

Review on: Crimean Congo Hemorrhagic Fever

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ARTICLE INFO	ABSTRACT
<p>Received: 26.12.2020</p> <p>Accepted: 15.01.2021</p> <p>Final Version: 25.01.2021</p> <p>*Corresponding Author: Email: jshpnd69@gmail.com</p>	<p>Crimean-Congo hemorrhagic fever (CCHF) is a vector-borne viral disease, widely distributed in different regions of the world. CCHF caused by a tick-borne virus (Nairovirus) which belongs to the Bunyaviridae family. The virus is highly pathogenic in nature, can be easily and has a high fatality rate of 10-40%. The reservoir and vector of CCHFV are the ticks of the Hyalomma genus. Therefore, the circulation of this virus depends upon the distribution of the ticks. The virus can be transmitted from the tick to an animal, animal to human and human to human. The major symptoms of CCHF are headache, high fever, abdominal pain, myalgia, hypotension and flushed face. As the disease progresses, severe symptoms start appearing, such as petechiae, ecchymosis, epistaxis, bleeding gums and emesis. CCHF can be diagnosed by Enzyme-linked immunosorbent assay, quantitative polymerase chain reaction, antigen detection, serum neutralization and isolation of the virus by cell culture. There is no specific antiviral therapy available for CCHF. However, ribavirin has been approved by the World Health Organization for the treatment of CCHFV infection. Awareness campaigns regarding the risk factors and control measures can aid in reducing the spread of this disease to a greater extent, particularly in developing countries.</p> <p>Keywords: Crimean Congo Hemorrhagic Fever, Bunyaviridae Family, Enzyme</p>

Introduction

Crimean Congo Haemorrhagic Fever (CCHF) is an infectious disease caused by a tick-borne virus (Nairovirus) which belongs to Bunyaviridae family. In 1944, CCHF was first characterized in the Crimea and named as "Crimean Haemorrhagic Fever". Later in 1969, the same disease was reported in the Congo, and thus named as "Crimean Congo Haemorrhagic Fever". CCHF is mostly found in Eastern Europe, particularly in former Soviet Union, throughout the Mediterranean, in north-western china, Central Asia, Southern Europe, Africa, the Middle East, and the Indian Subcontinent [1:2:3]. CCHF also occurs in several countries of Balkans [4]. In 2013, more than 50 cases were documented in Iran, Russia, Turkey, & Uzbekistan [5]. The risk of death amongst those affected is between 10-40% [4]. CCHF is a serious disease as it causes serious complications such as liver failure and may be fatal if not treated. It can be

described mainly as presence of blood in sputum, gums, rectum, and urine [6:4]. Symptoms of CCHF may include fever, muscle pain, headache, vomiting, diarrhoea, and bleeding into the skin. Onset of symptoms is less than 2 weeks following exposure [4].

Epidemiology

According to virological evidence CCHF was widespread in Asia, Eastern Europe, Middle East (except Israel, Lebanon and Jordan), central Africa, Western Africa, South Africa, and Madagascar. In 2008, more than 50 cases/year were reported from only four countries: Turkey, Iran, Russia, & Uzbekistan. 5-49 cases/year were present in South Africa, Central Asia including Pakistan and Afghanistan, in Middle East only in UAE and the

Balkan countries limited to Romina, Bulgaria, Serbia, Montenegro, & Kosovo-Albania [7].

