Emergence of CCHF Virus in Pakistan

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ABSTRACT

Crimean-Congo Hemorrhagic Fever (CCHF) is a zoonotic disease caused by a virus transmitted by ticks. In Pakistan, this illness has become a major concern due to various factors like changes in climate, tick population boom and transportation of carrier animals. CCHF outbreaks happen twice a year in Pakistan, mostly affecting areas that lack urbanization i.e., Baluchistan and Sindh. Pakistan is among the top countries with CCHF cases in Asia, and it has faced outbreaks since the 1960s.This disease presents significant challenges and widespread implications due to its potential to result in numerous fatalities and can be used as bioterrorism weapon. Challenges in controlling the disease include lack of awareness, poor hygiene standards, constrained diagnostic options and Inadequate disease monitoring and screening. Prevention of CCHF involves awareness among the people, use of protective gear, proper sanitation and monitoring of ticks regularly. Combining human, animal, and environmental health is crucial for stopping the disease. However, it's hard to coordinate everything, especially in places like Baluchistan where there aren't enough resources. To control CCHF from spreading enhanced inspection protocols, ticks control, and involvement of communities are important. This summary highlights the crucial necessity for joint endeavors focused on preventing, promptly detecting, and efficiently managing CCHF, ensuring the protection of public health and economic well-being.

Key words: zoonotic, amplifying host, ecchymosis, sporadic infections, surveillance.

CITATION

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1. INTRODUCTION

The term CCHF stands for Crimean-Congo Hemorrhagic Fever. CCHF is found to be a tick-borne viral zoonotic disease caused by Crimean-Congo Hemorrhagic Fever Virus. It is said to be asymptomatic in domestic and wild animals and both of them act as reservoirs of the virus (Fanelli and Buonavoglia 2021). Every year, Eid-al-Adha (a significant Muslim Festival of Sacrifice), along with the Hajj, occurs in Mecca. In the last 10-15 years, Eid-al-Adha, which generally occurs in autumn-winter months, will shift to the summer months when the CCHF virus is more prevalent. So, a massive increase in the number of cases is reported (Leblebicioglu et al. 2015).

During World War II (1944-45), the first recognition of CCHF occurred among Soviet Union military personnel in the Crimea, leading to its initial designation as Crimean Hemorrhagic Fever. In 1969, it was discovered that the virus causing Crimean Hemorrhagic Fever was the same as the one responsible for a febrile illness in the Belgian Congo, which was known as the Congo virus. As a result, the two names were merged into one, giving rise to the current name of the virus: Crimean-Congo Hemorrhagic Fever Virus (Hussain et al. 2016).

CCHF virus is an RNA virus characterised by a single-stranded, negative-sense genome. Its genome is divided into three segments: small (S), medium (M), and large (L) (Papa et al. 2017). CCHF is caused by a virus known as CCHFV (Crimean-Congo Hemorrhagic Fever virus), which belongs to the Orthonairovirus genus within the Bunyaviridae family. The transmission of this virus occurs through various tick species belonging to the (Hyalomma) Ixodidae family. These ticks can remain attached to the primary host for a maximum of 26 days, and in the case of migratory birds, they may serve as potential carriers of the virus over long distances (De Liberato et al. 2018). The enzootic cycle of the CCHF virus relies on an intricate network involving ticks and host populations, suggesting that the disease may be more widespread than what we can see from the number of reported clinical cases (Vescio et al. 2012).

The amplifying hosts of CCHF are various mammal species that remain asymptomatic. Humans get infected by tick bites or by direct contact with animal blood and other body fluids (Fillâtre et al. 2019). CCHF poses a significant danger to humans as it is perpetuated within various tick species and can be transmitted to both wild and domestic animals in their natural habitats (Saijo 2018). Of significant concern for human exposure is the virus's ability to infect livestock without causing any apparent disease (Hawman and Feldmann 2023). Cases of nosocomial transmission are notable in highlighting the spread of the CCHF virus within healthcare settings (Leblebicioglu et al. 2016).

