

# Factors affecting mortality in Crimean-Congo hemorrhagic fever

## Kırım Kongo kanamalı ateşinde mortaliteyi etkileyen faktörler

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### Abstract

**Aim:** Crimean-Congo hemorrhagic fever is a viral disease that is transmitted by infected ticks and has high mortality. We aim to determine the factors affecting mortality in patients with Crimean-Congo hemorrhagic fever (CCHF).

**Methods:** Age, gender, number of ticks, tick removal procedures, tick location, time to hospital admission, symptoms, physical examination findings, vital signs, laboratory parameters and factors affecting mortality were evaluated. The study was designed as a retrospective cohort study.

**Results:** The median age of the 172 patients was 46 (range, 18–78) years, and 73.8% of the patients were men. The mortality rate was high in patients with delayed time to hospital admission, those who were bitten on the head and neck region, those who had a high number of tick bites, those who had removed the tick themselves or had the tick removed by a relative and those who had impaired consciousness ( $P=0.001$ ,  $P<0.001$ ,  $P<0.001$ ,  $P<0.001$  and  $P=0.002$ , respectively). Bleeding was detected in 87.2% of cases. The frequency of ecchymosis, pleural effusion, hematuria, hematemesis and melena occurrence was high in non-survivors ( $P<0.001$ ,  $P<0.001$ ,  $P<0.001$ ,  $P=0.006$  and  $P=0.006$ , respectively). Fever and heart rate were significantly higher, systolic and diastolic blood pressure was significantly lower in non-survivors ( $P<0.001$ ,  $P<0.001$ ,  $P=0.006$  and  $P<0.001$ , respectively). Additionally, the white blood cell (WBC) count, international normalized ratio (INR), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were significantly higher and platelet count were significantly lower in non-survivors ( $P<0.001$  for all).

**Conclusion:** We found that in patients with CCHF, bleeding was a major factor associated with mortality. Factors such as a number of ticks, the number of people removing the ticks and tick location were found to affect mortality. We believe that blood tests and vital parameters can be used to predict mortality in patients with CCHF.

**Keywords:** Crimean-Congo hemorrhagic fever, Mortality, Emergency department

### Öz

**Amaç:** Kırım kongo kanamalı ateşi enfekte kenelerle bulaşan ve yüksek mortaliteye sahip viral bir hastalıktır. Kırım Kongo Kanamalı Ateşi (KKKA) hastalarında mortalite üzerinde etkili faktörleri belirlemeyi amaçladık.

**Yöntemler:** Hastaların yaş, cinsiyet, kene teması, kene sayısı, kenenin kim tarafından çıkarıldığı, kenenin vücuttaki lokalizasyonu, hastaneye başvuru süresi, semptomları, fizik muayene ve vital bulguları, laboratuvar parametreleri ve mortaliteye etki eden faktörler değerlendirildi. Çalışma retrospektif kohort olarak dizayn edildi.

**Bulgular:** 172 hastanın yaş ortancası 46 (18-78) yıl olup, olguların %73,8'i erkekti. Hastaneye başvurusu geç olan, baş ve boyun bölgesinden ısırılmış olan, ısırılan kene sayısı fazla olan, keneler kendisi veya yakını tarafından çıkartılan hastaların ve bilinç bozukluğu olan hastaların mortalite sıklığı yüksek saptandı (sırası ile  $P=0,001$ ,  $P<0,001$ ,  $P<0,001$ ,  $P<0,001$ ,  $P=0,002$ ). Olguların %87,2'sinde kanama saptandı. Mortal seyreden olgularda ekimoz, akciğerde sıvı, hematüri, hematemez ve melena sıklığı yüksekti (sırası ile  $P<0,001$ ,  $P<0,001$ ,  $P<0,001$ ,  $P=0,006$ ,  $P=0,006$ ). Mortal seyreden hastalarda ateş ve kalp hızı anlamlı olarak yüksek; sistolik ve diyastolik kan basınçları ise anlamlı olarak düşük saptandı (sırası ile  $P<0,001$ ,  $P<0,001$ ,  $P=0,006$ ,  $P<0,001$ ). Mortal seyreden hastalarda beyaz küre (BK) sayısı, uluslararası normalleştirilmiş oran (INR), aspartat aminotransferaz (AST) ve alanin aminotransferaz (ALT) düzeyleri anlamlı olarak yüksek, platelet sayısı, anlamlı olarak düşük saptandı (hepsi için  $P<0,001$ ).

**Sonuç:** Kanamanın mortalite gelişmesinde temel faktörlerden biri olduğu saptandı. Kene sayısı, çıkartan kişi sayısı ve ısırılma yeri gibi faktörlerin mortalite üzerine etkili olduğu saptandı. Kan tetkikleri ve vital parametrelerin KKKA tanısı olan hastalarda mortal seyredecek hastaların belirlenmesinde kullanılabileceği kanısındayız.

