Original Article

Characteristics of Patients with Crimean–Congo Haemorrhagic Fever in an Outbreak in Saurashtra region of Gujarat, India in 2013

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ABSTRACT

Background:CCHF (Crimean Congo Hemorrhagic Fever) is a severe fatal viral hemorrhagic fever similar to dengue fever but having potential to cause Nosocomial spread. CCHF virus belongs to RNA virus of Bunyaviridae family and its get transmitted by Hyalomma tick. Viral Illness presents as fever, severe body ache and bleeding manifestations along with thrombocytopenia, altered coagulation profiles and Liver Function Test. Ribavirin, antiviraldrug, if given in early stage may increases survival significantly.

Aims:

1) To Study Clinical, Pathological & Biochemical parameters in patients of CCHF
2) To Study the efficacy of Oral Ribavirin in CCHF.

Materials and Methods: This retrospective study included 10(ten) patients of RT-PCR confirmed CCHF admitted in Tertiary care teaching hospital of Gujarat, India. Their Clinical Parameters and laboratory finding studied on day to day basis. Oral Ribavirin given to 8 patients as 2 patients died before diagnosis of CCHF established.

Results: Almost all patients have had fever of short duration with most having bleeding manifestation with marked thrombocytopenia, altered PT &aPTT, decreased plasma fibrinogen and elevated FDP with mild to modest elevation in liver enzymes .Out of 8 patients who received ribavirin, only one died.

Conclusion: Oral ribavirin is to be started empirically in any patients involved in animal husbandry activity and develops acute hemorrhagic febrile illness in which tests for malaria and dengue are negative.

Keywords: Viral Hemorrhagic fever, Crimean Congo Hemorrhagic fever, Ribavirin

INTRODUCTION

Crimean Congo Haemorrhagic Fever (CCHF) is a zoonotic & potentially fatal acute viral infection occurring due to *Nairovirus* – RNA virus belonging to Bunyaviridae family. Wider distribution of disease correlates with the global distribution of *Hyalomma*tick, the vector responsible for viral transmission [1, 2]. CCHF is endemic in countries of Africa, Asia, Southeast Europe and Middle East. India's neighbourhood, Pakistan reports 50-60 cases annually. India was always under the potential threat of CCHF viral infection until an outbreak hit parts of Gujarat, taking four lives including treating medical personnel during 2010 – 2011, in Ahmadabad [3].Person-to-person transmission and instances of Nosocomial transmission were confirmed during 2010 (two cases), 2011 (eight cases), and 2012 (three cases) [4,5].

The disease is generally asymptomatic in infected animals but highly fatal in humans. Humans are the only known host of CCHF virus in which disease get manifested. The disease in humans begins as non-specific febrile symptoms, which may progress to Haemorrhagic syndrome. Although tick is a major vector in transmission of the disease, further secondary cases are frequently seen due to human to human transmission via percutaneous or per mucosal exposure to blood or body fluids containing the virus [6]. This uncommon transmission takes place most often among healthcare workers in hospital settings, thus posing a significant Nosocomial hazard [7]. Adhering to universal precautions while caring for patients, timely infection-control measures and administration of prophylactic therapy to healthcare workers after exposure can serve asimportant measures in limiting the spread of infection [8, 9]. Aim of the study is to evaluate clinical, pathological &biochemical parameters in patients of CCHF as

well as to study the efficacy of ribavirin (antiviral drug) therapy in such patients.

MATERIAL AND METHODS

In our retrospective study, we have included 10(ten) patients ofRT-PCR confirmed CCHF, having age>12 years and of both sex. They all were admitted and isolated in medicine department of P.D.U Medical College & Civil hospital – Rajkot, Gujarat, during Month of July – August 2013. 7(seven) patients were from single geographical area i.e. Karyana village, Amreli district. Other 3(three) were from different parts of Saurashtra region.Patients are classified according to categories that are suggested in literature [10]. All were coming into either Category B or Category C in which ribavirin therapy is indicated.

Intravenous form of ribavirin was not available at that time in Gujarat so, oral form was started according to World Health Organization (WHO) guidelines [11]. Oral ribavirin is to be started as dose of 30 mg/kg as stat dose (maximum up to 2 gm.) followed by 15 mg/kg in 4 (four) divided doses for 4 (four) days and then 7.5 mg/kg in 4 (four) divided doses for 6 (six) days(total of 10 days). Along with this, third generation cephalosporin and other supportive treatment including preparations of erythrocytes, fresh frozen plasma, and cryoprecipitate, according to laboratory parameters (shown in table 2) which were measured on twice daily basis after admission to the hospital.

RESULTS

Clinical characteristics of the patients are presented in table-1 and laboratory parameters are presented in table-2. Almost all patients were having history of moderate to high grade of fever for duration of 2 (two) to 7 (seven) days and they all were involved in animal husbandry activities. Most (60%) of them were having bleeding manifestations (in form of Petechiae, Ecchymosis, Haemoptysis, Hematemesis, Malena, Bleeding per rectum).Out of 10(ten) patients, 2(two) patients had respiratory complications (20%) and 3(three) patients had significant bradyarrythmia (30%) that requires continuous monitoring [table 1]. Most patients (70%) were having mild alterations in Liver Function Tests (LFTs) and having Normal Renal function Tests (RFTs) except 3 (three) expired patient (30%) were having modest to severe alterations in LFTs & mild alterations in RFTs. Modest to marked thrombocytopenia and leucopoenia observed in all the patients (100%) along with disturbed coagulation profile (Prolonged PT &aPTT, Higher D-Dimer & FDP) [table 2].Out of 10(ten) patients 2(two) patients having reactive Dengue IgM antibodies by ELISA and 1(one) had reactivity to Dengue NS1 antigen by ELISA .No one had malarial parasites on their peripheral smear OR having positive antigen –antibody malarial card test. Out of 10(ten) patients 8(eight) patients had received oral ribavirin therapy as per dosage guidelines as mentioned above and 1(one) patient died despite that treatment. Case fatality rate despite ribavirin therapy is thus around 12.5 %. No medical or paramedical staff had got infection of CCHF virus during treatment of these patients.