The disease usually has three phases: an incubation phase lasting 1 to 9 days, followed by hemorrhagic and hemorrhagic phases (in severe cases), and finally, the convalescence period. The hemorrhagic symptoms vary from small red or purple spots (petechiae) and nosebleeds (epistaxis) to widespread bruising (ecchymosis) and bleeding from different parts of the body (Papa et al. 2015). The symptoms of CCHF can vary from mild flu-like illness that resolves on its own to severe and life-threatening manifestations (Rehman et al. 2018). CCHF virus infection is characterised by fever and hemorrhage and is frequently accompanied by non-specific prodromal symptoms; these symptoms can include general malaise, fatigue, headache, muscle pain, and fever. These symptoms may precede the more specific manifestations of the disease, such as haemorrhage and organ dysfunction (Al-Abri et al. 2017). Severe CCHFV infection leads to the development of a condition which is distinguished by the presence of

petechiae, ecchymosis, epistaxis, gingival haemorrhage, and often gastrointestinal and cerebral haemorrhage (Zivcec et al. 2015).

In numerous countries, CCHFV has become a notable arboviral zoonotic disease, marked by the lack of specific antiviral therapies, a high mortality rate, and its capacity to spread through vectors (Dai et al. 2021). Due to the substantial genetic diversity observed among CCHFV strains, it is significantly essentialvital to focus on molecular protocols that can effectively detect all existing genetic lineages of the virus and in severe cases, there may be a delay or absence in the production of antibodies (Papa 2019). Due to the absence of an effective vaccination against the disease, disease prevention and treatment play a vital role. Consequently, immunotherapy is employed. Combining it with compensatory therapies such as blood and platelet replacement, water and electrolyte management, and Fresh Frozen Plasma (FFP) replacement, among other compensatory medicines, proves to be one of the most effective treatment approaches (Gholizadeh et al. 2022).

Although there is no treatment for CCHF and only anticipation is achieved through supportive therapy, it is observed that the use of proper PPE along with Ribavirin reduces CCHF virus infection among healthcare workers and also increases the chances of survival of infected person (Ergönül et al. 2018).

2. GLOBAL IMPACT OF CCHF

The epidemiology of Crimean-Congo Hemorrhagic Fever (CCHF) is being influenced by climatic and environmental changes, along with the growing global trade and mobility, leading to a risk for the continued transmission of the disease (Fanelli et al. 2022). Presently, Crimean-Congo Hemorrhagic Fever (CCHF) has been identified as endemic or potentially endemic in approximately 50 countries across Europe, Africa, and Asia. It leads to severe hemorrhagic syndrome and sporadic infections in humans (Nasirian 2019).

Evidence of Crimean-Congo Hemorrhagic Fever Virus (CCHFV) infection may have been documented as early as 1961 in Kenya, which was then known as British Kenya. Serological evidence of human CCHFV infection was initially obtained in the early 1980s (Temur et al. 2021). There was an outbreak in China in 1965, with an 80% case fatality rate (Ergönül 2006)

However, since the year 2000, the cases increased rapidly, and they have been reported in several countries, including Turkey, Iran, Pakistan, India, Greece, the Republic of Georgia, and some Balkan countries (Bente et al. 2013). From the year 2002 to 2004, it was declared that CCHF was endemic in Turkey with high mortality, and this outbreak was an alarming situation for all the countries near Turkey (Ozkurt et al. 2006). Furthermore, cases of CCHF imported from abroad were identified in France in 2004 and the United Kingdom (UK) in 2013 (Arteaga et al. 2020).

The frequency of CCHF outbreaks in Uganda is on the rise. Between 2013 and 2017, eight confirmed outbreaks were reported. Moreover, two additional outbreakattacks (not detailed in this manuscript) occurred in early 2018 (Mirembe et al. 2021). The affected regions of the world are represented in Fig. 1.

