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CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF);

PATTERN OF CLINICAL PRESENTATION AND PREDICTORS OF OUTCOME IN PATIENTS

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ABSTRACT... Background: Crimean-Congo hemorrhagic fever virus (CCHFV) from the Bunyaviridae family causes a highly contagious disease in human called as, Crimean-Congo hemorrhagic fever (CCHF). Infection in humans leads to a serious pyrexial illness that often results in death of the patient. **Objectives:** To evaluate the outcome of patients admitted to Khyber Teaching Hospital (KTH), Peshawar-Pakistan with CCHF. **Study Design:** Cross-sectional, retrospective, epidemiological study. **Setting:** Khyber Teaching Hospital (KTH), Peshawar-Pakistan. **Period:** 2016. **Methods:** On the basis of final outcome; death or recovery, a total of 11 patients diagnosed with CCHF in the year 2016 were divided into two groups. The demographic details and symptomatlogy of both the groups were evaluated. Continuous variables were analyzed using independent sample t-test on SPSS version 16. **Results:** Fever was common in patients who recovered. However, shock and coagulapathy were more commonly seen in patients expired. The mortality rate was 36.36%. Moreover, age and platelet count on admission were indicators of worse outcome, $P < 0.05$. However, total hospital stay did not predict the outcome, $P > 0.05$. **Conclusion:** The case fatality rate in CCHF is high. Moreover, mortality rate has an inverse relationship with platelet count on admission and a positive one with the patient's age.

Key words: Congo Fever, Platelets, Virus, Victor.

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INTRODUCTION

The first ever deadliest outbreak of Crimean-Congo hemorrhagic fever virus (CCHFV), was reported in the 1940s in the Crimean peninsula.[1] Crimean-Congo hemorrhagic fever virus (CCHFV), having a case fatality rate of around 50-60 % in humans, is caused by virus belonging to the family Bunyavirida.[2] Hyalomma ticks are the natural vector.[3] It is transmitted to humans by tick bites directly or through contact with the blood or body fluids of diseased animals or human as in the hospital. CCHF is endemic in different regions of the world including Africa, Southeast Europe, Middle East and Asia.[4]

On the basis of genetic variability, the Congo virus has been divided into seven serotypes including; Africa-1, Africa-2, Africa-3, Europe-1, Europe-2, Asia-1 and Asia-2.[5] Because of very high fatality rates and alarming pathogenic nature of CCHFV, there is a possible risk of this virus being used as an agent of bioterrorism or as biological warfare. Therefore, the culturing of this virus is only permitted in bio-safety level four (BSL-4) and in maximum secured laboratories.[4-50]

It must be noted that, CCHFV has been recognized as a global health threat. As the virus is widely distributed in the world, Pakistan has experienced the epidemics of this disease every now and then, covering almost all four provinces namely; Punjab, Baluchistan, Khyber Pakhtunkhwa (KPK), and Sindh.[6] Considering the widespread geographic distribution of CCHFV in Pakistan, there is an immense need for preventive measures on emergency basis. Such measures are crucial eradicating the virus from the country, as subsequent to poliovirus, CCHFV may become a serious threat Pakistanis.[6-7] It must be noted that, in September 2010, an epidemic

was reported in the KPK province of Pakistan. Although, the record keeping was not standard, but some reports indicated cases in excess of hundred, with a case-fatality rate above 10%.[8]

Considering the importance of CCHF in Pakistan, we conducted this epidemiological study on CCHF in Peshawar Pakistan in the year 2016.

MATERIAL AND METHODS

This cross-sectional, retrospective, epidemiological study was conducted on 11 patients admitted to Khyber Teaching Hospital Peshawar Pakistan. The study was approved by the hospital's ethics' review committee and informed written consent was obtained from every participant or their attendants before their inclusion in the study.

The inclusion criteria included; both genders, any age and positive polymerase chain reaction (PCR) for Congo virus. Any one not fulfilling the above criteria was excluded. Similarly, those with coexisting or separate diagnosis of infectious diseases like dengue fever, yellow fever, malaria, infectious mononucleosis, HIV and so forth were excluded. Those with liver cirrhosis, hypersplenism, hematological or solid organ malignancy were excluded. Conditions leading to a decline in platelets like immune thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), and medications like methotrexate and others were also excluded.

