

# Evaluation of Crimean-Congo Hemorrhagic Fever Disease in Amasya Region “Are We Afraid of Ticks?”

## Amasya Bölgesinde Kırım-Kongo Kanamalı Ateşi Vakalarının Değerlendirilmesinde “Biz Keneden Korkmalı mıyız?”

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**ABSTRACT Objective:** Crimean-Congo hemorrhagic fever in Turkey has attracted attention in recent years due to its high mortality in people who were completely healthy before. The aim of this study was to determine the risk and mortality rates of Crimean-Congo hemorrhagic fever (CCHF) in patients who have contact with ticks in our region. **Material and Methods:** In this study, cases with contact with the tick were examined retrospectively between 01.01.2010 - 31.12.2010 at the Hospital Emergency Clinic. The data were obtained from State Hospital Emergency Service Registry and the clinical files of the hospitalized patients. **Results:** In 2010, 3,018 patients (1%) who had presented to the State Hospital Emergency Department complained of contact with ticks. The majority of the presentations were in June. When the obtained data were evaluated, the likelihood of infection with the virus was 1%, the mortality rate from CCHF due to tick exposure was 0.2%, and the fatality rate of CCHF was 17.64%. **Conclusion:** In terms of reflecting the panic of the people, especially of those living in endemic regions, emergency hospital patient presentations are an important criterion. Mortality from tick exposure is not as high as it is expected.

**Keywords:** Emergency medical services; nairovirus; crimean-congo hemorrhagic fever; tick

**ÖZET Amaç:** Ülkemizde son yıllarda Kırım Kongo kanamalı ateşi, daha önce tamamen sağlıklı olan kişilerde, yüksek mortalitesi nedeni ile dikkat çekmektedir. Bölgemizde kene ile temas şikayeti ile başvuran hastalarda, Kırım Kongo Kanamalı Ateşi (KKKA) gelişme riski ve mortalite oranlarının belirlenmesi amaçlanmıştır. **Gereç ve Yöntemler:** 01.01.2010 - 31.12.2010 tarihleri arasında acil servisimize başvuran, kene ile temas hikayesi olan olgular retrospektif olarak incelendi. Veriler acil servis kayıtları ve hastanede yatan hastaların klinik dosyalarından elde edildi. **Bulgular:** Devlet Hastanesi Acil Servisine 2010 yılında, 3018 hasta (%1) kene ile temas şikayeti nedeniyle başvurmuştur. Başvurular en çok haziran ayındaadır. Elde edilen veriler değerlendirildiğinde, kene ile temas sonrası virüsle enfekte olma ihtimali %1, mortalite %0,2 iken fatalite oranı %17,64 olarak tespit edilmiştir. **Sonuç:** Acil servise yapılan başvurular, özellikle endemik bölgelerde yaşayan halkın paniğini yansıtmaları açısından önemli bir kriterdir. Mortalite zannedildiği kadar yüksek değildir.

**Anahtar Kelimeler:** Acil servis; nairo virüs; kırım kongo kanamalı ateşi; kene

In Turkey, the Crimean-Congo hemorrhagic fever has attracted attention in recent years due to its high mortality in those who are completely healthy. The Crimean Congo hemorrhagic fever virus carried by ticks is a member of the Nairovirus family.<sup>1</sup> Acute emergence; symptoms of wide-spread body pain, fever, nausea, vomiting, abdominal pain, diarrhea, ecchymosis and bleeding, and laboratory findings of elevated aspartate

aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH), thrombocytopenia and leukopenia. Diagnosis, is usually made by viral culture, detection of antibodies against the virus or molecular methods.<sup>1</sup>