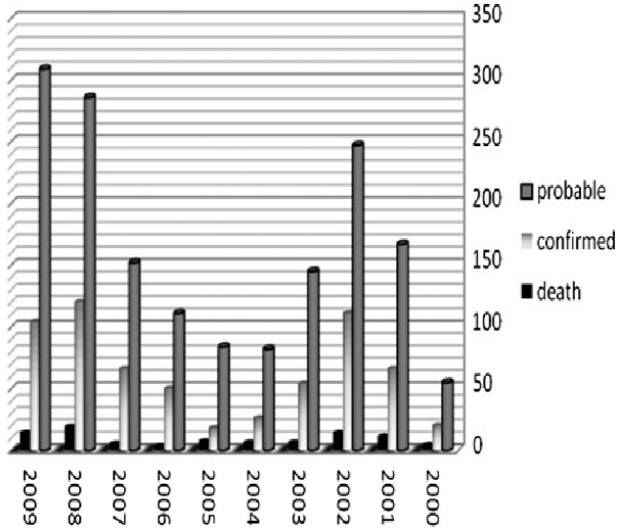


Fig. 1: Epidemiology of CCHF

Transmission

Ixodid (hard) ticks, especially those of the genus, *Hyalomma*, are both a reservoir and a vector for the CCHF 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 [1:2:3].

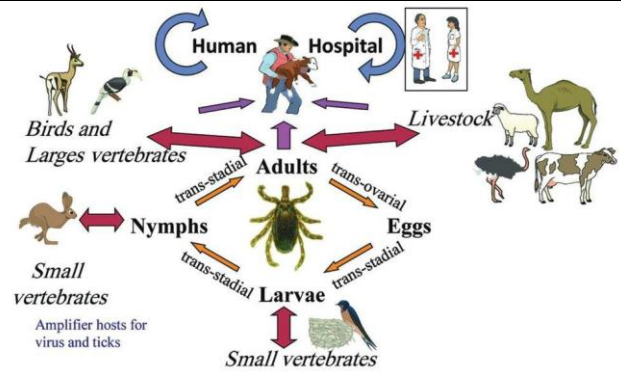


Fig. 2: Transmission of CCHF

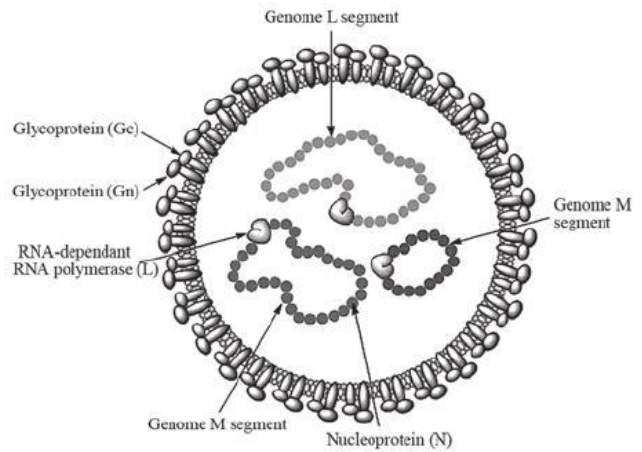


Fig. 3: Structure of CCHF Virus

Literature Review

Incubation Period

Incubation period depends on the mode of acquisition of the virus. The incubation period following infection by a tick bite, is usually 1-3 days, with a maximum of 9 days. The incubation period following contact with infected blood or tissues is usually five to six days, with a maximum of 13 days [8].

Pathogenesis

- Virus enters in the body through hosts
- Replication of virus
- Pro-inflammatory Response
- Endothelial Damage
- Activation of intrinsic coagulation cascade
- DIC & Multi organ failure
- Death

Sign and Symptoms

Prehemorrhagic Phase

- High fever
- Chills
- Myalgia
- Neck pain & stiffness
- Headache, Nausea, Vomiting
- Abdominal pain
- Hypotension
- Relative bradycardia
- Conjunctivitis
- Pharyngitis
- After 2-4 days, the agitation may be replaced by sleepiness, depression, and the abdominal pain may be localized to the upper right quadrant, with detectable hepatomegaly.

Hemorrhagic Phase

- Petechial Rash
- Petechiae
- Ecchymoses
- Epitaxis
- Hematemesis
- Haemoptysis
- Haematuria

Convalescent Phase

- Generalized weakness
- Tachycardia
- Lymphadenopathy

Risk Factors

Animal herders, livestock workers and slaughterhouse workers are at high risk of CCHF.

