

Detailed Evaluation of Patients Admitted To Emergency Department With a Tick Bite Complaint

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Summary. *Background and Objective.* A tick bite has been an emergency of increased importance in recent years since it can cause a progressive, fatal disease such as Crimean-Congo hemorrhagic fever (CCHF). This issue should be considered by physicians working not only in endemic areas but also in the entire world, taking into account immigration, overseas trips, etc. In our study, we aimed to increase the awareness of the issue by evaluating the emergency department admissions of tick bite complaints in an endemic area.

Material and Methods. In total, 251 patients who had been admitted to the emergency department with a complaint of a tick bite within 10 months were included into the study. The data were obtained by collecting main complaints, demographic characteristics, cell counts on admission, and biochemical tests as well as CCHF findings in the RT-PCR test. The patients were divided into 2 groups according to the results of real-time polymerase chain reaction (PCR+ and PCR–).

Results. All the patients complained of tick bites. As for the additional complaints, 46% of the overall study population had fatigue and 36% experienced fever. Fever was the most common complaint in the PCR+ group (39%). The platelet and white blood cell counts were significantly lower and the AST level was significantly higher in the PCR+ group than the PCR– group ($P < 0.01$).

Conclusions. In CCHF, where an early diagnosis is very important in reducing mortality, and the symptoms such as a tick bite, fever, and fatigue should be taken seriously by emergency medicine physicians. Leukopenia and thrombocytopenia and higher levels of enzymes in the liver function tests should be taken into account.

Introduction

There are many tick types in Turkey, especially in the Kelkit valley (1). In addition, an increase in the tick population has been observed for the last decade in the region (2, 3). Tick bites may result in many diseases, such as Lyme disease, Rocky Mountain spotted fever, ehrlichiosis, Colorado tick fever, babesiosis, etc., in humans because of their carrier (vector) roles (4). Crimean-Congo hemorrhagic fever (CCHF) with an increasing incidence and high mortality rate is one of the most important diseases that is transmitted via a tick bite.

The virus that causes CCHF is a member of the *Nairovirus* genus in the family *Bunyaviridae* (5). This virus may be transmitted among humans in 3 ways (6). The first one is through the bite of a carrier tick. In particular, ticks in the genus *Hyalomma* are responsible for this (1, 7, 8). Second, a patient who developed CCHF can transmit it during the acute phase of the disease. Finally, it can also be transmitted by means of the blood and the tissues of viremic farm animals.

The disease is characterized by 4 phases during its clinical course (9–11). The first, which is the incu-

bation period, varies from 2 to 9 days. The prehemorrhagic period is clinically silent and nonspecific. Generally, it is shorter than a week. Patients may experience the symptoms such as fever, malaise, fatigue, muscle pain, rash, headache, and nausea. The hemorrhagic period is even shorter. Petechiae, conjunctival hemorrhage, hematuria, hematemesis, or melena may occur. During this period, the symptoms of the central nervous system from delirium to coma may also occur. Besides, disseminated intravascular coagulation or shock can develop in patients in this period and can be fatal. The recovery period begins 10–20 days after the onset of the disease. During this period, symptoms such as tachycardia, polyneuritis, breathing difficulty, and blurred vision can be seen or patients can be asymptomatic after recovering from the hemorrhagic period. Patients are usually hospitalized for about 9 to 10 days.

An early diagnosis is one of the important factors in reducing mortality from CCHF (12). The definitive diagnosis is made by identifying specific IgM antibodies or detecting a 4-fold increase in the IgG antibody level by the enzyme-linked immunosorbent assay (ELISA). The identification of the viral DNA in the blood with the help of real-time polymerase chain reaction (RT-PCR) is another diagnostic method (12).

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The contact with a virus should be avoided first, as in other viral diseases, in order to prevent the development of CCHF. It is important to apply strict isolation measures in hospitals in order to increase the awareness of people living in endemic areas, especially those at risk (farmers, livestock workers, etc.).

The province of Tokat is located in the Kelkit Valley and is considered to be an endemic region for CCHF (Fig. 1) (13). The first CCHF case was identified in the province of Tokat in 2002 (14). Emergency services play a critical role in the management of this disease, especially in endemic areas. Patients with complaints of a tick bite are admitted to emergency departments first. A tick is removed from the body by emergency medicine physicians, and the first systemic examinations of patients are performed in emergency departments. If these examinations show no abnormalities, patients are discharged from the hospital and warned to present immediately in case of the symptoms such as fever, fatigue, and nausea. Thus, the first diagnosis is performed by emergency services in CCHF, as in case of many diseases. In endemic regions, although there is no a complaint of a tick bite, CCHF has to be considered in patients with fever of unknown origin.

