islamic calendar and now days, it is coinciding with summer season when environmental conditions are suitable for tick growth, development ultimately increases tick population carrying CCHF virus^[2]. Movement of animals from rural areas to urban areas increases CCHFV transmission to the humans. Due to lack of polices for prevention against CCHF, number of cases are increasing day by day.

Before few days of Eid-ul-Azha, it is a tradition to keep animals at houses and this increases the chance of transmission through the bite of the infected tick. Mostly people slaughter animals by themselves or appoint a butcher at their homes, so, during slaughtering chances of transmission also increases^[38]. Furthermore, butchers also act as source of CCHF transmission by providing services from home to home. Another major problem is the waste material of slaughtered animals, which is kept in open places and there is no proper disposal system.

Besides these sacrificial activities, accidental death of animals is also a major source of transmission. Animals are kept on roads or open places for weeks and lack of proper disposal system also aggravate the condition^[7]. Although, the Ministry of National Health Services Pakistan has started an awareness scheme and regarding this, a letter has been issued in June 2015 focusing on preventive measures against CCHF. But unfortunately, it did not describe any guidelines for slaughtering and animal movements across boundaries^[2].

Special precautions must be taken while buying the sacrificial animals like inspection of the animal body for ticks, each day and avoidance from crushing of ticks with bare hands. Do not try to remove the tick with your fingers. Wear light colored, full sleeve clothes and shoes with socks. Apply an insect repellent on the exposed area of body. Take a shower and change your clothes as soon as you return home.

5. Prevention and control

Difficulty in the control of CCHF infection is due to un-

noticed transmission of virus in domestic animals during tick-animal-tick cycle and further due to wide range of tick vectors. Due to unavailability of vaccines against these vectors, acaricides are the only option for control of these vectors at livestock farms. So in this scenario, public awareness regarding this disease and its vector is the only way to reduce the burden of exposure to CCHF.

One of the primary reasons for the spread of CCHF is the lack of reasonable facilities and care center to accommodate quality care for animals. Proper monitoring of animals which imported from other countries or endemic regions, especially during Eid ul Azha, should be done to control CCHF. One of the best ways to reduce the transmission of CCHF virus from animal to human is the use of gloves and proper protective clothes. Try to avoid direct contact with infected person and infected body fluids. Media should provide awareness regarding symptoms, route of transmission and preventive measures against CCHF i.e. avoid direct contact with tick, and use proper clothing during animal cleaning, use spray to protect your animals against ticks, avoid backyard animal slaughtering practices, cover mouth and nose during start of slaughtering, slaughtering should be done in abattoirs or restricted places. If hands are blood stained, do not rub eyes or nose. The offal and leftovers of the animal should be disposed-off properly. Slaughtering area should be washed and cleaned after the sacrificial activities.

Besides these awareness programs, informative lectures, training workshops are also necessary to properly educate the health care professionals. Government should also play its role by implementing the strategies and providing financial resources to the research institutes for development of vaccines against livestock and agricultural infectious diseases. During the religious occasion of Eid-ul-Azha, it is necessary to provide suitable diagnostic facilities and quarantine measures to help in prevention of the disease spread and reduction in the causality rate due to CCHFV. There is need to provide registry and tracking system for monitoring of animals and people from endemic areas to other provinces and across the country borders. Epidemiological survey should be conducted to get familiar with the prevalence of tick fauna and other associated factors which can aggravate the condition by providing suitable environment and transmission route for vector-borne diseases. Environmental hygiene and personal protection are also the essential components of prevention.

6. Conclusion

Crimean-Congo hemorrhagic fever is highly prevalent disease across the world and Pakistan is at high risk due to higher abundance of ticks and suitable environment for

their growth. Flaws in health care system policies, high prevalence in rural community engaged with livestock rearing and association of livestock with Eid-ul-Azha also increase the risk of CCHF. Moreover, workers in diagnostic laboratories are also at risk to develop infection through contact with viral samples during routine dealings. For all these reasons, Center for Disease Control and Prevention has characterized CCHFV as a BSL-4 pathogen. Some of these factors belong to culture and some are physical, so, they should be dealt in different ways. It is suggested to devise some policies to educate the community about CCHF and its transmission routes. This will be helpful for minimizing the risk factors and will help to stop the nosocomial transmission.

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