Editorial

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Crimean-Congo hemorrhagic fever outbreak affecting healthcare workers in Pakistan: an urgent rising concern

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Introduction

The Crimean-Congo Hemorrhagic Fever (CCHF) was first discovered in 1944 in the Crimea region of the former Soviet Union and in 1956 in the Belgian Congo (presently Democratic Republic of the Congo)[1]. The first reports of this disease emerged separately in two distinct geographical areas. Subsequently, these findings were connected, leading to the present naming of the virus. This historical discovery, occurring in two different geographical regions, acted as a first indication of the potential extensive occurrence of CCHF and its causative agent, Crimean-Congo Hemorrhagic Fever Virus (CCHFV), belonging to the Nairoviridae family. CCHFV has been recorded in several countries since its identification, expanding its geographic distribution over Europe, Asia, and Africa[2].

Etiology

CCHF is a disease caused by the arbovirus CCHFV. The virus has an enclosed structure, a segmented genome, and a single-stranded RNA with a negative sense. Based on the latest taxonomic classification influenced by advancements in viral genomic and metagenomic comparative analysis, it is classified under the genus Orthonairovirus in the family Nairoviridae, which belongs to the order Bunyavirales[3,4]. The viral genome has three RNA segments, namely short, medium, and large. The segments include the genetic information for the viral nucleoprotein, the precursor of the glycoprotein, and the RNA-dependent RNA polymerase, respectively[5]. Compared to other viruses transmitted by ticks, CCHFV has a higher level of genetic diversity, indicating its extensive dissemination[6].

Epidemiology and outbreak of Congo in Pakistan

Over the last two decades, there have been instances of the development or reappearance of certain diseases in several countries, such as Greece in 2008, Georgia in 2009, Spain in 2016, and Turkey in 2002. The countries in Southern Asia (Afghanistan, Iran, and Pakistan) and Western Asia (Iraq and Turkey) frequently report the highest numbers of cases globally[7,8]. The primary carrier of the CCHFV, which infects many animals, including humans, is primarily the ixodid ticks, namely those belonging to the genus Hyalomma. The ticks Hyalomma marginatum, H. turanicum, and H. rufipes have been identified as the primary carriers of CCHFV[9,10].

The Pakistani province of Baluchistan is currently dealing with a significant outbreak of CCHF, also known as the Congo virus. There have been 20 documented fatalities as of now, including a tragic occurrence involving a doctor who died while being evacuated to Karachi for treatment. Out of 200 suspected instances, 73 have tested positive for the tick-borne virus, with 12 healthcare personnel receiving treatment in Karachi and four doctors in critical condition. Given the severity of CCHF, with mortality occurring in up to 40% of cases, there is an urgent need for vaccine development to curb the spread of the virus. In the absence of a vaccine, public awareness and preventive measures become paramount. The necessity of utilizing certified acaricides and wearing protective gear, as well as the risks connected with the virus, must be emphasized to those working in the livestock industry. Furthermore, preventing the spread of the infection from person to person is essential, calling for actions like avoiding close quarters, ensuring hand hygiene, and wearing protective gear in medical facilities. The lives of medical professionals and the public are at risk, as evidenced by the temporary prohibition on private slaughterhouses in densely populated areas that have been implemented[11].

Specifically in South Asian countries, the current surge of CCHF cases, notably observed in Pakistan, is particularly prominent during Eid-up-Azha[12]. This annual challenge is compounded by Pakistan's unique geographical location and the widespread involvement of its population in animal husbandry activities[13]. Moreover, as a developing nation, Pakistan faces

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formidable obstacles in acquiring the necessary resources and financial capacity to establish a robust healthcare infrastructure, which is crucial during epidemics and health crises[14]. These factors collectively pose significant risks for healthcare workers, increasing their susceptibility to viral infection.

Clinical signs and symptoms

Most infections caused by CCHFV either have no symptoms or generate moderate clinical symptoms. Less severe instances often display unspecific signs such as headaches, muscle discomfort, joint pain, fever, nausea, and vomiting. Occasionally, there may be severe occurrences where abrupt bruising and bleeding appear at the injection sites. The illness has the potential to be lethal within a few days of its beginning, with the case-fatality rate varying between 5 and 80%. Age, pre-existing medical problems, availability of supportive care, virus strain, and method of transmission are all determinants that might impact the severity and prognosis of CCHF. It is crucial to emphasize to those employed in the cattle industry the need to use certified acaricides and wear suitable protection gear, as well as the associated hazards related to the virus.

Moreover, it is crucial to take measures to halt the transmission of the virus between individuals. These measures include avoiding crowded spaces, maintaining proper hand hygiene, and using personal protection gear in medical settings. The temporary ban on private slaughterhouses in densely populated regions poses a significant threat to the lives of medical professionals and the public[15].

