Crimean-Congo haemorrhagic fever: An outbreak in India

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EDITORIAL

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Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic viral disease that is asymptomatic in infected animals, but a serious threat to the health of humans. Human infections begin with non-specific febrile symptoms, but progresses to a serious haemorrhagic syndrome with a high case fatality rate.[1,2] CCHF is caused by the CCHF virus (CCHFV), a member of the genus Nairovirus in the family Bunyaviridae. The virus is stable for up to 10 days in blood kept at 40°C.

Although the causative virus is often transmitted by ticks, animal-to-human and human-to-human transmission also occurs. CCHF affects mostly adults (no case has been reported in children under 15 in South Africa since 1993)[3] and is endemic in many countries in Africa, Europe and Asia. During 2001, cases or outbreaks were recorded in Iran, Pakistan, South Africa with the latest being in India.[4] It has also been found in parts of Europe including southern portions of the former USSR (Crimea, Astrakhan, Rostov, Uzbekistan, Kazakhstan, and Tajikistan), Turkey, Bulgaria, Greece, Albania and Kosovo (a province of the former Yugoslavia).[5-10] Limited serological evidence suggests that CCHFV might also occur in parts of Hungary, France and Portugal. The most recent CCHF outbreak occurred in January 2011 in the state of Ahmedabad (India).

In this outbreak this rare deadly virus killed three people. The three victims included an adult female, a nurse, and the doctor who treated the adult female at a private hospital in Ahmedabad (India).[11] The patients died due to multiple organ failure, specifically failure of the liver and kidney. The National Institute of Virology (NIV), (Pune, India) confirmed that all three patients were infected with the CCHF virus.[11] The NIV is testing some 50 samples from the area, and the Gujarat government, warning of a possible outbreak, has begun a screening exercise covering approximately 16,000 villagers.

No CCHF case has ever been reported in India before.[12] Reasons for the outbreak of CCHF in India include climate and anthropogenic factors such as changes in land use, agricultural practices or hunting activities, and movement of livestock that may influence host-tick-virus dynamics.

The CCHF virus may infect a wide range of domestic and wild animals, with the occurrence of this virus correlated with the distribution of a particular species of tick. A number of tick genera are capable of becoming infected with the CCHF virus, but the most efficient and common vectors for CCHF appear to be members of the Hyalomma genus. Trans-ovarial (transmission of the virus from infected female ticks to offspring via eggs) and venereal transmission have been demonstrated amongst some vector species, indicating one mechanism which may contribute to maintaining the circulation of the virus in nature.[3] Many birds are resistant to infection, but ostriches are susceptible and may show a high prevalence of infection in endemic areas. Animals become infected with CCHF from the bite of infected ticks.

However, the most important source for acquisition of the virus by ticks is believed to be infected small vertebrates on which immature Hyalomma ticks feed. Once infected, the tick remains infected through its developmental stages, and the mature tick may transmit the infection to large vertebrates, such as livestock. Domestic ruminant animals, such as cattle, sheep and goats, are viraemic (virus circulating in the bloodstream) for around one week after becoming infected.[4]

Humans acquire CCHF in two different ways; through a tick bite or contact or by contagion. The sources of exposure include being bitten by a tick (happening, occasionally when individuals squash them between their fingers as a means of self-protection), contacting animal blood or tissues, and drinking unpasteurised milk. Human-to-human transmission can occur, particularly when skin or mucous membranes are exposed to blood during haemorrhages or tissues during surgery. This disease is a particular threat to farmers and other agricultural

workers, veterinarians, laboratory workers and hospital personnel.[3] Infection more commonly occurs in people who have outdoor occupations such as farmers, dairymaids or woodsmen.

The first sign of CCHF is a sudden onset of fever and other non-specific symptoms including chills, severe headache, dizziness, photophobia, neck pain, myalgia and arthralgia and the accompanying fever may be very high. Gastrointestinal symptoms including nausea, vomiting, non-bloody diarrhoea and abdominal pain are also common. It is followed, after several days, by the haemorrhagic phase.[13]

The hemorrhagic phase develops suddenly. It is usually short, lasting on average two to three days. A petechial rash may be the first symptom. The rash is followed by petechiae, ecchymoses and large bruises on the skin and mucous membranes. Hematemesis, melena, epistaxis, haematuria, haemoptysis and bleeding from venepuncture sites are also common. Some patients die from haemorrhages, haemorrhagic pneumonia or cardiovascular disturbances. In patients who survive, recovery begins 10 to 20 days after the onset of illness.[3]

CCHF can be diagnosed by isolating CCHFV from blood, plasma or tissues. It is often diagnosed using RT-PCR on blood samples. This technique is highly sensitive. Viral antigens can be identified with enzyme-linked immunoassay (ELISA) or immunofluorescence, but this test is less sensitive than PCR.[14] CCHF can also be diagnosed by serology. Tests detect CCHFV-specific IgM, or a rise in IgG titres in paired acute and convalescent sera.[12]

The average case fatality rate is 30–50%, but mortality rates from 10% to 80% have been reported in various outbreaks. The mortality rate is usually higher for nosocomial infections than after tick bites; this may be related to the virus dose.[12] Particularly high mortality rates have been reported in some outbreaks from the United Arab Emirates (73%) and China (80%). Due to the high case fatality rates and difficulties in treatment, prevention, and control, CCHF is a disease which should be notified to the public health authorities immediately. CCHF virus is also in the list of agents for which the Revised International Health Regulations of 2005 call for implementation of the decision algorithm for risk assessment and possible notification to the World Health Organization (WHO).[15]

General supportive therapy is the mainstay of patient management in CCHF. Intensive monitoring to guide volume and blood component replacement is required. The WHO recommends Ribavirin for the treatment of CCHF cases.[16,17] Ribavirin is believed to improve the prognosis if administered before day five after the onset of illness. Both oral and intravenous formulations seem to be effective. Passive immunotherapy with hyperimmune serum has been tested in a few cases, but the value of this treatment is controversial.[12]

Prevention and control:[18]

- Personal protective measures like avoidance of areas where tick vectors are abundant and when they are active (spring to autumn); regular examination of clothing and skin for ticks, and their removal; and use of repellents in those persons living in endemic areas.
- Persons who work with livestock or other animals can take protective measures like the use of repellents on the skin (e.g. DEET) and clothing (e.g. permethrin) and wearing gloves or other protective clothing to prevent skin contact with infected tissue or blood.
- When patients with CCHF are admitted to hospital, there is a risk of nosocomial spread of infection. In the past, serious outbreaks have occurred in this way and it is imperative that adequate infection control measures be observed to prevent this disastrous outcome. Patients with suspected or confirmed CCHF should be isolated and cared for using barrier nursing techniques.
- Specimens of blood or tissues taken for diagnostic purposes should be collected and handled using universal precautions. Sharps (needles and other penetrating surgical instruments) and body wastes should be safely disposed of using appropriate decontamination procedures.
- Healthcare workers (HCW) who have had contact with tissue or blood from patients with suspected or confirmed CCHF should be followed up with daily temperature and symptom monitoring for at least 14 days after the putative exposure.
- Contact tracing and follow up of family, friends and other patients, who may be exposed to a CCHF virus through close contact with the infected HCW is essential.
- There is no safe and effective vaccine available for human use. Although an inactivated, mouse brain-derived vaccine against CCHF has been developed and used on a small scale in Eastern Europe. The acaricides (chemicals intended to kill ticks) is only a realistic option for well-managed livestock production facilities.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

CONSENT

The authors declare that:

1. They have obtained informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committee.