EVALUATION OF THE CRIMEAN-CONGO HEMORRHAGIC FEVER CASES FOLLOWED AND TREATED IN OUR CLINIC BETWEEN 2009-2013

Abstract

Objectives: The Crimean-Congo hemorrhagic fever virus (CCHFV) belongs to the family *Bunyaviridae*, genus *Nairovirus*, and causes severe disease in humans; the reported case-fatality rate is 3%–30%. The aim of this study was to determine the epidemiological and clinical characteristics of the CCHF cases in our clinic between 2009-2013.

Material and Method: Thirty-three patients with the diagnosis of CCHF were followed up in Kayseri Training and Research Hospital between January 2009 and September 2013. Demographic, geographic, climatic, and clinical and laboratory characteristics of all patients were investigated. Patient serum samples were tested for anti- CCHF Ig M and immunoglobulin Ig G antibodies by ELISA and polymerase chain reaction (real-time PCR).

Results: According to our reports 33 CCHF cases were followed in our clinic. Of the CCHF cases, 63.6% were male. Thirty patients (90.9%) were from rural regions. Seventeen patients (51, 5%) were farmers. The median age was 46.7 years (range18-71 years). On admission, 97% of patients experienced high fever, 100% had weakness, 93.9% had a headache. The disease was more usual in May, June, July. Of the CCHF cases, 69.7% had a history of tick bite. On admission, all of the patients had thrombocytopenia, 87.9% had leucopenia, 27.3% had anemia, and 87.9% had elevated AST and ALT. Oral ribavirin treatment was used in 33.3% of the CCHF cases. The case-fatality rate was 12.1% (4/33 patients).

Conclusions: CCHF remains a seasonal problem in the Mid-Eastern Anatolia region of Turkey. The mortality rate in our patients was higher than reported in other studies in our country (12% vs 5%). CCHF should be accompanied with supportive care, especially including early platelet replacement.

Keywords: Crimean-Congo Hemorrhagic Fever, case-fatality rate, tick-bite.

INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne viral zoonosis with the potential of human-to-human transmission with case fatality rates from 3% to 50% (1). It is an endemic disease in Turkey and large outbreaks have been observed during spring and summer months since 2002 (2). In Turkey, 5% case fatality rate (CFR) had been reported by the Ministry of Health of Turkey (3). The primary transmission route of the virus to humans is known to be tick bite. Moreover, contact with patients at the viremic phase of the disease or exposure to tissue or blood of an infected animal can lead to the disease (4).

In the present study, demographic, geographic, climatic, clinical and laboratory features of the CCHF cases in our clinic followed up 5 years were analyzed and risk factors were measured.

METHODS

The patients with acute febrile syndrome characterized by fever, malaise, bleeding, leucopenia, and thrombocytopenia in spring and summer of 2009 and 2013 were admitted. The patients, who had positive IgM and polymerase chain reaction (RT-PCR) results for CCHFV in blood, were included in the study. Virologic studies were performed at Refik Saydam National Hygiene Center, which is the national

reference laboratory in Ankara, Turkey. Demographic data of the data of patients, as well as clinical and the laboratory results, were recorded and transferred to the SPSS 20.0 (Statistical Package for the Social Sciences 20.0) statistical package program.

RESULTS

The epidemiological characteristics of patients are shown in Table 1. Specific antibodies against CCHF virus were found in all patients' sera. The number of confirmed cases, according to the year include 2009 (4), 2010 (13), 2011 (8), 2012 (2) and 2013 (6). All patients took on in the springtime and summer months when air temperatures climb above 20 °C. The disease was most common in the months May, June and July. The greatest number of patients (30.3%) was accepted in July (Figure 1).

