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The Epidemiological Aspect of Crimean-congo Hemorrhagic Fever in Southeast of Iran

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This study was conducted in order to determine the epidemiologic aspect of CCHF in this province. In this retrospective study, we evaluated the prevalence of epidemiological factors in the 182 patients with CCHF, who were admitted to Boo-Ali Hospital in a time period of 6 years from January 1999 to June 2005. Out of 182 cases with CCHF, 81.3% were male and 18.7% female. Ninety one cases (49.5%) had an age more than 35 years and 47% were between 18-35. Only 3.5% cases had an age less than 18 years (between 5-18 year). More over, 77% were Iranian patient and 23% of the cases were non-Iranian (immigrants from Afghanistan and Pakistan). Sixty eight percent of patients were animal holders and there was a significant difference between job and frequency of infection ($p = 0.00001$). 19.7% of cases had history of tick bite. Eighty nine percent of patients had bleeding in skin and mucus membranes. Therefore, in endemic area, any patient with history of fever of less than two week duration, history of contact with animals and with bleeding in the skin and orifices should arouse suspicion of CCHF.

Key words: Crimean-congo hemorrhagic fever, epidemiological factors, out break, Zahedan

INTRODUCTION

Crimean-Congo Hemorrhagic Fever (CCHF) is caused by a virus that is widely distributed in wild and domestic mammals, birds and ticks in many regions of Africa, Europe and Asia (Kelly *et al.*, 2004; Alavi-Naini *et al.*, 2004). CCHF was first observed in the Crimea in 1944 by Russian scientists. Then virus was first isolated in Africa from the blood of a febrile patient in Zaire in 1956. CCHF Virus (CCHFV) (genus *Nairovirus*, family *Bunyaviridae*) is spread by the tick *Hyalomma* sp. or via blood transfusion and contaminated blood of human and animal or by contact with infected tissue (Alavi-Naini *et al.*, 2004; Flick *et al.*, 2003). CCHF can produce a severe hemorrhagic fever with shock, Disseminated Intravascular Coagulation (DIC), frequent extensive bleeding and severe thrombocytopenia. Following an incubation period of two to nine days, patients have a sudden onset of fever, nausea, severe headache and myalgia, petechial rash and hemorrhagic signs such as hematemesis and melena supervene on three to six days of the illness (Peters, 2000; Fisher-Hoch and Simpson, 1985; Sheikh *et al.*, 2004; Anonymous, 1988; Baron *et al.*, 1983). Other sites of bleeding, such as intracranial hemorrhage may occur (Alavi-Naini *et al.*, 2004). Despite high mortality rate (60% up of clinically apparent cases), up to 80% of the infections may be subclinical (Kelly *et al.*, 2004; Alavi-Naini *et al.*, 2004; Flick *et al.*, 2003). Diagnosis of the infection may be based on the detection of CCHF Antibody by ELISA, which possesses high sensitivity and specificity and PCR (Saijo *et al.*, 2002; Saluzzo and Guenno, 1987; Burt *et al.*, 1998). Epidemics of CCHFV have previously been reported from Eastern Europe, Africa and central Asia (Kelly *et al.*, 2004; Alavi-Naini *et al.*, 2004). Many cases have been reported from the countries around Iran including Turkey, Iraq, Russia, Afghanistan and Pakistan (Kelly *et al.*, 2004; Alavi-Naini *et al.*, 2004; Baron *et al.*, 1983; Chinikar, 2004; Nadeem *et al.*, 2003). Although serologic evidence indicated the existence of CCHF in Iran several decades ago, no clinical cases have been documented. Herein, we describe 182 patients with CCHF from the Sistan and Baluchistan province in Southeast of Iran.

MATERIALS AND METHODS

The present study was conducted at Department of Infectious Diseases in collaboration of Department of Microbiology and Arboviruses Center, Boo-Ali Provincial Teaching Hospital, Zahedana, the largest tertiary care hospital in the province of Sistan and Baluchistan, Iran. The study expanded over a time period of 6 years between January 1st, 1999 and June 2005.