The virus is usually transmitted to humans through the bite of infected horns or by contact with blood and tissues of viremic animals. In addition, nosocomial transmission from infected persons has also been mentioned.<sup>2</sup> The Crimean Congo Hemorrhagic Fever (CCHF), also known as rural disease, is seen in spring in farmers engaged in animal husbandry.<sup>3</sup> While 90% of the cases in our country are farmers, health workers constitute the second most frequently affected group. The mortality rate varies depending on the country and the hospital conditions. The first case in Turkey was defined in 2002, and until the middle of 2008, about 3,000 cases with a mortality rate of 5% were reported by the Turkish Ministry of Health.<sup>4</sup>

The endemic regions are mostly subdivided settlements in the valley where the mountains separating the sea and the inner regions come to an end ending in rivers reaching the sea.<sup>5</sup> People living in the same region and in the same geographical area can be surpassed without displaying any symptoms at a rate of 13.5 percent. What is interesting is that these are not individuals of the same living in the same household, but individuals who live in the same environment as CCHF patients, ie farmers and livestock workers.<sup>5</sup>

The clinical stages of CCHF comprises incubation, prehemorrhagic, hemorrhagic and the healing stages. In the literature, it is seen that CCHF cases have increased AST, ALT, LDH and creatine kinase (CK) values, activated partial thromboplastin time (aPTT) and prothrombin time (PT), and a decrease in the platelet count, which have been defined as poor prognostic criteria.<sup>3</sup>

In this study, it was aimed to determine the risk of mortality and the risk of developing CCHF in patients who had contact with ticks in the region.

## MATERIAL AND METHODS

In this study, cases with contact with the tick were examined retrospectively between 01.01.2010 and 31.12.2010 at the State Hospital Emergency Clinic. Ethical approval was obtained from the Medical Faculty Clinical Investigation Ethics Board on the 26.05.2011 and numbered 2011/165. The data were obtained from the State Hospital Emergency Department Registry and the clinical files of the hospitalized patients. Only the latest presentations of patients who were subsequently followed-up with ticks were included in the study.

Doubtful cases in terms of **CCHF**; fever, muscle aches, nausea, vomiting, bleeding, and laboratory findings accompanying thrombocytopenia and leukopenia; blood samples were sent to the Hıfzısıhha Center, Ankara, Turkey were evaluated as having CCHF polymerase chain reaction (PCR) (+) or CCHF Ig M (+).

## RESULTS

In 2010, a total of 245,578 patients had presented to the State Hospital Emergency Department. More than 1% of these presentations (3,018) had the complaint of tick exposure. When follow up appointments were excluded, 1,498 new cases were identified (806 males-692 females). The distribution of cases according to the months has been shown in Figure 1. According to the obtained data, the most presentations were in June.

Of these 1,498 cases, 66 were admitted, 41 of them were male and 25 were female. The serum samples from these patients suspected of CCHF were sent to the Hıfzısıhha Center for serological examination. According to these results, a total of 17 patients, 8 male and 9 female, tested positive. Three of these cases died. The assay-positive cases and deaths have been displayed in Figure 2. The assay-positive cases were all from the Göynücek county and neighboring villages in this county. None of our patients diagnosed with CCHF had any definitive knowledge of the duration tick exposure.

Among the biochemical values of the serologically positive cases, AST (52,8-819), CK (182-752) and

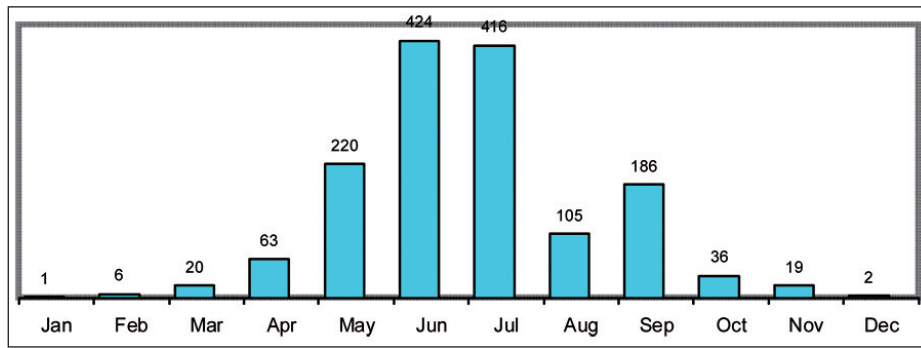


FIGURE 1: Dispersion of cases applied with tick exposure according to the month.