Table1: Clinical characteristics for 10 patients with CCHF

Most common symptoms	Number of patients (% in bracket), n=10
Fever	9 (90)
Headache	5 (50)
Myalgia	4 (40)
Diarrhoea	3 (30)
Nausea +/- Vomiting	1 (10)
Abdominal pain	3 (30)
Physical Findings	
Fever, temperature > 100^0 F	2 (20)
Maculopapular rash	0 (0)
Bleeding signs	
Petechiae	4 (40)
Haematemesis	2 (20)
Malena	4 (40)
Haemoptysis	2 (20)
Haematoma	1 (10)
Haematuria	0 (0)
p/v bleeding	0 (0)
Epistaxis	0 (0)
Hypotension	3 (30)
Brady-arrhythmia	3 (30)
Respiratory findings	2 (20)
Convulsions	1 (10)
Stupor	3 (30)

Table2: Pathologic laboratory findings for 10 Patients with CCHF

Laboratory findings	Mean Values (range in bracket)
Lowest platelet count	16,600/cumm (1000-30000)
Lowest WBC count	2630 /cumm (1100-4900)
Longest PT in sec.	19.4 sec (12.7 – 30.4)
Longest aPTT in sec.	56.10 sec (28.5 – 84.2)
Highest SGPT (ALT)	705 U/L (61 – 3912)
Highest S.Bilirubin	2.3 mg% (0.65-5.34)
Highest B.urea	55 mg% (32-97)
Highest S.creatinine	1.4 mg% (0.93-3.8)
Lowest P. Fibrinogen	92.3mg%
Highest FDP level	27.4 microgram%
Highest D-dimer level	11.8 microgram%

DISCUSSION

The presence of fever, malaise, and headache concomitant with laboratory findings of leucopoenia and thrombocytopenia is a common clinical picture for zoonotic diseases of bacterial and viral origin. The important viral hemorrhagic fevers (VHF) in India spread by an arthropod vectors are Dengue fever/Dengue hemorrhagic fever and Kyasanur forest disease [12]. There is also an increasing recent interest in the Ebola virus as the current 2014 epidemic in the African subcontinent may soon spread beyond its boundaries and indeed some cases have already been reported from outside of the main affected region. Crimean Congo haemorrhagic fever (CCHF) is a viral haemorrhagic fever (VHF) that having overall case fatality of 9-50% in various studies with its potential to have Nosocomial spread. India was always under the potential threat of CCHF viral infection but to our knowledge, no case of CCHF has been reported until 2011[13, 14].

In 2004, Ergonul O et al. [15] submitted their study of 35 confirmed cases of CCHF in which mean lowest WBC count was 1740 /cumm, mean lowest platelet count was 26000/cumm, mean longest Prothrombin time (PT) was 13 seconds, mean longest activated partial Thromboplastin Time (aPTT) was 45 seconds and mean highest ALT level was 383 U/L which are more similar to our findings stated in table 2. They have also reported bleeding manifestations in form of epistaxis and Haematemesis in 29%, Malena in 6%, hematuria in 5%, hemoptysis in 2% of case which are also more similar to our findings stated in table 1. Ergonul O et al. did not observe renal failure in any of their patients while in our study we found mean highest S.creatinine 1.4 mg% (0.93-3.8 mg). They have had given ribavirin to 8 (eight) of 30 patients that having severe disease and all 8(eight) patient survived which shows their overall case fatality of 2.8% while in our study 2(two) out of 10(ten) patients died before diagnosisof having CCHF was made and ribavirin therapy started and so, only 8(eight) patient received oral ribavirin. Out of that 8(eight) patients only 1(one) patient died that resulted in case fatality of 12.5% in our study. This shows possible effectiveness of ribavirin in CCHF treatment though statistical significance not established with such small sample size. However, many studies showing no efficacy of ribavirin in form of reduction of viral load or altering disease progression [16], there are also other studies available that showing role of ribavirin in terms of mortality reduction particularly when its administered earlier in disease course[17,18]. WHO has recommended its use in treatment of CCHF and we also favours it as per our study results. One interesting thing that we noticed in our study is that 2(two) patients having reactive Dengue IgM antibodies by ELISA and 1(one) had reactivity to Dengue NS1 antigen by ELISA. Though studies are not available for cross reactivity between CCHF & Dengue antibodies, this might be possible because of high endemicity of Dengue Virus in our country.

CONCLUSION

CCHF cannot be ignored in differential diagnosis of any patient who had regular contact with cattle,withor without history of tick bite, presenting with fever or history of fever, along with significant thrombocytopenia (<50,000/cumm), Leucopenia, Negative results for Malaria and dengue (preferably by PCR), Modest alterations in LFTs & in coagulation Profile (Markers of DIC), Normal to Mild alterations in RFTs**.** It is better to start empirical oral ribavirin in such patients than to lose them before laboratory confirmation of infection arrives.

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