In this study, the objective was to examine the patients with complaints of a tick bite admitted to the Emergency Department of the University Hospital in Tokat province, an endemic region for CCHF, and to share our annual analysis in order to contribute literature in Turkey and the world as well as to raise the awareness of emergency medicine physicians about CCHF.

Material and Methods

In the study, the patients who were admitted to the Emergency Department of the University Hospital because of tick bite complaints between January 2012 and October 2012 were evaluated retrospectively. The hospital ENLIL-HIS database was used, and the patients who were admitted within this 10-month period with a diagnosis of A98.0, T63.8, T63.9, X25, and X27 according to the International Classification of Diseases were screened in order to obtain the list of the patients admitted with complaints of a tick bite, and their information was recorded in the prepared study forms. The following data were considered in the study form: patients' gender, age, main complaints, vital signs, hemoglobin level, platelet and white blood cell counts, AST and ALT levels, whether they were hospitalized with the CCHF prediagnosis or not in the Department of Infectious Diseases, and whether they were diagnosed with CCHF or not by the PCR results in the ongoing process. This information was collected from the patients' records obtained from both the ENLIL-HIS database and the hospital archives.

Based on the results of RT-PCR, the patients were divided into 2 groups: PCR+ and PCR-.

Statistical Analysis. The chi-square tests were used to evaluate categorical variables used in the study (Fisher exact chi-square test was used if the expected values were lower than 5 in 2×2 tables). Categorical variables are expressed in numbers and percentage. Continuous variables are presented as mean (standard deviation) with the range. The normal distribution of continuous variables was analyzed by the Kolmogorov-Smirnov normality

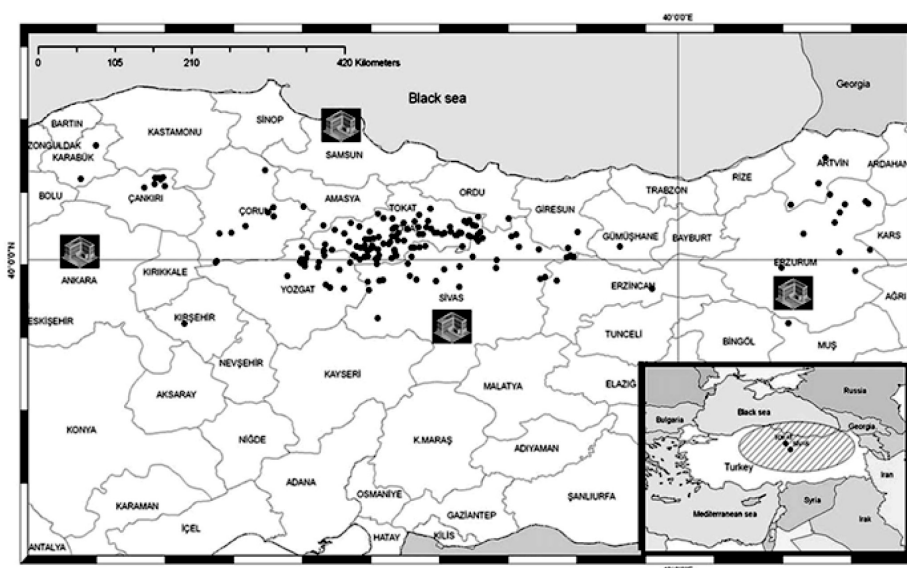


Fig. 1. Geographic locations (dots) of all the patients with Crimean-Congo hemorrhagic fever and the participating centers (symbols) between 2003 and 2004 in Turkey (13)

test. *P* values below 0.05 were considered statistically significant. Statistical analysis was performed with the statistical software (PASW ver.18. SPSS inc.15.0.).

Results

A total of 251 patients were admitted to the emergency department due to tick bites between January 2012 and October 2012. Their mean age was 38.51 years (SD, 7.2; coefficient of variation, 18%). In total, 136 (54.2%) men and 115 (45.8%) women were admitted, and the male-to-female ratio was 1.18 to 1.