Diagnosis had been confirmed by hemorrhagic fever reference laboratories of south Africa, Sengal and pasteur

institute of Iran using ELISA antibody test and RT-PCR. We evaluated the epidemiological factors in the patient with CCHF including sex, age, nationality, job and history of contact and clinical symptoms such as fever, myalgia, bleeding and the out come.

RESULTS

Among 182 cases with CCHF who were confirmed by serology and RT-PCR, 147 cases (81.3%) were male and 57 cases (18.7%) were female. Most of our patients were male, because males are outside more and are in contact with animals. Ninety one cases (49.5%) had an age more than 35 years and 47% were between 18-35. Only 3.5% cases had an age less than 18 years (between 5-18 year). Only one case was more than 65 years old (Table 1). There was no significant statistical difference in the age and frequency of infection between the male and female ($p = 0.22$). Moreover, 77% were Iranian and 23% of the cases were non-Iranian (immigrants from Afghanistan and Pakistan). Sixty eight percent of patients were animal holders and there was a significant difference between job and frequency of infection ($p = 0.00001$) (Table 2). 19.7% of cases had history of tick bite and other patients had history of contact to animal, tissue or blood of livestock. Sixty one percent of the cases were urban.

The mean period for first clinical manifestation in CCHF cases before hospitalization was 4.62 ± 0.73 days. One hundred and forty four cases (79%) were recovered and 38 cases (21%) were died. Common symptoms included fever (96.5%), myalgia (90.2%) and bleeding (89%).

DISCUSSION

CCHF infection is reported from many countries, in particular in the Persian Gulf region but also from countries on various continents (Alavi-Naini *et al.*, 2004).

The characteristics of CCHF virus infection in domestic animals are often unapparent, while human

Table 1: Frequency of patients with CCHF according to age and sex

Age/year	5<	5-19	20-34	35-50	>65	Total
Male	0	5	63	78	1	147
Female	0	2	21	12	0	35
Total	0	7	84	90	1	182

There is no significant difference in the age and frequency of infection between the male and female ($p = 0.22$)

Table 2: Frequency of patients with CCHF according to job

	Student	Farmer	Health care		Animal holder	Total
			worker	Housewife		
Male	5	21	1	-	120	147
Female	1	1	1	28	4	35
Total	6	22	2	28	124	182

There is significant difference between job and frequency of infection ($p = 0.00001$)

infections often result in severe hemorrhagic fevers. Activities related to herding i.e., sleeping outside during seasonal migrations and having contact with sick animal) also seem to be risk factors for infection (Kelly *et al.*, 2004; Alavi-Naini *et al.*, 2004; Nadeem *et al.*, 2003).

The incubation period for CCHF virus infection in humans is commonly 1 week, but varies depending on the type of exposure (tick bite, contact with blood, or skin of infected animals) (Chinikar, 2004; Nadeem *et al.*, 2003). Viruses are only detectable during the first week of illness so analysis of the humoral response is the best mode of detection for the disease (Kelly *et al.*, 2004; Chinikar, 2004).

Our patients were from 6 of the 8 city in Sistan and Baluchistan province. However, the majority of the confirmed cases were from Zabol (69%), which is located in neighborhood of Afghanistan.

In multivariate analysis, in Ozkurt study in turkey, farming (OR, 11.4), living in a rural area (OR, 10.05) and being bitten by tick (OR, 6.75) were determined as risk factors for CCHF. Despite high mortality rate (60% up of clinically apparent cases), in this study, mortality rate was 21%. Death from CCHF usually occurred on 5 to 14 days of illness. All death, in this study was occurred between 3 to 11 days. In Turkey study, as present study, rates of fever during hospitalization, bleeding from multiple sites and presence of petechia/ecchymosis were higher in the patients who died than in surviving ones. In other study by Nadeem *et al.* (2003) mortality rate was 23%. In recent survey also rates of bleeding from multiple sites and presence of petechia/ecchymosis were higher in the patients who died than in surviving patients. In Nadeem *et al.* (2003) study, 60% of patients were male and age of patients varied from 4-75 years. Our result showed that 81% of cases with CCHF were male and age of patients was between 5-59 years.

Therefore, any patients residing in endemic area, presenting with history of fever of less than two week duration, history of contact with sick animal and with bleeding in the skin and orifices should arouse suspicion of CCHF.

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