LDH (285-1,389) enzymes were found to be higher in patients who died at the emergency department. The average platelet counts of the positive cases were 126,000/mm<sup>3</sup>, while the mean platelet counts of those who died were 83,600 (Table 1). When the obtained data were evaluated, the likelihood of infection with the virus after tick exposure was 1%, the mortality rate from tick bite due to CCHF was 0.2%, and the case-fatality rate of CCHF was 17.64%.

## DISCUSSION

Crimean Congo Hemorrhagic Fever (CCHF) is a serious disease with a mortality rate of 5-30%, which

is the causative agent of a virus identified in the Nairovirus species of the Bunyaviridae family. The mortality rate by the Ministry of Health in Turkey has been reported to be 5%.<sup>6</sup> The mortality rate in Turkey is lower than that of other countries, the reason for which is considered to be due to many factors. The most important of these are: differences in virulence of different strains, access to health care and host factors. Those who engage in professions such as livestock, agriculture, slaughterhouse and veterinary are at the highest risk of contracting the infection by the CCHF virus.<sup>7,8</sup> In the last decade, the number of sporadic cases and

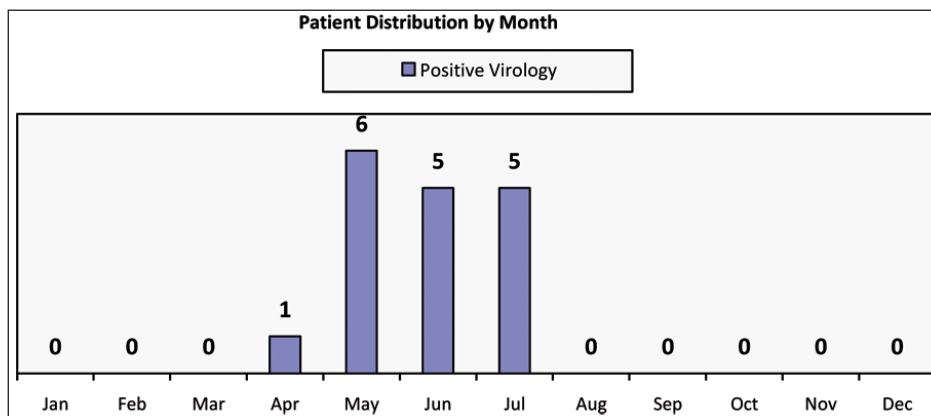


FIGURE 2: Distribution of CCHF patients by month.

TABLE 1: Mean laboratory results of patients who were followed-up with CCHF pre-diagnosis.

AVERAGE	WBC 10 <sup>9</sup> /L	HgB g/dL	Plt 10 <sup>3</sup> /μl	LDH U/L	AST U/mL	ALT U/mL	CK U/L	CK-MB U/L
Negative serology	7.6±(4.6)	13.2±(1.6)	187000±(103.000)	296±(241)	60.8±(49)	51±(46)	372±(575)	24.5±(21)
Positive serology	4.1±(1.69)	12.85±(1.54)	126.000±(45.000)	285±(115)	52.8±(44)	31.8±(19.6)	182±(218)	19±(7.7)
Patients who died	4.8±(1.56)	11.6±(0.37)	83.600±(60.000)	1.389±(1.674)	819±(1.133)	287±(337)	752±(711)	43±(26)

outbreaks related to CCHF has increased in endemic regions. Turkey is one of these endemic countries. The first case was reported in 2002 in Turkey, and with a confirmed diagnosis by serology or polymerase chain reaction towards the middle of 2008, around 3,000 cases were reported with a mortality rate of 5%.<sup>4</sup>

The province where the study was carried out is located in the Yeşilirmak valley of the Middle Black Sea Region, with a population of 350,000 and a high level of agriculture and animal husbandry. It is also one of our endemic disease for CCHF, which is also referred to as rural disease, and 1% of the urgent cases constitute a complaint of exposure with ticks. All of the positive cases came from Göynücek District and nearby villages neighboring Çorum, Yozgat and Tokat provinces.