3. CCHF IN PAKISTAN

Over time, Pakistan has been grappling with the burden of both communicable and non-communicable diseases. Among these threats, CCHF is particularly concerning, exhibiting biannual peaks during March to May and August to October. Currently, cases of CCHF have been confirmed in all regions of Pakistan (Yousaf et al. 2018). Isolated cases of CCHF are documented in of the rural areas of Punjab, Azad Jammu Kashmir, and Khyber Pakhtunkhwa, as well as in neighbouring Afghanistan, where cattle herding is a common practice (Noreen et al. 2020).

Pakistan is classified as an endemic country for CCHF, ranking as the fourth highest in reported cases of CCHF infection in Asia, following Turkey, Russia, and Iran (Ince et al. 2014). The first isolation of the CCHF virus in Pakistan occurred during the 1960s, originating from ticks found in the Changa-Manga Forest located near Lahore (Saleem et al. 2016). In 1976, the first case of CCHF was reported in Pakistan at Rawalpindi General Hospital (Atif et al. 2017). As a consequence, the outbreak in the hospital gave rise to 11 additional cases, leading to the death of three individuals (Tabassum et al. 2023). During the period from 1976 to 2010, 14 outbreaks were reported in Pakistan (Qidwai 2016).

An outbreak was reported that from 1st January 2013 to the middle of June, and 16 cases of CCHF were outlined, and 6 of these died (ul Islam et al. 2014). In May 2017, an outbreak occurred in the Karak district of Khyber Pakhtunkhwa in which six individuals exhibited symptoms such as nausea, vomiting, and diarrhoea. Four out of six died within four days (Jamil et al. 2022). From January 2014 to May 2020, cases of CCHF rose in Pakistan, with approximately 356 instancespoints with a mortality rate of 25%. Among these patients, Baluchistan accounted for 38%, Punjab for 23%, Khyber Pakhtunkhwa for 19%, Sindh for 14%, and Islamabad for 6% (Ahmed et al. 2021). The data is represented in Fig. 2.

Pakistan has observed a higher incidence of CCHF virus since August 2016 (Wahid et al. 2019). In 2016, a surgeon and nurse who had been working at Bahawalpur Hospital lost their lives due to CCHF during their treatment at Agha Khan University Hospital (Ahmed et al. 2018). From January 2017 to December 2019, another outbreak of CCHF was recorded; a total of 244 patients displaying symptoms suggestive of CCHF were admitted to prominent hospitals in Rawalpindi. Among them, 45 patients (18.4%) tested positive for CCHF according to the diagnostic results (Ahmed et al. 2021).

A cross-sectional study was undertaken at Public Hospital Quetta from 2015 to 2020. Among the 480 suspected cases of CCHF, PCR was conducted on 73% of the cases. Of those, 52% were CCHF positive, with a Case Fatality Rate (CFR) of 25% (Saeed et al. 2021). It is observed that Baluchistan is most affected throughout the country on an annual basis. In 2021, 19 suspected cases were reported, of which 14 were confirmed positive and five resulted in fatalities. However, in 2022, there were a total of four confirmed cases in Punjab and Sindh (Tariq et al. 2023). The first case of CCHF in Peshawar was reported in mid-June 2022, and a total of 13 confirmed cases were reported from different regions of the country (Waris et al. 2022).

It is noted that CCHFV is endemic in two provinces of Pakistan, i.e. Baluchistan, which shares a border with Afghanistan and Iran, and Sindh, specifically Karachi. However, cases of the virus have also been reported in other provinces of the country (Umair et al. 2020).