All the patients complained of tick bites. As for the additional complaints, 116 (46%) patients had fatigue, 91 (36%) patients had fever, 18 (7.1%) patients experienced abdominal pain, 15 (5.9%) patients had only tick bites, and 11 (4.3%) patients had hemorrhage (Fig. 2).

Of the 251 patients who had been admitted to the emergency department with a complaint of a tick bite, 82 (36%) were hospitalized to the Department of Infectious Diseases with the prediagnosis of CCHF. There were 63 (76.8%) patients who had positive results of RT-PCR. The male-to-female ratio was 1.625:1. The mean age was 39.6 years (SD, 9.6; coefficient of variation, 23%), and the patients were hospitalized for a mean of 7 days (SD, 2.3). In the PCR+ group, the platelet and white blood cell counts were significantly lower compared with those in the PCR– group, and the AST level was significantly

higher in the PCR+ group than the PCR– group ($P < 0.01$) (Table).

According to the complaints of the PCR+ patients on admission, 25 (39%) patients developed fever, 22 (34%) patients experienced fatigue, and 16 (25%) patients had bleeding (Fig. 3). The mean temperature was 38.6°C (SD, 3.4°C; coefficient of variation, 8.8%).

Death occurred in 2 (0.8%) of the 251 patients who had been admitted to the emergency department during hospitalization in an intensive care unit. The results of PCR were positive in these 2 patients, and they accounted for 3.2% of all the PCR+ patients.

Discussion

CCHF, which has been reported in about 30 countries around the world, is a fatal, hemorrhagic viral disease (15). Although CCHF is endemic and observed frequently in some areas, it is important to increase the awareness of CCHF when considering situations such as immigration and overseas trips in the entire world. The tick bite, which is the most important mode of transmission, is frequently encountered in emergency departments. Although the most common complaint was fatigue, accompanying a tick bite in our study, the presence of patients with no additional complaints may show that people now visit a health care institution instead of removing ticks by themselves. Thus, the knowledge and the awareness of the society, which has had frequent

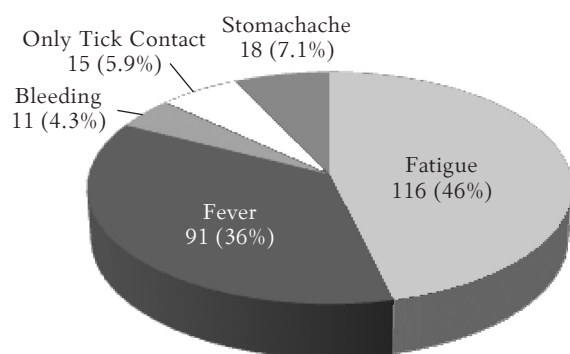


Fig. 2. Distribution of the patients admitted due to tick bites according to symptoms experienced

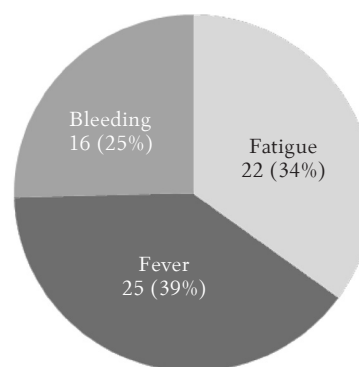


Fig. 3. Distribution of the PCR+ patients according to symptoms experienced

Table 1. Laboratory Values of the Patients Admitted due to Tick Bites Based on the Results of Polymerase Chain Reaction

Parameter	PCR+	PCR–	<i>P</i>
PLT count per μL	74000 (9250) [55870–92130]	292000 (11002) [270436–313564]	<0.01
WBC count per μL	3200 (880) [1475.2–4924.8]	9400 (740) [7949.6–10850.4]	<0.01
AST, U/L	155 (17.7) [120.3–189.7]	24 (4.114) [15.9–32.1]	<0.01
ALT, U/L	77 (14.7) [48.2–105.8]	38 (2.3) [33.5–42.5]	0.534

Values are mean (standard deviation) [95% confidence interval].

PCR, polymerase chain reaction; PLT, platelet; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

exposure to ticks for several years, about CCHF has increased.

In our study, CCHF was identified in 25.1% of the patients with a complaint of a tick bite admitted to the emergency department. In a study by Yardan et al., where the incidence of tick bites in the emergency department was examined, CCHF was documented in 3% of the cases. The percentage of patients with CCHF in our study was higher because the other study was performed in a nonendemic province (16).