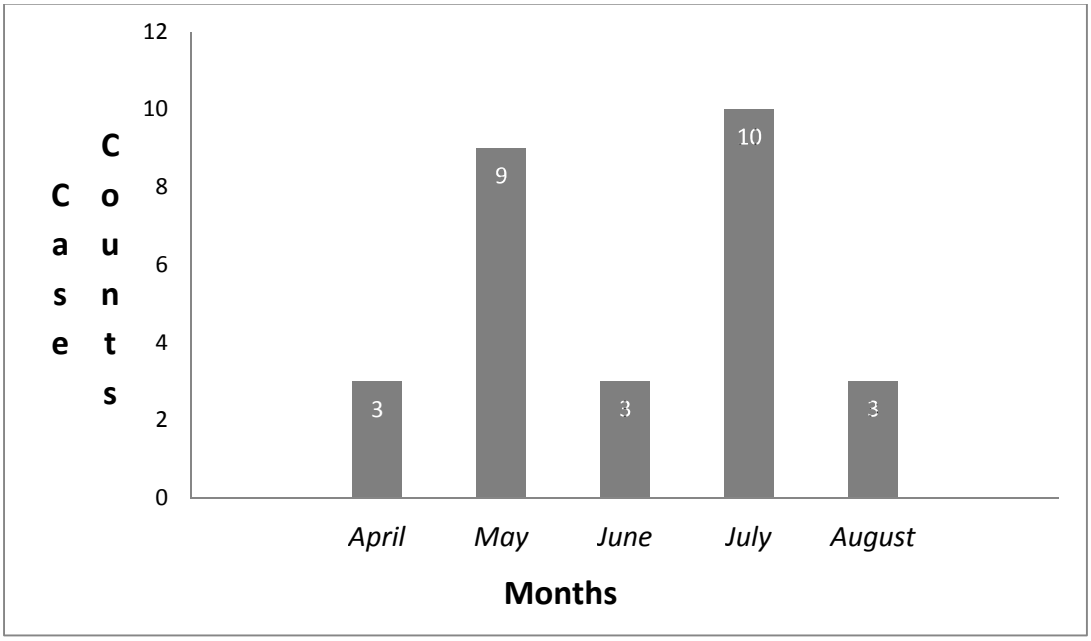

Figure. *Seasonal distribution of our CCHF cases; all the cases were followed in April to August; no cases were attended in other months.*

Baseline clinical characteristics and laboratory are presented Table 2, Table 3 and Table 4.

According to the case report forms, oral ribavirin treatment was employed in 33.3% of the CCHF cases (Table 3). Hospital admission period after beginning symptoms was 3.2±1 days. The case-fatality rate was 12.1% (4/33 patients).

Table 1. The epidemiological characteristics of patients with a diagnosis of CCHF

Age (year±SD)	46.7±14.7	
	n	%
Gender		
Male	21	63.6
Female	12	36.4
Inhabiting in the rural region	30	90.9
Location		
County of Kayseri	15	45.5
County of Yozgat	8	24.2
County of Adana	5	15.2
County of Sivas	2	6.1
Center of Nevşehir	1	3
Center of Kayseri	1	3
Center of Niğde	1	3
Occupation		
Farmer	17	51.5
Housewife	7	21.2

Working in animal agriculture or as a sheepherder	7	21.2
Student	1	3
Unemployed	1	3

Table 2. Potential risk factors for transmission and clinical of CCHF cases

Possible risk factors for transmission	n	%
Tick bite	23	69.7
Tick contact	19	57.6
Close contact with animals	32	97
Contact with the body fluid of a CCHF case	1	3
Living in the rural area	31	93.9
Activities in the nature	33	100
Symptoms and signs		
Fatigue	33	100
Fever	32	97
Headache	31	93.9
Myalgia	32	97
Nausea	25	75.8
Vomiting	17	51.5
Abdominal pain	11	33.3
Diarrhea	10	30.3
Hemorrhage	7	21.2
Body temperature >38 ºC	28	84.8

Hypotension	16	48.5
Tachycardia	15	45.5
Epistaxis	2	6.1
Gingival hemorrhage	3	9.1
Hematuria	6	18.2
Vaginal bleeding	1	3
Gastrointestinal system hemorrhage	2	6.1
Maculopapular rash	2	6.1

Table 3. Laboratory findings, treatment and outcome in patients with a diagnosis of CCHF.