All those fulfilling the strict inclusion and exclusion criteria were recruited in the study. By adapting to universal precautions, every participant was worked up with detailed clinical assessment and laboratory. A structured questionnaire specifically designed for this purpose was used. The questionnaire included questions related to demographic details, platelet count, liver enzymes, coagulation profile and so forth. The outcome was measured in terms of death or recovery of the patient.

All the data was entered into and analyzed by SPSS Version 16. Frequencies and percentages were calculated for qualitative variables like gender, location and occupation. Means and standard deviations were determined for continuous variables like age, admission platelet count and so forth. The disease outcome (death or recovery) was stratified amongst the dependent variables by using Chi-squared test.

RESULTS

CCHF infected more males [(N=10), (90.9%)], than females [(N=10), (9.1%)]. The mean age of all the patients was 36.82 ± 11.74. The minimum age was 25 against a maximum of 60 years. By profession, butchers, farmers and others, constituted 45.5%, 18.2% and 36.4% of the sample population respectively. 45.5% of the patients each belonged to Peshawar or other parts of Khyber-Pakhthunkhwa, while 9.1% of the cases were from Afghanistan. Of all the cases of CCHF, 63.6% recovered and were discharged. Moreover, the rest of 36.4% died. The mean hospital stay in days was 7.91± 7.44. The minimum hospital stay was 1 day against a maximum of 27 days. Moreover, the mean platelet count on admission was 64300/mm^3 ± 21256. An overview of the mode of transmission (Figure-1) and seasonal variations (Figure-2) in the incidence of CCHF are given below. Moreover, the main clinical manifestations of the patients are summarized as follows (Table-I).

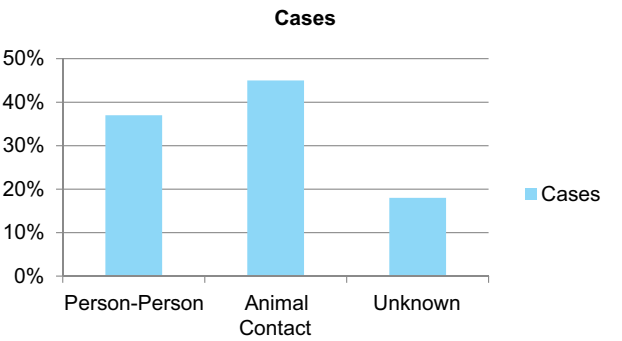
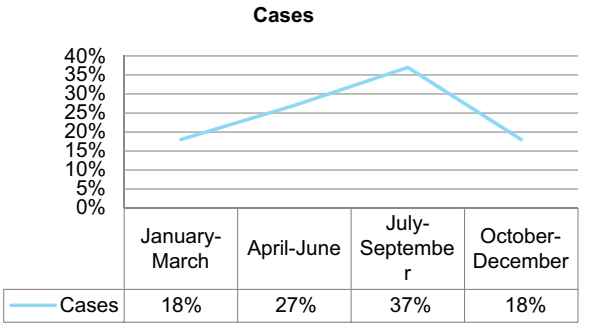


Figure-1. An overview of the mode of transmission.

An independent sample t-test was run to assess the relationship of outcome (death or recovery) with age, admission platelet count and total hospital stay. The results showed that, age of the patients who died was higher (M=45.75, SD=14.29), than those who survived, (M=31.71, SD=6.62), at a statistically significant level, t (9)

= 2.27, P= 0.04. Nevertheless, the total hospital stay was higher in patient who recovered, (M=11.43, SD= 7.23), than those who died, (M= 1.75, SD= 0.5). Again the difference in hospital stay between the two groups was statistically significant, t (9) =2.61, P=0.02. Although, the platelet count on admission was higher in the recovery group, (M= 70700, SD=21876), than the expired group, (M=53000, SD=16812), but the difference between the two study groups was not significant statistically, t (9) = 1.39, P>0.05.



Fgirue-2. An overview of confirmed cases of CCHF at different times of the year.

