ORIGINAL ARTICLE

CRIMEAN CONGO HEMORRHAGIC FEVER IN HAZARA DIVISION

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Background: Crimean-Congo Hemorrhagic fever (CCHF) is endemic in certain areas of Pakistan with 14 outbreaks in addition to many sporadic cases so far. It is highly fatal zoonotic disease caused by bite of infected tick. The objective of our study is to describe clinical features, treatment and outcome of CCHF positive cases during its outbreak in Hazara division, with the intention to bring focus to this fatal emerging disease. **Methods:** This study was conducted in Medical A Unit of Ayub Teaching Hospital, Abbottabad for a period of three months. All patients presenting with fever and platelet count less than 50,000/mm^3 were included in the study. Apart from baseline investigations their blood samples were sent for the detection of CCHF virus. All patients were given supportive treatment including fresh frozen plasma and were started on oral Ribavirin. All patients were isolated and barrier personal precautions were observed by health care givers **Results**: Eighty-eight patients with fever and thrombocytopenia were included. Among these, 8 were found to be positive for CCHF. Supportive treatment with oral Ribavirin was given to all patients. One patient with CCHF died. One left against advice and six patients recovered completely. **Conclusions:** All patients presenting with acute fever and thrombocytopenia should be suspected and evaluated for CCHF. Oral Ribavirin is safe and effective in the treatment of CCHF.

Keywords: Crimean Congo Hemorrhagic fever, Pakistan, Ribavirin

INTRODUCTION

Viral hemorrhagic fevers are acute infections with high mortality rates. Important viruses include Ebola, Lassa, Marburg, Crimean Congo Hemorrhagic Fever (CCHF) virus, Rift Valley fever virus, Dengue and Yellow fever virus.[1] Crimean Congo hemorrhagic fever was first recognised in western Crimea, USSR, in 1944. Around that time more than 200 cases of serious acute febrile illness with severe bleeding occurred and many of them were soviet troops who were helping locals with the summer harvest. In 1970 Casals showed that Crimean hemorrhagic fever virus strains were antigenically and biologically closely related to Congo fever virus, first isolated in Zaire in 1956.[2]

Crimean Congo hemorrhagic fever has since been described in parts of Africa, Asia, Eastern Europe and Middle East. The virus belongs to the genus Nairo virus in the Bunyaviridae family. Humans become infected through the bites of ticks, by contact with a patient with CCHF during acute phase of infection, or by contact with blood or tissues from viraemic live stock.[3]

Crimean Congo hemorrhagic fever is endemic in Pakistan with sporadic out breaks. In Pakistan it was initially reported in 1976, when a laparotomy was performed on a patient with abdominal pain, haemetemesis and malena in a general hospital in Rawalpindi. Since then 14 outbreaks in addition to sporadic cases have occurred in different parts of the country.[4,5]

In September 2010 a breakout of Congo Crimean hemorrhagic fever occurred in Hazara division, Pakistan. The outbreak came into notice after a young doctor working in Bisham region of the Hazara division contracted the virus from a patient and ultimately died of the disease. His blood samples revealed to be CCHF virus positive. In this study we present clinical characteristics and outcome features of patients presenting in Ayub Teaching Hospital Abbottabad with the objective to focus attention on this fatal disease.

MATERIAL AND METHODS

This study was conducted in Medical A unit of Ayub Teaching Hospital Abbottabad. All patients admitted during September 2010 to November 2010 with fever and thrombocytopenia (platelet counts less than $50{,}000\times10^9$/L) were included in the study. All patients were treated as suspected cases of CCHF. Protective personal precautions including protective gloves, gowns, mask etc. Age, gender and address were recorded. Thorough history was taken and clinical examination performed. Blood samples of all the patients with platelet counts less than $50{,}000\times10^9$/L were sent to NIH (National Institute of Health) Islamabad, for the diagnosis of CCHF virus infection. Other relevant laboratory investigations like full blood count, liver function tests, blood urea, serum creatinin, fibrinogen degradation products (FDP's), prothrombin time (PT), activated partial prothrombin time(APTT) were also performed in the patients.

Supportive treatment was started along with a broad spectrum antibiotic. The patients were given whole blood preparations, fresh frozen plasma and platelet concentrates according to their haemostasis. As results from NIH were not available for one week; therefore, 1 Ribavirin therapy was initiated before laboratory evidence of CCHF infection. Oral Ribavirin

was administered (4 gm four times daily for 4 days followed by 2.4 gm four times daily for 6 days). Intravenous Ribavirin was not available. All suspected cases were kept in separate section of the ward with instructions to observe barrier care. Data was analysed using SPSS-10, descriptive statistics were applied to analyse data.

RESULTS

A total of 88 patients were admitted with fever and thrombocytopenia (platelet count less than $50,000\times10^9$/L) during the study period, from various regions of Hazara division. Of these 70 (79.55%) were male and 18 (20.45%) were female. Ages of female patients ranged from 16–65 years with majority 38.88% (7 patients) in the third decade of life. All of the female patients were house wives. Ages of male patients ranged from 16–70 years with most of them being in third decade (18 patients 25.71%) followed by 17 patients (24.28%) in twenties. None of the male patients were involved in agriculture or veterinary business. Common symptoms of patients are shown in Table-1. Geographical distribution of the patients is shown in Tabble-2.