CCHF is an endemic disease in Turkey in terms of central, eastern Anatolia and the Black Sea region. Furthermore, while it has been reported from the western and southern parts of the country, the presence of a number of studies is limited to examining new emergency room presentations. In the current studies, the infectivity rate was not given to the patients who had been admitted with ticks attached.<sup>9,10</sup> In particular, emergency presentations to the State Hospital Emergency Department are an important criterion for reflecting the panic of the people living in endemic areas. In 2010, a total of 245,578 patients were admitted. 1% of these presentations (3,018) complained of tick exposure. When follow up examinations were excluded, 1,498 of new cases were identified (806 males-692 females). 70.7% (1,060) of these cases had presented in May, June and July. Only 17 (8 males-9 females) of the patients had viraemia. After exposure with ticks, the probability of infection with the virus is 1% (17/1,498), the mortality rate from tick exposure due to CCHF is 0.2% (3/1,498), while the rate of fatality of CCHF is 17.64% (3/17).

According to the surveillance study results of the Ministry of Health in 2010, the total number of cases of CCHF was determined as 868, and 50 cases had died (Mortality 5-6%). In the region, a total of 36 cases were determined and 4 cases

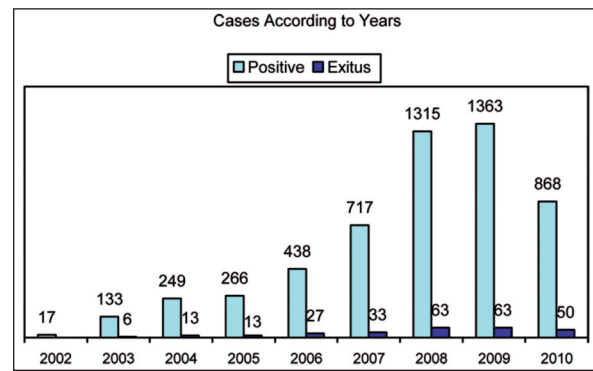


FIGURE 3: The number of cases reported over the years in Turkey.

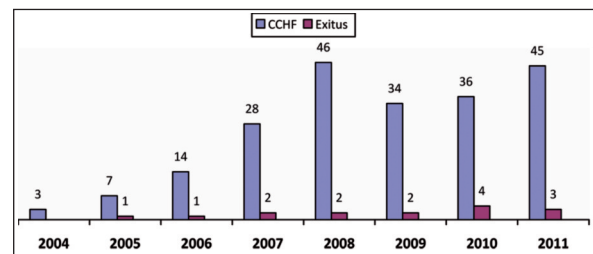


FIGURE 4: Number of CCHF cases having occurred in the Amasya region over the years (cut of 24.08.2011).

died.<sup>11,12</sup> As of July 2011, compared to the previous year, an increase in the number of cases has occurred, with 655 cases having been reported, and 33 cases having died (Figures 3, 4).<sup>12</sup>

Climate change can be shown as a result of the appearance of endemics in our country since 2002. It is one of the factors that facilitates the proliferation of tick populations and thus increases the incidence of tick-borne diseases.<sup>4</sup> In the northern hemisphere, *Hyalomma marginatum* ticks are active mainly in spring, especially in April and May, and the immature state is active between May and September.<sup>13</sup> It has been found in our country that the number of days in which the temperature exceeded 5°C in April and the average temperature in April increased has gradually in the previous years.<sup>14</sup> However, it is suggested that the climate change has been unable to explain the increase in tick-borne diseases in Europe over the last 20 years.<sup>15</sup> Beyond climate change, outbreaks of CCHF can develop under the influence of a number of environmental factors on the basis of favorable climatic conditions that can be experienced by *Hyalomma* species in various stages.<sup>1</sup>

The seasonal development of the cases reported in our country, according to the data of the Ministry of Health, is observed between May and September.<sup>12</sup> In our study, the cases were followed in May, June and July. More than 70% of our total emergency presentations were again within these three months.