4. FACTORS INFLUENCING THE EMERGENCE OF CCHF IN PAKISTAN

The reported emergence of CCHF is linked to climate change, environmental shifts, rising tick populations, increased presence of wild animals, the movement of domestic and trans-national animals, and the transportation of virus-carrying ticks through migratory birds (Leblebicioglu et al. 2016). Factors that are influencing the emergence of CCHF are:

5. ENVIRONMENTAL FACTORS

5.1. TICK-BORNE TRANSMISSION

Among environmental factors, ticks are the ones that may hold much more importance; ticks are the vectors for the CCHF virus and play a vital role in the spread of CCHF. In order to prevent CCHF, there should be strategies to control ticks during their peak periods (Iqbal et al. 2017).

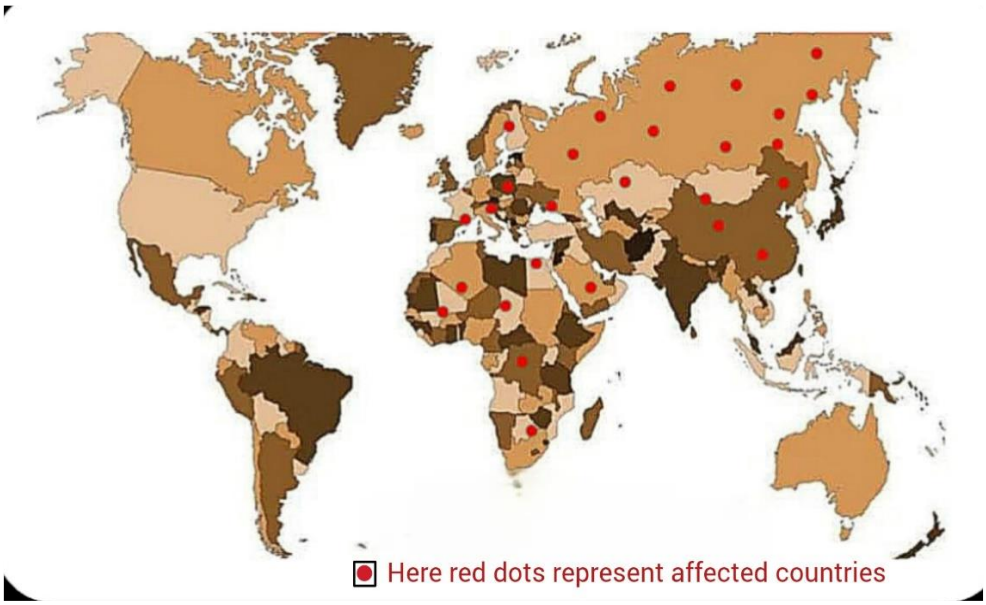

Fig. 1: Affected regions of the World.