Fifty-four (61.36%) patients had platelet count between 21 to $50,000\times10^9$/L, while 34 (38.63%) had platelet counts below $20,000\times10^9$/L. Of total 88 patients 8 were found to be positive for CCHF, giving frequency of 9.09%. Among the 8 positive cases one was female and seven were male. All CCHF virus positive cases had platelet counts less than $30,000\times10^9$/L. Regarding outcome of these 8 patients, 1 patient died in the hospital, giving mortality of 12.5%. One patient left against medical advice while the rest 6 were discharged after successful treatment. None of the doctors or paramedical staff became infected.

Table-1: Common symptoms of the patients

Symptoms	No of patients	Percentage
Fever	88	100
Epistaxis	9	10.22
Bodyaches	56	63.63
Purpuric spots	4	4.45
Bleeding gums	2	2.27
Pain abdomen	10	11.36
Vomiting	12	13.63
Malena	2	2.27
Hematuria	2	2.27
Irritability	2	2.27
Upper GI bleed	2	2.27

Table-2: Geographical distribution

Area	Number	Percentage
Abbottabad	5	5.68
Mansehra	38	43.18
Haripur	30	34.09
Havelian	8	9.09
Batagram	3	3.04
Oghi	4	4.54

DISCUSSION

Crimean-Congo hemorrhagic fever (CCHF) is endemic in certain rural areas of Pakistan. Since CCHF virus discovery in the country in 1976 cases have been reported from Rawalpindi[4], Balochistan[6], and Karachi[7]. In Abbottabad first case of CCHF was seen in December 2005.[8]

An outbreak of CCHF occurred in Hazara division. The highly contagious disease came into limelight after the death of a doctor working in the northern area of Bisham region. The first case appeared in September 2010. Majority of the cases occurred in the month of October. In the areas with endemic CCHF, the disease may occur most often in the spring or summer. A similar outbreak occurring in Baluchistan in 2001 showed maximum number of cases occurring in June and tapered off in October.[9] Majority of the cases were reported from the Mansehra and Haripur districts of the Hazara division. The seasonal trend of the disease differed in our study. As the Hyalomma ticks are better adapted to surviving in warm dry conditions, it is reasonable to suggest that recent climatic and socioeconomic changes including large scale migration to the towns especially after the 2005 earthquake in the region may have promoted the outbreak. This needs to be further investigated by the epidemiologists.

The CCHF is notorious for causing nosocomial outbreaks, typically after admission of the index case. Most of the outbreaks in Pakistan were nosocomial resulting in deaths of health care workers.[4,10] Fortunately in our study after a single secondary case of doctor, no health care worker became infected with the virus. Although basic knowledge of CCHF among health care workers is poor[10], with knowledge assessing survey showing only 66% of the health care workers having some knowledge about CCHF.[11] Ayub Teaching Hospital took immediate notice of the disease and all suspected cases were placed in isolation with barrier nursing. Regarding airborne transmission of the disease, data is insufficient with most evidence ruling out airborne transmission except two nosocomial cases being reported in South Africa without any evidence of direct exposure to infected material.[12] Our study also supports against airborne transmission, as none of the contacts developed the disease.

In humans CCHF typically presents with high grade fever of sudden onset, malaise severe headache and gastrointestinal symptoms. Prominent haemorrhages may occur in the late stages of the disease with published fatality rates ranging 10–50%.[3] The mortality rate in our study was 12.5%. Main signs and symptoms were fever, abdominal pain, vomiting, myalgias and bleeding manifestations. The CCHF is diagnosed by detection of viral RNA in blood and secretions of the patient, which requires at least one

week. Clinical assessment is the main stay of diagnosis. Acute fever with bleeding manifestation in endemic areas warrants further workup for CCHF. In our study 9.09% of the suspected cases proved to be positive for CCHF on serology and molecular studies. Another study showed 30% CCHF cases positive on serology.[9] Most of the studies conducted in Pakistan suggest that history, clinical findings and supportive baseline investigations may be sufficient for early detection and treatment of CCHF cases.[5,13]

In our study response to treatment which included oral Ribavirin, fresh frozen plasma and platelets was good. All CCHF cases except one had satisfactory recovery. Oral Ribavirin has proven to be effective in the treatment of CCHF in our study which is in favour with other studies conducted.[9,14] However Ribavirin use in CCHF cases has not been tested in randomised control trials owing to the severity of the disease.

Limitation of our study is that we have reported only those cases presented in Medical A unit of the hospital, although during the outbreak other Medical units also received CCHF positive cases but due to lack of sufficient data we were not able to include those cases in our study.

CONCLUSION

Pakistan being the endemic area for CCHF, patients presenting with acute fever, thrombocytopenia and bleeding manifestations should be suspected and evaluated for CCHF. Ribavirin along with haematological support is the main stay of treatment with good prognosis.

RECOMMENDATIONS:

CCHF is highly contagious with high mortality rate so definite guidelines for the prevention of the disease should be designed including measures to increase awareness among public and specially among health care workers regarding common presentations and mode of spread of the disease. Hospitals should ensure proper isolation of all suspected and confirmed cases with strict contact precautions. All health care workers should use protective equipment for entering the isolation area. Blood samples of suspected cases should be sent for confirmation of CCHF. Ribavirin can be given orally to all suspected or confirmed cases. Contact tracing should be ensured and health care authorities should be informed. Climate and environmental factors that may influence CCHF epidemiology and spread should be further studied. There is need to develop veterinary surveillance in high risk areas, mapping of endemic areas and risk assessment for CCHF in order to strengthen preparedness and response of CCHF.

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