**Anahtar kelimeler:** Kırım Kongo kanamalı ateşi, Mortalite, Acil servis

## Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic disease first described in the 12th century. The causative microorganism is the orthonairovirus from the Nairoviridae family that is carried by ticks in the genus *Hyalomma* [1,2]. CCHF is endemic to the Balkans, Middle East and Asian regions [1,2]. Although ticks are considered as the principal vector in disease transmission, the transmission of the virus via blood and other body fluids has also been reported [2,3]. Although the pathogenesis of the disease is still unclear, the host immune response, endothelial injury and inflammatory cytokines in infected tissues are believed to play a role in pathogenesis [4].

A CCHF often presents with mild, non-specific findings, but it may also progress to the hemorrhagic stage and result in mortality. The mortality rate associated with this disease is 5%–30%; however, the mortality rate is lower in endemic regions such as Turkey and Russia. It remains unclear whether the differences in mortality are related to regional differences or case management strategies [5,6].

In the present study, we aimed to determine the factors affecting mortality in patients diagnosed with CCHF and contribute to the existing literature.

## Materials and methods

The ethical compliance of this study was approved in accordance with the Helsinki Declaration by the Hospital Local Ethics Committee, Ankara, Turkey.

Between January 2014 and January 2019, 1592 patients with tick bites were admitted to our emergency department; 172 patients with the tick bites recorded on the hospital automation system in whom a definitive diagnosis of CCHF. Serum samples taken from patients during the application Jelsa standard tube, Turkey Institute of Public Health, Department of Microbiology Reference Laboratory, and the National Arbovirus Reference and Research on Viral Zoonosis Laboratory was made. The viral RNA extraction assay was performed with the EZ1 Virus Mini Kit (QIAGEN). The real-time PCR analysis was performed with Applied Biosystems, LightCycler® 480 Instrument II (Roche) and Rotor-Gene™ 3000/6000 (Corbett Research). Patients with a Crimean Congo viral antigen were found to be positive.

Age, gender, number of ticks, tick removal procedure, tick location, time to hospital admission, physical examination findings, vital signs, laboratory parameters and factors affecting mortality were evaluated. Patients aged >18 years with complete records were included in the study, whereas those with bleeding disorders for any reason (hemophilia, gene mutation, etc.), those with trauma-related bleeding signs (ecchymosis, hematoma, etc.) and those with missing records were excluded from the study.

### Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software (IBM SPSS 22.0, IBM Corporation, Armonk, NY, USA). Median, minimum and maximum values of quantitative data; in the analysis of qualitative data, frequency, and ratio values were used. Mann-Whitney U test was used for the analysis of quantitative data; the Chi-Squared test was used for the analysis of qualitative

independent data and, Fisher's Exact test was used when the Chi-Square test conditions were not provided. The Receiver operating characteristic (ROC) curve was used to calculate the cut-off, sensitivity and specificity values of the data. Logistic regression analysis was used to analyze the factors affecting mortality.  $P < 0.05$  was considered statistically significant.

## Results

The median age of the 172 patients included in the study was 46 (18–78) years, and men comprised 73.8% of patients. The mortality rate was found to be 8.1%. There was no relationship between age, gender and mortality ( $P = 0.836$  and  $P = 0.999$ , respectively). The mortality rate was found to be significantly higher in patients with delayed admission to the hospital ( $P < 0.001$ ). The most common bite localization was the upper extremity, and the mortality rate of head and neck bites was significantly high ( $P < 0.001$ ). Although a single tick was detected in 97.7% of patients, the mortality rate was higher in patients with a higher number of tick bites ( $P < 0.001$ ). In 97.1% of patients, the tick was removed by the doctor; in these patients, the mortality rate was found to be lower compared with patients in whom the tick was removed by the patient/relatives ( $P < 0.001$ ). The most common symptom was fever (72.1%), followed by abdominal pain (40.1%) and diarrhea (34.9%). The mortality rate was higher in patients with impaired consciousness ( $P = 0.002$ ). Bleeding was detected in 87.2% of patients. There was no correlation between bleeding and mortality ( $P = 0.135$ ). The frequency of ecchymosis, pleural effusion, hematuria, hematemesis and melena occurrence was found to be higher in non-survivors ( $P < 0.001$ ,  $P < 0.001$ ,  $P < 0.001$ ,  $P = 0.006$  and  $P = 0.006$ , respectively); whereas epistaxis, gingival bleeding and petechiae were not associated with mortality ( $P = 0.145$ ,  $P = 0.137$  and  $P = 0.293$ , respectively). Fever and pulse rate were significantly higher, systolic and diastolic blood pressure was significantly lower in non-survivors ( $P < 0.001$ ,  $P < 0.001$ ,  $P = 0.006$  and  $P < 0.001$ , respectively). White blood cell (WBC) counts, international normalized ratio (INR) and aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were significantly higher and platelet count were significantly lower in non-survivors ( $P < 0.001$  for all) (Table 1).