When evaluating the cases infected with CCHF in Turkey with regard to the route of infection in 2008, there was a history of a tick bite in 71% of cases seen until the end of June. However, lack of a history of exposure in 48% of cases in 2010 indicates that contamination of the animals with blood and body fluids can be expected at a high rate. In addition, since CCHF can be associated with different tabulations such as pharyngitis and brucellosis, the alarm situation in the emergency departments is higher than expected.<sup>1</sup> This situation creates panic among both the health personnel and the public. The tick needs time to be able to insert the CCHF virus to humans. The tick sucks the blood through the excess liquid from the salivary gland, which takes 6-12 hours to process.<sup>12</sup> The fact that none of our cases knew the time of having been bitten by the ticks indicates that even if we are in the endemic region, the public education is not good.

When laboratory values are considered, leukopenia and thrombocytopenia are noteworthy. Increases in alkaline phosphatase (ALP), gamma glutamil transferase (GGT), LDH, AST, ALT, CK and Bilirubin values are observed. PT, PTT and other clotting tests show significant impairment.<sup>16</sup> The enzymes AST (188-819), CK (283 - 752) and LDH (480-1,389) were significantly higher in patients who died.<sup>8</sup>  $AST \geq 700$  U/L and  $ALT \geq 900$  U/L were determined as weight criterion.<sup>1</sup> The number of platelet counts  $\leq 20,000/mm^3$  is defined as independent risk factors associated with mortality.<sup>17</sup> In our study, the mean platelet counts of positive cases was  $118,000/mm^3$ , while the mean value of those who died was  $83,600/mm^3$ .

## RESULT

The alarm situation in the emergency departments is higher than predicted because the disease can be detected not only by holding the ticks, but also by taking in viruses in blood and body fluids of viremic

animals and by associating with other diseases such as pharyngitis and brucellosis. In particular, in terms of reflecting the panic of the people living in endemic regions, the number of emergency department presentations is an important criterion. In view of the increasing threats, emergency physicians should be prepared for the intensity of this infection.

As in all infectious diseases, it is very important and necessary to take preventive and control measures in CCHF. Determination of the epidemiological risk factors for CCHF has a critical value in terms of development of prevention strategies, since CCHF is a seasonal problem in our region. Combating ticks is the first step. According to the geographical regions and species, the hyalomonic lineages that infect with CCHF are generally active in April and October; this is also the reason for the epidemics in these periods. For this reason, hosts should be kept away from the edges.

In the endemic public education in particular, the fact that mortality after exposure with ticks is much less than it was thought, and the simplicity of the methods of prevention will prevent panic and fear.

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### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

**Idea / Concept:** Emine Doğan; **Design:** Emine Doğan, Abdullah Sadık; **Introduction:** Serap Çakar; **Supervision / Consultancy:** Abdullah Sadık Giriş; **Data Collection and / or Processing:** Emine Doğan, Abdullah Sadık; **Introduction:** Serap Çakar; **Analysis and / or Interpretation:** Emine Doğan, Abdullah Sadık; **Introduction Source Browsing:** Emine Doğan, Abdullah Sadık; **Author of the Article:** Emine Doğan, Abdullah Sadık; **Critical Review:** Emine Dogan, Serap Çakar; **Resources and Funding:** Emine Doğan, Serap Çakar; **Materials:** Emine Dogan, Serap Çakar.

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