Although CCHF affects people of all ages, it is often reported in men in various studies performed as in our study as well; however, it is usually a disease of young adults (9, 17, 18). Considering active lifestyles of this age group, in parallel with their contact possibility with ticks, a possibility of CCHF development is expected.

Our study included only the patients admitted to the emergency departments, who complained of tick bites. Thus, the cases of contaminations through blood and tissues were not included, and this can be considered as the limitation of our study.

Fever and malaise are the most common complaints of patients with CCHF, as reported in many studies (15, 17, 19). High fever and fatigue documented with a tick bite should alert emergency medicine physicians for the diagnosis of CCHF. In our study, fatigue was the most common complaint in terms of additional complaints of the patients admitted with tick bites, and the most frequent complaint of the patients diagnosed with CCHF was fever. The presence of fever, especially in those living in endemic regions even if there is no complaint of a tick bite, should suggest CCHF. Hemorrhage should also be a warning sign in addition to fever and fatigue. In a few studies, where survivors and nonsurvivors were compared, it has been reported that hemorrhage is an important factor for higher mortality rates (20–22). Since it has been reported that the hemorrhagic period of CCHF is a sign of poor prognosis, emergency care should be given immediately to hemorrhagic patients.

If a tick is still on the body of patients admitted to the emergency department, the tick is removed properly from the body first. The incubation period of the disease (2–9 days) makes it necessary for patients to be careful of the symptoms such as malaise, fatigue, headache, muscle pain, and bleeding. They should be admitted to emergency services immediately in case of any complaint. In order to achieve this, CCHF has to be accepted as a public health issue, and emergency medicine physicians should keep informed the patients admitted with a complaint of a tick bite.

Laboratory testing is of great importance for

patients admitted with complaints such as malaise, fever, or hemorrhage in the diagnosis of CCHF. In our study, the mean platelet count and the white blood cell count were lower in the CCHF-positive group. Similarly, Gozalan et al. reported in one of their studies that thrombocytopenia and leukopenia were frequently documented in patients with CCHF. Although a significant difference in the leukocyte count was detected between the CCHF+ and CCHF– groups, no statistical significance was reported in the platelet counts (19). Ergonul et al. also reported in one of their studies that leukopenia and thrombocytopenia were observed in patients with CCHF (20). Similarly, leukopenia and thrombocytopenia were identified in 65% of the patients in a study by Ertugrul et al. (17). In the light of all this information, it is suggested that leukopenia and thrombocytopenia can be used as indicators of CCHF in the emergency department.

Our study showed the AST and the ALT levels were higher in the CCHF-positive group, but the difference was significant only in the AST level. In a study by Gozalan et al., although 77.8% and 47.4% of the patients had higher AST and ALT levels, respectively, there were no significant differences between the CCHF-positive and CCHF-negative groups (19). In a study by Ozturk et al., where they examined CCHF patients, 98.3% and 83.6% of the patients had higher AST and ALT levels, respectively (23). Bakir et al. performed the study where they developed a scoring system to grade the severity of the disease and reported that the higher values of both the AST and ALT levels showed a poor prognosis of CCHF (21). Ergonul et al. linked higher AST and ALT levels to mortality in a study where they evaluated risk factors in CCHF (20).

The mean follow-up of patients with CCHF generally varies between 7 and 10 days, and our study results are also consistent with these data (21).

The mortality rate of 5% due to CCHF was reported in the study by Duygu et al., and the same rate during the 5-year follow-up was documented in the study by Uyar et al. (24). The data of the Ministry of Health of Turkey indicated 6396 cases of CCHF diagnosed between 2002 and 2011, and 5% of them were fatal (25). In our study, the mortality rate was significantly lower than these figures. We suggest that such a lower mortality rate was because of early visits of the patients to emergency departments due to right warnings and guidance given to the tick-bitten patients studied.

Conclusions

An early diagnosis of CCHF, which has a high mortality rate, is important for emergency medicine physicians, especially in endemic areas. The symp-

toms such as a tick bite, fever, and fatigue should be taken seriously, and leukopenia and thrombocytopenia and higher levels of enzymes in the liver function tests should be taken into account. At the same time, creating a public awareness with public

health activities is very important to ensure that this disease is kept under control.

Statement of Conflict of Interest

The authors state no conflict of interest.

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