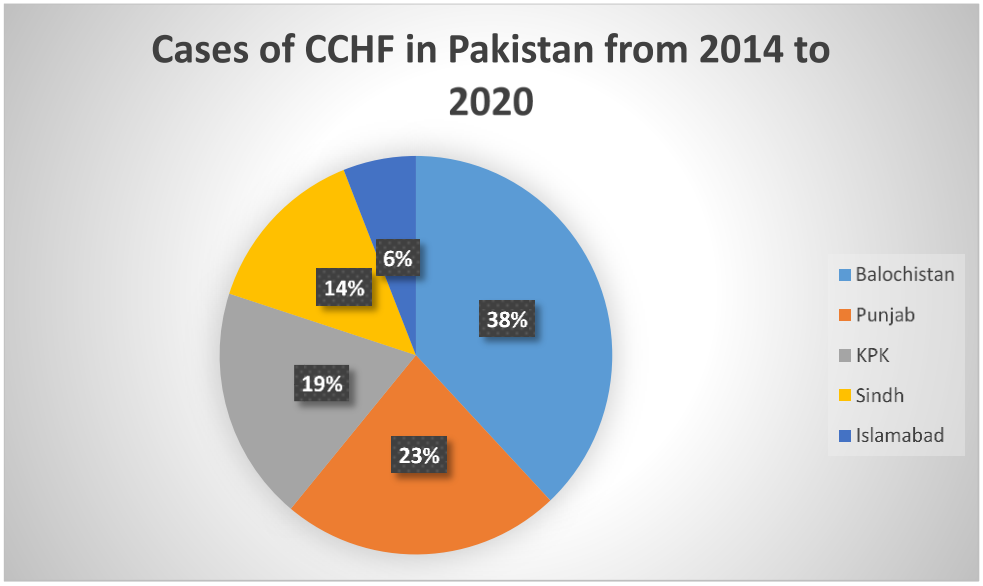

Fig. 2: Cases of CCHF in Pakistan from 2014 to 2020 (Self-designed figure; Data taken from Ahmed et al. 2021).

5.2. CLIMATE CHANGE

As far as the environment is concerned, the climate of the region matters. The escalating effects of climate change in Pakistan have led to a rise in CCHF incidence, attributed to intensified industrialisation, agricultural and occupational practices, and population density (Yasmeen et al. 2022). Ticks thrive in warm and arid environments, making an increase in temperature and a decrease in rainfall favourable conditions for their growth and reproduction (Hussain et al. 2016).

5.3. MIGRATION

Another critical factor which leads to a risk of transmitting the CCHF virus is migratory birds as they act as an amplifying host. They also spread tick species especially, especially hyalomma (Nili et al. 2020).

6. ANIMAL HUSBANDRY AND LIVESTOCK TRADE PRACTICES

6.1. LACK OF AWARENESS

Rural inhabitants exhibit a lower literacy rate and lack awareness about tick-borne illnesses. They inhabit their livestock without implementing any preventative measures and rely on both milk and meat for sustenance while also utilizing cattle dung for wound-healing purposes (Dashti 2012).

6.2. UNHYGIENIC CONDITIONS

Poor sanitation and unhygienic conditions play a pivotal role in facilitating the transmission of CCHF virus. In areas where proper sanitation practices are lacking, infected ticks and animals can easily contaminate water sources, leading to the virus's introduction to the human population. Addressing these issues through improved sanitation measures is crucial in preventing and controlling the outbreak of CCHF (Lea M 2023).

6.3. PASTURE CONTAMINATION

Factors like the grazing system and the age of the livestock can significantly affect the likelihood of disease occurrence. In the stable grazing system, only a small number of animals are affected by the CCHF virus, but this rate can increase up to 30% in the nomadic system (Ahmadkhani et al. 2018).

6.4. TRANSPORTATION

However, another major cause of propagation of the CCHF virus is the transportation of animals from rural to urban areas for business purposes, and it generates the potential to result in viral spillover, where viruses can be transmitted from animals to humans in urban settings (Mallhi et al. 2017). The swift advancement of transportation and the frequent global movement of people and goods have significantly accelerated the rapid spread of infectious agents across the world (Grout et al. 2017).

7. PUBLIC HEALTH IMPACT

CCHF virus poses a significant risk to public health and has been recorded as a potential bioterrorism threat. The community should remain vigilant concerning the possibility of importing CCHF cases from areas where the disease is enzootic (endemic) and the potential for human-to-human transmission, particularly in nosocomial situations (Suchal et al. 2018). The Centre for Disease Control and Prevention (CDC) has identified and categorized several viral agents as potential biological terrorism agents, including CCHF virus and considered them as weapons of mass destruction (Bronze et al. 2002).

As far as the public health impact of CCHF is concerned, there is an utmost requirement to conduct serological surveys on animals in regions identified as high-risk for CCHF occurrence (Fanelli et al. 2022). In the various areas of the country, the reporting quality of CCHF virus infection varies, leading to inconsistencies. Additionally, there is limited active surveillance of human CCHF virus infection, making it challenging to assess the extent and intensity of transmission accurately (Dreshaj et al. 2016).