Clinical Feature	Recovered Patients (n=7)	Expired Patients (n=4)
Fever	85.7%	50%
Myalgias	71.4%	75%
Headache and eye pain	71.4%%	75%
Conjunctival Ingestion	57.14%	75%
Hepatomegally	42.85%	50%
Coagulapathy & Shock	42.85%	100%
Purpura	28.5%	75%

Table-I. An overview of the chief clinical characteristics of the patients

DISCUSSION

CCHF is zoonotic disease. It is endemic in Africa, the Balkans, the Middle East and Asia. The responsible virus is harbored by several domestic and wild animals. While clinically significant disease is a rarity in infected animals, it is devastating in infected humans, with a mortality rate of 10-40%. It is noteworthy that, the mortality rate is our study was 36 %.[8-9]

In Pakistan, the virus was first isolated for the first time in 1960 from hayaloma species of the ticks.[10] Since 1960, repeated sporadic cases and even outbreaks have been reported in people who deal with livestock. The genotype, Asia-1 is the most common genotype of CCHFV in Pakistan. However, Asia-2 genotype has been isolated from patients in Baluchistan.[11] Moreover, beyond any shadow of doubt confirmed first ever case of CCHF in Pakistan was reported in 1976, at a general hospital of Rawalpindi.[12-13] Between 1976 and 2000, only 23 cases of CCHF were reported in Pakistan with a case fatality rate of 39%.[13-14] It is interesting to note that, only in the year 2016, 11 cases were confirmed at Khyber Teaching Hospital Peshawar-Pakistan alone with a case fatality rate comparable to the previous statistics. This might explain either an increase in the burden of CCHF in our country or unreported previous cases or both. Moreover, the better and widespread availability of diagnostic tests for CCHF may be another plausible explanation. The increase in the incidence of CCHF in Pakistan in recent years has also been reported in other studies.[1,15,16]

The CCHF virus is transmitted to human either by tick bites or through intimacy with blood or tissues of the infected animal during or immediately after slaughter. That's said, the vast majority CCHF cases have been reported in people involved in the livestock industry, such as farmers, slaughterhouse workers and veterinarians.[17] Similarly, human-to-human spread of the disease can results from close contact with the blood, tissues, secretions and so on of the infected persons.[18] Moreover, healthcare staff can acquire the infections while handling or treating such patients.[19] It must be noted that, majority of patients in our study sample (81%), had evidence of known contact with livestock or infected person.

Although, the incubation period depends upon the mode of transmission. For tick bite, it generally ranges from 1-3 days with a maximum of 9 days. The incubation period following contact with infected blood or tissues is usually 5-6 days, with a reported maximum of 13 days.[20] For our study, the incubation period is unknown as the patients

or their attendants could not recall the time of contact precisely.

Clinically, there is sudden onset of fever, myalgia, dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia. Patients may report nausea, vomiting, diarrhoea, abdominal pain and so forth. In less than a week, the patient may go into drowsiness, agitation and lassitude, and the abdominal pain may start localizing to the upper abdomen, with clinically apparent hepatomegaly. This may soon be followed by signs of shock, bleeding tendency and multi organ failure.[21-22] When this approaches, the chances of death are extremely high with mortality rate reaching 30% in the second week of illness. Moreover, those who are to ultimately recover, the signs of improvement ensue on the roughly the ninth day of illness.[19-22] These observations are comparable to our study.

The diagnosis of CCHF can be confirmed in a number of ways. The available laboratory tests include serology, antigen detection, PCR for CCHFV, and virus isolation by culture.[23] We confirmed all the cases by doing PCR for CCHFV. Treatment is through general supportive measures. Moreover, there is still some controversy regarding the effectiveness of Ribavarin in the treatment of CCHF. There is no effective vaccine available for protection against CCHF.[24] Nevertheless, preventive measures like wearing protecting clothing, use of insecticides to kill the vector and adapting universal personal protective precautions and so forth, are the only source of hope against this deadly disease.[25-26]

CONCLUSION

The incidence of CCHF is higher in the latter half of the year. Moreover, the mortality rate is as high as 36%. Mortality is influenced by patient's age and platelet count on admission. However, total hospital stay is not a predictor of worse outcome.

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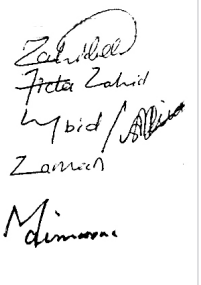
1	Zahidullah Khan	Concept & design.	
2	Zahid Fida	Drafting.	
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