Healthcare workers in endemic areas are at high risk of infection. Individuals and international travellers who come in contact to livestock in endemic regions may also develop infection [1:2:3]. Rubbing the infected tick on skin or slaughtering the infected animal/hosts is also the one of the risk factors

Diagnosis

CCHF can be diagnosed by different lab. Tests, such as:

Enzyme-Linked Immunosorbent Assay

IgG & IgM antibodies can be detected in serum by enzyme-linked immunoassay (EIA) or ELISA from the sixth day of the illness. Either the presence of IgM or a 4-fold rise in the titre of IgG antibody in serum samples between the acute and convalescence phases can be helpful in diagnosis of the disease. IgM remains detectable for up to four months, and IgG levels decline but remain detectable up to five years. Patients with fatal disease do not usually develop a measurable antibody response and in these individuals, as well as in patients in the first few days of illness, diagnosis is achieved by virus detection in blood or tissue samples [19].

Antigen Detection

Viral antigens can be sometimes seen in tissue samples by immunofluorescence or EIA [19].

Reverse Transcriptase Polymerase Chain Reaction [RT-PCR]

• Virus Isolation by cell culture:

The virus may be isolated from blood or tissue specimens in the first five days of illness, and grown in cell culture [19].

Results and Discussion

Treatment

The treatment of CCHF depends on the severity of the disease. Currently, there are no such antiviral that can be used for the treatment of CCHF that is approved by the US Food and Drug Administration [21]. However, Ribavirin a guanosine analogue is only the drug which can be used to treat CCHF [23:24]. Ribavirin inhibits replication of RNA & DNA of the virus. The drug is first phosphorylated to 5 phosphate derivatives, the major product being the compound ribavirin triphosphate, which exerts its antiviral action by inhibiting guanosine triphosphate formation, preventing viral messenger RNA (mRNA) capping, & blocking RNA dependent RNA polymerase [25:26]. Despite of various insufficient efficacy of ribavirin for CCHF patients, WHO has approved antiviral ribavirin for the treatment of CCHF based on in vitro data [26:29]. Ribavirin can be taken orally or intravenously. For effective results, it can be given along with interferons [30]. In numerous in vitro studies, interferon type-I is shown to have antiviral activity, however, no clinical data is available on interferon use [27:31]. A recent study utilized modified vaccinia virus Ankara (attenuated poxvirus vector) to develop a recombinant vaccine that expresses glycoproteins of CCHFV in two mouse strains. A cellular and humoral immune response was confirmed against this vaccine, which protected the recipient model animals from developing the lethal disease [32]. Studies were also conducted to determine the role of immunotherapy in the treatment of CCHF. A new immunoglobulin,

Venin, which is specific to CCHFV, has been prepared from the plasma pool of boosted donors through ethanol-polyethylene glycol fractionation and an ion-exchange purification step [33]. However, in the case of CCHFV, the beneficial effects of immunotherapy are extremely limited [34:35].

Prevention

For the individual, use of effective personal protective measures against tick bites and limiting animal exposure are the best ways to avoid the infection. Use of permethrin- impregnated clothing and gear, tucking trousers into boots or socks, wearing light-coloured clothing to facilitate tick identification, insect repellents on exposed skin, and daily skin inspection for ticks are mainstays of prevention. A suspected patient should be placed in a private room, and negative-pressure respiratory isolation should be considered, particularly if coughing, vomiting, or other activities generating large-droplet aerosols occur. Those entering the patient's room should wear gloves and gowns, and those approaching within one meter should wear face shields or surgical masks and eye protection to prevent contact with blood or other body fluids [36]. Experience with vaccines against CCHFV is limited and the vaccine would not be suitable for use in many countries because of its method of preparation [37].



Fig. 4: Prevention of Crimean Congo Hemorrhagic Fever

Conclusion

CCHF is a harmful disease as there is no specific treatment. The only way to avoid this infection is prevention. In a developing country, the disease poses more serious effects due to inadequate resources. Reinforcing the control measures to prevent the transmission of the disease to new areas is necessary. The animal and health sectors, by taking solid steps, can contribute to reduce the spread of this disease across the country. Awareness campaigns regarding risk factors and control measures can aid in apprising the public of the ill effects of this virus.

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