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Epidemiological risk factors for Crimean-Congo hemorrhagic fever patients

Aim: The aim of this study was to evaluate the epidemiological risk factors for Crimean-Congo hemorrhagic fever (CCHF) patients admitted to our hospitals between January 2004- December 2006.

Materials and methods: This was a study of 63 CCHF patients whose definitive diagnosis was based on the detection of CCHF virus-specific IgM by ELISA and/or of genomic segments of the CCHF virus by real time polymerase chain reaction (RT-PCR) and 50 healthy controls. Related data were collected prospectively.

Results: Twenty-two (50.8%) of the patients were female, and 31 of them (49.2%) were male. The mean age of the patients was 46 years. Anti-CCHF virus IgM was positive in 52 patients, and RT-PCR was positive in 13 patients. Thirty two patients (50.8%) had a tick-bite history before the onset of fever. Fifty-nine (93.6%) patients were involved farming/handling livestock, and they were living in rural area. In univariate analysis of epidemiological factors of the patients and healthy controls, farming ($P < 0.001$), handled livestock ($P < 0.001$), living in rural area ($P < 0.001$), and history of tick-bite ($P < 0.001$) were determined as the risk factors for CCHF in this study. Multivariate logistic regression analysis revealed only farming (OR = 59.9) and tick-bite history (OR = 5.9) as risk factors for CCHF. The disease was observed between April and August (most frequent in July, 2005 and June, 2006).

Conclusions: We saw that CCHF appears to be an increasing seasonal problem in our region, and obtaining the epidemiological factors of CCHF is important for determining the prevention strategy.

Key words: Crimean-Congo hemorrhagic virus, epidemiology, risk factors

Kırım-Kongo hemorajik ateşi hastalarında epidemiyolojik risk faktörleri

Amaç: Bu çalışmanın amacı Ocak 2004-Aralık 2006 arasında hastanemize kabul edilen Kırım-Kongo kanamalı ateşi (KKKA) hastalarının epidemiyolojik risk faktörlerini değerlendirmektir.

Yöntem ve gereç: Bu çalışma tanısı ELISA ile virüs spesifik IgM ve/veya RT-PCR ile genomik segment analizine dayanan 63 KKKA'li hasta ve 50 sağlıklı kontrol vakasına uygulandı. Veriler prospektif olarak toplandı.

Bulgular: Hastaların 32'si (% 50,8) kadın, 31'i (% 49,2) erkekti. Hastaların yaş ortalaması 46 idi. Elli iki hastada anti-CCHF virüs IgM, 13 hastada RT-PCR pozitifliği. Otuziki (% 50,8) hastada ateş öncesi kene ısırığı öyküsü mevcuttu. Elli dokuz hasta (% 93,6) çiftçilik, hayvancılıkla uğraşiyor ve kırsal kesimde yaşıyordu. Univaryans analizi ile hasta ve sağlıklı kontroller arasında çiftçilik ($P < 0,001$), hayvancılık ($P < 0,001$), kırsal kesimde yaşama ($P < 0,001$) ve kene ısırığı öyküsü ($P < 0,001$) risk faktörü olarak belirlendi. Ancak multivaryans lojistik regresyon analizinde yalnızca çiftçilik (OR: 59,9) ve kene ısırığı öyküsü (OR:5,9) KKKA hastalarında risk faktörü olarak belirlendi. Bu seride hastalık Nisan-Ağustos ayları arasında görüldü (en sık Temmuz 2005 ve Haziran 2006).

Sonuç: Bölgemizde KKKA'ini mevsimsel bir problem olarak gördük ve KKKA için epidemiyolojik risk faktörlerinin belirlenmesi hastalığın önlenmesi için önlem stratejilerinin belirlenmesinde önemli parametreler olacaktır.

Anahtar sözcükler: Kırım-Kongo hemorajik ateş virüsü, epidemiyoloji, risk faktörleri

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Introduction

CCHF is a widely distributed potentially lethal disease caused by a virus belonging to Bunyaviridae family (1,2). The distribution of these viruses is generally limited and the viruses are therefore endemic in certain areas of the world. Infection is transmitted to humans via the bite of ticks (mainly of the genus *Hyalomma*) or through unprotected contact with blood or tissues from infected animals or humans (1-3). The most common clinical signs of CCHF are fever, nausea, headache, diarrhea, myalgia, petechial rash, and bleeding, and it causes severe disease in humans and results in an approximately 30% fatality rate (2). Although confirmed CCHF patients or serological evidence of the virus were reported from neighboring countries, there is no evidence of CCHF case in Turkey before 2002 (4,5). CCHF has recently been detected in about 30 countries including Turkey, Bulgaria, Albania, and Greece, (6-9). Treatment options for CCHF are limited.

The number of cases has been increasing over the years in Turkey (4). Therefore, the aim of the present study was to evaluate the epidemiological factors of CCHF patients in this region and to make a contribution in the selection of control and prevention strategies.

Materials and methods

Between January 2005 and December 2006, we carried out a prospective study including 50 healthy controls and 63 patients with acute febrile syndrome, characterized by malaise, bleeding, leukopenia and thrombocytopenia who were admitted to the Infectious Diseases and Clinical Microbiology Department of Atatürk University Research Hospital, a 1200-bed tertiary hospital in Erzurum, Turkey. Patients with positive IgM antibody and/or detection of viral RNA by RT-PCR in blood or tissue were included in this study. Acute and convalescent sera from all the acute cases were sent to the Refik Saydam Hygiene Center of Ankara, Turkey for ELISA and RT-PCR tests. Related data were collected prospectively.