Tick-borne viral diseases (TBVDs), specially CCHF virus in domestic livestock, present significant risks to global food security, national economies, and public health, as they have adverse impacts on farmer's income and act as a socio-economic factor in the emergence of CCHF virus (Oluwayelu et al. 2023). The main challenge faced by this endemic region is the insufficient coordination between the animal and

human sectors concerning disease control. Additionally, there is a scarcity of laboratory kits for diagnosing CCHF, especially at the district level. This can result in misdiagnosis or delayed treatment, leading to an increase in fatalities (Jafar et al. 2022).

8. PREVENTION AND CONTROL

Lack of consultancy, not caring about essential safety measures, and not having enough isolation rooms for sick people may contribute to nosocomial disease outbreaks. When people with a highly contagious disease are admitted to the hospital, it often generates anxiety, confusion, and fear among hospital staff, and this negligence lead to the spread of a disease (Smego et al. 2004). In order to prevent CCHF infection proper public awareness is needed; one should know how to avoid such risk factors that may lead to that febrile infection, i.e., farmers must use long sleeves and pants and reduce their work in ticks loaded environments (Hawman and Feldmann 2023).

Laboratory staff handling materials from suspected CCHF cases must adhere to good laboratory practices and maintain a high level of adequate biosafety precautions. This is necessary to mitigate the potential for sample-to-person or indirect transmission (Al-Abri et al. 2019). It is mandatory to use proper PPE, but it was observed that only PPE is not sufficientfor. This hazardous virus also getsenters the body through aerosol, and this PPE set does not protect the conjunctiva and upper respiratory tract against aerosols, which could contain the particles of sputum streaked with infected blood from the patient (Pshenichnaya and Nenadskaya 2015).

It is of utmost importance to raise public awareness about the modes of transmission and the symptoms to be vigilant about, as it plays a vital role in disease prevention. Implementing measures to restrict the entry of wild animals into human-inhabited areas has proven effective in reducing disease transmission and controlling infection cases (Greene et al. 2022). In order to lessen the risk of animal-to-human transmission, it is essential to implement quarantine measures while importing animals and ensure regular treatment with pesticides. Furthermore, maintaining hygienic conditions during slaughtering, whether in slaughterhouses or at home, is also crucial (Al-Rubaye et al. 2022).

For control of CCHF virus, active tick surveillance is required. To achieve this goal, it is essential to monitor the distribution, occurrence, and frequency of CCHF virus infection among the ticks in specific geographical areas. The use of pesticides should be encouraged in the habitats of ticks (Sah et al. 2022). At present, there is a lack of a surveillance system to report the condition, particularly in Baluchistan promptly. This surveillance is crucial for conducting risk assessments, disease mapping, and forecasting related to CCHF (Aziz et al. 2020). Both community leaders and technical experts should collaboratively raise awareness about disease prevention and control, ensuring the community receives sufficient knowledge. Employing a One Health approach is essential to effectively implement prevention and control strategies (Ayebare et al. 2023).

9. CONCLUSION

Crimean-Congo Hemorrhagic Fever (CCHF) is a significant tick-borne viral zoonotic disease with a rising incidence in Pakistan and global concern. The disease's enzootic cycle, involving ticks and host populations, indicates its likely broader prevalence beyond reported clinical cases. The emergence of CCHF in Pakistan is influenced by environmental changes, climate shifts, and increasing tick populations, along with human activities like animal husbandry and livestock trade. Preventing and controlling CCHF necessitates public awareness, strict quarantine measures for imported animals, and regular use of pesticides.

A comprehensive One Health approach is vital for disease prevention. Surveillance, serological surveys, and active tick monitoring can aid early detection and tracking. While specific antiviral therapies are lacking, advances in immunotherapy and proper use of PPE have shown promise in managing severe cases and protecting healthcare workers.

Socio-economic factors, such as livestock and agriculture impact, require attention in disease control strategies. In conclusion, a collaborative approach, investment in surveillance and research, and a focus on public awareness are essential in combatting CCHF's spread in Pakistan, safeguarding public health, and mitigating its impact on society and agriculture.

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