Laboratory findings	n	%
Anemia	9	27.3
Leukopenia	29	87.9
Thrombocytopenia	33	100
Elevated AST and ALT	29	87.9
Elevated CK	24	72.7
Elevated LDH	22	66.7
Abnormality at chest x-ray	5	15.2
Treatment		
Ribavirin	11	33.3
Supportive	24	72.7
Outcome		
Cured	29	87.9

Died	4	12.1
Duration of hospitalization (days ± SD)	7.81±2.9	

Table 4. The baseline laboratory of the patients with CCHF

Laboratory findings	Median ± SD
Leukocyte (10^3/µL)	2.6±1.7
Platelet (10^3/µL)	71.4±37.2
Hemoglobin (g/dL)	13.8±1.8
Aspartate-Aminotransferase (IU/mL)	287±322
Alanine-Aminotransferase (IU/mL)	142±135
Creatine phosphokinase (IU/mL)	710±749
Lactate dehydrogenase (IU/mL)	520±354
Prothrombin time (sec)	13.7±2.4
Activated partial thromboplastin time (sec)	37.6±17.1
International normalized ratio	1.1±0.2

DISCUSSION

CCHF was found to be endemic in the middle, northern, and eastern Turkey between the months of March and October (5, 6). Our cases were living in the similar area (Kayseri, Yozgat, Adana, Nevşehir, Sivas, Niğde) in the months May, June and July.

The virus can be transmitted to humans by tick bites or by contact with blood or tissue of CCHF patients or infected livestock (7). Of the CCHF cases 69.7% of

our cases had a history of tick-bite or tick contact, 97% patients' had a history of close contact with animals. The occupations at risk for CCHF have primarily been those that are engaged in animal husbandry and farming, which involve the risk of contact with ticks (8). In our series, cases were mostly farmers (17 cases, 51.5%). The incidence rate of the disease among healthcare workers is very low in Turkey. In this study followed by 33 cases which there was no health worker.

In the present study, male patients were dominant (63.6%). In our region, men work in all types of farming household tasks and tend livestock in rural regions.

Evaluation of clinical findings showed that the most common symptoms were tiredness, fever, myalgia and headache (8-11). In this study, the most common reported complaints were fatigue, myalgia, headache and fever. The hemorrhages observed in patients may be in the form of epistaxis, hematemesis, melena, hematuria, gingival hemorrhage, vaginal bleeding, petechial or ecchymosis as well as occult hemorrhage without any significant signs (4). The result and symptoms of patients in the case series described in the literature showed consistent with the results and symptoms noted in our study (5, 6, 8).

The treatment efficacy of ribavirin in CCHF remains unclear. Some studies from our country have reported a decreased mortality rate among the severe cases that were given oral ribavirin treatment, while other studies have reported that ribavirin has no effects on mortality (9, 11, 12). Only eleven patients received oral ribavirin and our patients died who treated with oral ribavirin.

There is a broad range (2-80%) in the mortality rate in different countries (10). The average fatality rate for Turkey is around 5% (6). These rates lower than the reported series from other parts of the world. Unfortunately, the case-fatality rate

of our patients was higher than others series reported from other regions of our country (12% vs. 5%).

CONCLUSION

In conclusion, the CCHF virus causes severe viral hemorrhagic fever outbreaks. CCHF remains a seasonal problem in the Mid-Eastern Anatolia region of Turkey. In the absence of a vaccine, the only way to reduce infection in people is by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the virus. Particularly in cases coming from regions categorized as endemic, it is concluded that mortality can be brought down by carefully taken medical history and practice medical treatment and replacement therapies in consideration of CCHF pre-diagnosis.

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