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Review Article

Crimean-Congo Hemorrhagic Fever: An Endemic Sporadic Zoonotic Viral Infection in Uganda

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Abstract

Crimean-Congo Hemorrhagic Fever is an Arboviral zoonosis responsible for sporadic outbreaks of hemorrhagic fever in endemic areas. The control of CCHFV calls for multidisciplinary approach involving partners like WHO and OIE. Mmultidisciplinary research will allow better understanding of the epidemiology of CCHF in ticks, domestic livestock and wild animal populations, and will support the identification of human risk factors for infection and the development of better diagnostics, antiviral drugs and vaccines. Also, the identification of an animal model for testing would facilitate any further research, and allow studying host response to infection and evaluating intervention and control strategies. Finally, the role of environmental change, including climate change, needs further assessment. Support CCHF surveillance, diagnostic capacity and outbreak response activities. Reduce infection in people by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the virus.

Keywords: *Crimean-Congo hemorrhagic fever, CCHFV, Zoonosis, Seroprevalence, ELISA, Ixodid ticks, Uganda*

Background and Aim

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne viral zoonotic disease caused by Crimean Congo hemorrhagic fever virus (CCHFV), a member of the genus *Nairovirus* in the family *Bunyaviridae* and order *Bunyavirales*. CCHF is typically asymptomatic in animals but can be highly fatal in humans approaching case fatality rate of approximately 30%. The disease is distributed in many countries of Asia, Africa, the Middle East and south-eastern Europe. As the distribution of CCHFV coincides with the distribution of its main vector, Ixodid (hard) ticks of the genus *Hyalomma*, both a reservoir and a vector for the CCHF virus; the spread of infected ticks into new, unaffected areas facilitates the spread of the virus. Numerous wild and domestic animals, such as cattle, goats, sheep and hares, serve as amplifying hosts for the virus. Transmission to humans occurs through contact with infected ticks or animal blood. CCHF can be transmitted from one infected human to another by contact with infectious blood or body fluids. Documented spread of CCHF has also occurred in hospitals due to improper sterilization of medical equipment, reuse of injection needles, and contamination of medical supplies. Occupational groups with an elevated risk of Crimean Congo hemorrhagic fever include farmers, shepherds, veterinarians, abattoir workers, healthcare personnel and laboratory workers, as well as anyone at elevated risk of exposure to ticks. Seasonality can result from seasonal changes in tick numbers or increased human exposure to slaughtered livestock. The case fatality rate is thought to be approximately 5-30% in most instances, although rates as high as 80% have been reported occasionally in limited outbreaks. Factors such as the availability and quality of healthcare, virus dose, route of exposure, coinfections, and possibly the viral strain, are thought to influence mortality.

A person with CCHF can have the following signs & symptoms: Sudden on-set of high fever, Headache, Back pain, Joint pain, Abdominal pain, Dizziness (feeling that you are losing your balance and about to fall), Neck pain and stiffness. The person who has been in contact with a person who has similar symptoms or animals infested with ticks, or has had a tick bite. In addition, the person can also have any of the following: Nausea, Vomiting, Diarrhoea, Sore throat, Sharp mood swings, Confusion, Bleeding, bruising or a rash After 2 or 4 days, the patient may experience sleeplessness and depression. Following a bite from an infected tick, the infection can establish in the animal with brief illness. The Crimean Congo Hemorrhagic Fever virus can then be passed on to the tick which can in turn pass the virus to human or other animals [1-7].

Uganda is divided into ten agroecological zones: Southern highlands, Southern dry lands, Lake Victoria crescent, Eastern, Mid-Northern, Lake Albert crescent, West Nile, Western highlands, South East, and Karamoja drylands. Mid-Northern: Flat terrain covered by thick Savannah grassland. Lira, Apac, Kitgum, Gulu, Pader districts. Agriculture remains the major source of livelihood in Uganda. According to the Uganda National Household Survey (UNHS) 2016/17, the bigger proportion of the working population is engaged in agriculture, forestry and fishing (65%). Among the females in the working population, 70% are engaged in agriculture compared to 58% of the males. Furthermore, 38% of persons in employment were in paid employment with a higher proportion of males (46%) compared to females (28%). The Agricultural sector accounted for the largest share of employment (36%).The agriculture sector had a total contribution to GDP at current prices of 24.9 percent in the FY 2016/17 compared to 23.7 percent in FY 2015/16. This indicated that the population at risk of CCHFV in Uganda is large.