Diagnosis

Timely diagnosis remains a cornerstone in effective medical management. The diagnostic process encompasses meticulous evaluation of clinical manifestations, thorough laboratory investigations, and precise utilization of radiological modalities. Clinical scrutiny involves the assessment of prominent symptoms, including headache, pyrexia, abdominal discomfort, myalgia, hypotension, and facial erythema. Disease progression may unveil additional clinical signs such as petechiae, ecchymosis, epistaxis, gingival hemorrhage, and emesis[16]. The principal diagnostic modality for suspected CCHF cases entails employing RT-PCR assays, offering optimal sensitivity for early detection of active viral infection. Further confirmation can be sought through serological profiling via ELISA methodology targeting specific IgM and IgG antibodies against viral antigens[17]. Radiological investigations, particularly thoracic CT scans, have elucidated notable pulmonary manifestations, including parenchymal infiltrates and pleural effusions in CCHF patients[18].

Treatment

Currently, no specific antiviral therapy is tailored for CCHF. The primary therapeutic approach revolves around providing supportive care, necessitating hospitalization for continuous vital sign surveillance, and prompt intervention against organ dysfunction symptoms[19]. Paracetamol, recognized for its antipyretic properties, mitigates fever-related discomfort[19]. The cornerstone of treatment for CCHF patients lies in fluid replacement and transfusion strategies. This encompasses the administration of intravenous fluids, electrolytes, and blood components, including platelets, erythrocyte concentrates, and fresh frozen plasma (FFP) in cases of hemorrhage.

Furthermore, vigilant monitoring of laboratory parameters and clinical status remains imperative[20]. While several investigations suggest the potential efficacy of Ribavirin in CCHF management, conclusive evidence is yet to be established[21]. Additionally, animal trials have shown the potential use of favipiravir (T-705) in suppressing viremia and viral shedding of the pathogen in cynomolgus macaques (Primates)[22].

International efforts

The Third International Conference on CCHF was held in Thessaloniki, Greece, from 19 September to 21 September 2023, and attracted a varied group of worldwide stakeholders. The meeting, which drew 118 attendees from 24 countries and represented subjects such as public health, clinical medicine, ecology, epidemiology, immunology, and virology, encouraged strong debates and partnerships. The talks covered the multidimensional terrain of CCHF, including epidemiology in human populations, the role of CCHFV in ticks, insights into wild and domestic animal hosts, molecular virology advances, pathophysiology elucidation through animal models, immunological responses defining treatment approaches, and novel ways for CCHF prevention in people[23].

Prevention

To prevent and manage CCHF infection, one may avoid or limit exposure to infected ticks by using tick repellents. For effective control of the spread of disease, protective gear and swift removal of ticks are recommended[24]. The prevalence of CCHV is notably high among individuals whose occupations include direct contact with animals, such as animal breeders, veterinary healthcare personnel, and agricultural workers. Therefore, the use of personal protective equipment such as gloves and masks has been found advantageous in preventing infection[25]. Utilizing educational campaigns to raise public awareness may be an effective technique in managing the transmission of diseases[14].

There are a few recommendations for the future that should help us better understand how the CCHFV spreads and devise effective response tactics. To aid with early diagnosis, they include harmonizing case definitions between endemic and nonendemic nations, creating quick diagnostic tests for CCHF RNA quantification appropriate for resource-constrained environments, and carrying out randomized controlled trials to confirm novel therapies such as ribavirin and monoclonal antibodies. Furthermore, considering the overlap of symptoms with other illnesses, the development of clinical diagnostic algorithms is necessary to facilitate the timely identification of CCHF patients. While collaborative efforts will center on generating evidence-based risk communication messages for high-risk groups, sero-epidemiological investigations will be critical for determining illness prevalence in both human and animal populations. Vaccines against ticks and animals, as well as best practices for animal health surveillance, will support preventative efforts even more. Ultimately, pre-emptive interventions in high-risk regions that have been selected will be guided by spatial-temporal forecasting, which will be utilized to predict circulation patterns and outbreaks. The combined goal of these projects is to improve the region's capacity for reaction and readiness against the spread of CCHFV.

Conclusion

Congo Virus Disease necessitates a comprehensive strategy, including laboratory proficiency, clinical attentiveness, and public health strategies for diagnosis, treatment, and prevention. Effective cooperation among healthcare practitioners, researchers, and public health institutions is crucial, and early detection is vital. Essential components include hospitalization, alleviation of symptoms, and provision of supportive care. In addition, it is essential to take preventative steps such as wearing protective eyewear and preventing tick bites. To effectively address the Congo Virus Disease, a comprehensive approach, including research, community engagement, and public health measures, is necessary.

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