Data analysis

Chi-squared and Fisher's exact tests were used for categorical variables. A multivariate analysis was

performed for the prediction of risk factors. A P value of <0.05 was considered statistically significant. SPSS 10.0 was used for statistical analyses.

Results

Anti-CCHF virus IgM was positive for 52 patients, and RT-PCR was positive for 13 patients. Twenty-two (50.8%) of the patients were female and 31 (49.2%) were male. The mean age of the patients was 46 ± 16.9 (age range 21-83) years. Thirty two patients (50.8%) had a tick-bite history before the onset of fever. Fifty nine (93.6%) patients were involved farming/handling livestock, and they were living in rural area. In univariate analysis of demographic variables of the patients and healthy controls, farming, handled livestock, living in rural area, and history of tick-bite were determined as the risk factors for CCHF in our region (Table 1). Multivariate logistic regression analysis revealed that only farming and tick-bite history as the risk factors for CCHF (Table2). The disease occurred from April to August (most frequent in July, 2005 and June, 2006) (Figure 1).

Discussion

CCHF is an often fatal viral infection described in about 30 countries, and it has the most extensive geographic distribution of the medically important tickborne viral diseases, closely approximating the known global distribution of *Hyalomma* spp. ticks (2,3,10). CCHF virus has probably been circulating in Turkey for many years (5). Serologic evidence of CCHF virus in Turkey was reported in the 1980s; however, public awareness did not focus on the disease (11). Although epidemics have been reported from neighboring countries since the 1970s, patients with CCHF were first reported in Turkey in 2002 (5,12,13). Between 2002 and 2007, a total of 1820 confirmed cases, including 92 resulting in death, were reported to the Ministry of Health (MoH) of Turkey, showing an increasing trend over the years (6).

There are several groups of individuals who are considered to be at-risk of contracting CCHF (2). Epidemiologically, CCHF cases are distributed mainly among actively working age groups exposed to tick populations (3). Gender distribution varies between

Table 1. Epidemiological data for 63 patients with CCHF and controls.

	CCHF Patients <i>n</i> : 63, (%)	Control <i>n</i> : 50, (%)	P value
Age	46 ± 16.9	48.4 ± 20.2	0.499*
Female	31 (49.2%)	23 (46%)	0.739*
Male	32 (50.8%)	27 (54%)	0.290*
Farming	59 (93.6%)	14 (28%)	0.000*
Handled livestock	59 (93.6%)	24 (48%)	0.000*
Living in rural area	59 (93.6%)	22 (44%)	0.000*
Tick-bite	32 (50.8%)	12 (24%)	0.004*
Contact with a patient with CCHF	No	No	-
Camping	No	No	-

*by Chi-squared test.

Table 2. Epidemiological risk factors for CCHF in multivariate analysis.

Variable	OR	95% CI	P value
Farming	59.9	26.255-1074.990	0.000*
Tick-bite	5.9	0.039-9.25	0.015*

*Multivariate logistic regression analysis was used (OR: odds ratio, CI: confidential intervals).

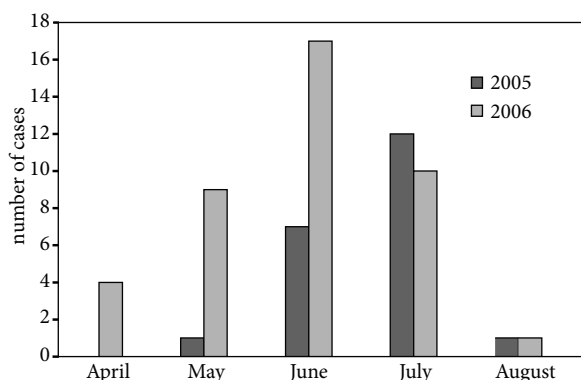


Figure 1. In this series, the disease occurred from April to August.

countries, depending on the participation of women in agricultural work. In this region, women in rural areas are active workers in the agricultural and animal husbandry sectors. Comparison of gender and age characteristics of 63 patients and control group showed that the male to female ratio was close to 1

and there were no significant differences with respect to gender and age.

The main transmission routes of the virus are tick-bite, crushing infected ticks, and contact with tissues, body fluids, and blood of CCHF patients or infected animals. The major at-risk group is farmers living in endemic areas; most of the affected cases deal with agriculture and/or animal husbandry (3). Most of our patients were farmers and handling livestock in rural areas as previously presented (14). One study indicates that the seroprevalence of CCHF virus is higher in people living in rural areas compared to urban areas of the CCHF virus epicenter in Turkey (12.8% vs 2.0%) (15).

Ticks are very common in this region; 47% of the tick species collected from domestic animals were *Rhipicephalus bursa* and 46% were *Hyalomma marginatum marginatum* (16). Both tick species play a role in CCHF transmission (2). In our study, nearly 50% of cases have a history of tick bites. Farming and being bitten by tick were determined as risk factors for CCHF in the multivariate analysis in this study. Many studies also determined that the occupations of animal husbandry and farming were significantly associated with CCHF seropositivity (14,15, 17)

Infected humans can spread the disease via close contacts, which may result in community outbreaks and nosocomial infections (18). In our study there was no nosocomial infection. In Turkey, there have

been 6 reported nosocomial infections; all had a history of contact with CCHF patients (6).

In the northern hemisphere, *H marginatum marginatum* is usually activated by increasing temperature in spring, particularly in April or May, and the immature stages are active in summer between May and September (10). In this series, cases were diagnosed between May and August with peak levels in June and July in each year, which corresponds with the tick season.

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To conclude, from the results of our study we report that, the most important epidemiological risk factors for CCHF are farming (OR:59.9) and tick-bite (OR:5.9), and the disease is a seasonal problem in this region like other regions of Turkey.

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