Materials and Methods

CCHFV is thought to infect animals with few or no clinical signs. No illnesses have been attributed to this virus in naturally infected animals. However, the disease is zoonotic. Serum samples are collected from susceptible animals. The host range includes: human, domestic and wild animals. Sera samples are tested for the presence of CCHFV-specific immunoglobulin G (IgG) antibodies using enzyme-linked immunosorbent assay (ELISA), virus isolation or detecting its nucleic acids and antigens in blood samples or tissues. Urine, saliva and other secretions and excretions may also contain nucleic acids, but the suitability of these samples for diagnosis has not been fully investigated. At autopsy, CCHFV can be found in a variety of tissues, such as liver, spleen, lung, bone marrow, kidney and brain. Clinical cases are often diagnosed with a combination of reverse transcription-polymerase chain reaction (RT-PCR) tests and serology. CCHFV strains are highly variable, and many RT-PCR tests only recognize local variants or a subset of viruses. However, tests that can detect most or all known variants, including the highly divergent AP92 strain, have also been developed. Other published assays to detect nucleic acids include microarray and macroarray-based techniques and loop-mediated isothermal amplification. In fatal cases, viral RNA tends to increase as the disease progresses. Immunohistochemistry can be used on tissues collected at autopsy. Animal inoculation into newborn or immunodeficient mice is more sensitive than cell culture, and has been used occasionally in clinical cases, though it is generally discouraged if there are alternatives. Either specific IgM or rising titers should be seen. Virus neutralization is rarely employed, due to the hazards of handling live CCHFV. Treatment is mainly supportive. Seriously ill patients require intensive care. The antiviral drug ribavirin has been used to treat CCHF infection with apparent benefit. Both oral and intravenous formulations seem to be effective.

There are no vaccines available for use in animals. Although an inactivated, mouse brain-derived vaccine against CCHF has been developed and used on a small scale in eastern Europe, there is currently no safe and effective vaccine widely available for human use. Tests on patient samples present an extreme biohazard risk and should only be conducted under maximum biological containment conditions. However, if samples have been inactivated (e.g. with virucides, gamma rays, formaldehyde, heat, etc.), they can be manipulated in a basic biosafety environment. Patients with fatal disease, as well as in patients in the first few days of illness, do not usually develop a measurable antibody response and so diagnosis in these individuals is achieved by virus or RNA detection in blood or tissue samples.

Results

A study by Nurettin *et al.* (2022) screened domestic animals for IgG prevalence, and compared their results with those for wild animals (14.01% vs. 9.84%, respectively) indicating that wild animals and livestock are equally important for circulating the CCHF virus in endemic areas such as seen in Turkiye. Mirembe *et al.* (2021), identified 14 confirmed cases (64% males) with five deaths (case-fatality rate: 36%) from 11 districts in western and central region Uganda. Of these, eight (73%) case-patients resided in Uganda's 'cattle corridor'. Atim *et al.* (2022), detected CCHFV seropositivity of 221/800 (27·6%) in humans, 612/666 (91·8%) in cattle, 413/549 (75·2%) in goats and 18/32 (56·2%) in dogs. Human seropositivity was associated with livestock farming and collecting/eating engorged ticks. In animals, seropositivity was higher in cattle versus goats, CCHFV was identified in multiple tick pools of *Rhipicephalus appendiculatus*. A cross sectional study was conducted to determine the prevalence of CCHF and to identify the potential risk factors associated with CCHFV seropositivity among the one-humped camel (*Camelus dromedaries*) in Central Sudan. A total of 361 camels selected randomly from six localities were employed in the study. Sera sampled were tested for the presence of CCHFV-specific immunoglobulin G (IgG) antibodies using enzyme-linked immunosorbent assay (ELISA). CCHFV seropositivity was recorded in 77 out of 361 animals accounting for a prevalence rate of 21.3%. The prevalence of CCHF is significantly high among camels in Khartoum State, Sudan. Age, breed, locality and tick control are considered as potential risk factors for contracting CCHF (Suliman et al., 2017). This study aimed at providing knowledge and awareness about the disease to reduce the impact on the livelihood of pastoral communities and ultimately avoid disease spread in human.

Crimean-Congo haemorrhagic fever (CCHF) is the most widespread, tick-borne viral disease affecting humans (Al-Abri et al., 2017).

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