ROC analysis results and specificity/sensitivity ratios of WBC count, INR, platelet count, AST and ALT levels, fever, systolic blood pressure, diastolic blood pressure and pulse rate are shown in Figure 1 and Table 2.

A regression analysis performed on non-survivors revealed that none of the factors were predictive of mortality (Table 3).

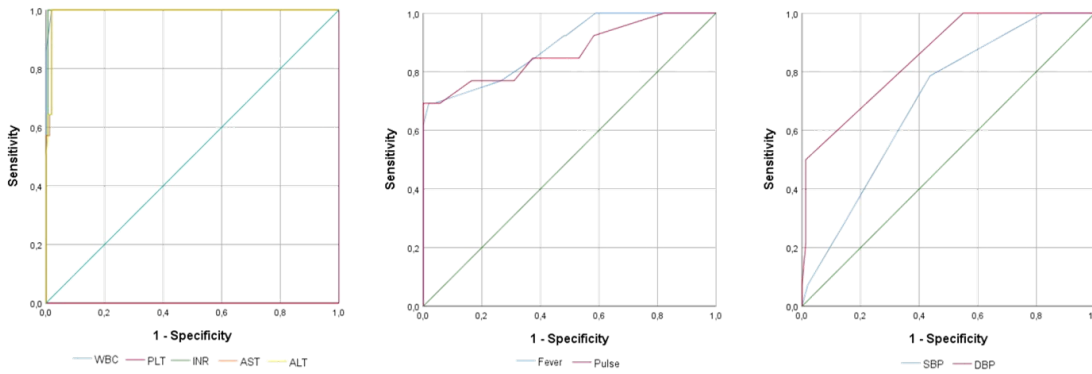


Figure 1: ROC analysis of vital signs and blood values

Table 1: Mortality analysis of influencing factors

	Total (n:172)	Survival (n:158)	Non-survivors (n:14)	P-value
	Median (min-max)/n (%)	Median (min-max)/n (%)	Median (min-max)/n (%)	
Age (years)	46 (18-78)	45.5 (21-78)	0.836 <sup>b</sup>	
Gender				>0.999 <sup>a</sup>
Male	127 (73.8)	116 (73.4)	11 (78.6)	
Female	45 (26.2)	42 (26.6)	3 (21.4)	
Time to hospital admission (day)	3 (1-9)	5 (1-9)	0.001	0.001
Tick location				<0.001 <sup>a</sup>
Head and neck	10 (5.8)	1 (0.6)	9 (64.3)	
Body	15 (8.7)	12 (7.6)	3 (21.4)	
Upper extremity	90 (52.3)	89 (56.3)	1 (7.1)	
Lower extremity	57 (33.1)	56 (35.4)	1 (7.1)	
Ticks number				<0.001 <sup>a</sup>
1	168 (97.7)	158 (100)	10 (71.4)	
2	4 (2.3)	0	4 (28.6)	
Tick removal				<0.001 <sup>a</sup>
Doctor	167 (97.1)	158 (100)	9 (64.3)	
Patient/relatives	5 (2.9)	0	5 (35.7)	
Symptoms				
Fever	124 (72.1)	111 (70.3)	13 (92.9)	0.116 <sup>b</sup>
Subfebrile fever	48 (27.9)	47 (29.7)	1 (7.1)	0.323 <sup>b</sup>
Abdominal pain	69 (40.1)	63 (39.9)	6 (42.9)	0.827 <sup>b</sup>
Diarrhea	60 (34.9)	55 (34.8)	5 (35.7)	>0.999 <sup>b</sup>
Muscle/joint pain	30 (17.4)	25 (15.8)	5 (35.7)	0.073 <sup>b</sup>
Headache	29 (16.9)	26 (13.5)	3 (21.4)	0.708 <sup>b</sup>
Dizziness	28 (16.3)	26 (16.5)	2 (14.3)	<0.999 <sup>b</sup>
Dizziness				
Nausea/vomiting	24 (14)	21 (13.3)	3 (21.4)	0.418 <sup>b</sup>
Impaired consciousness	13 (7.6)	8 (5.1)	5 (35.7)	0.002 <sup>b</sup>
Impaired consciousness				
Others*	26 (15.1)	23 (14.6)	3 (21.4)	0.448 <sup>b</sup>
Bleeding	150 (87.2)	136 (86.1)	14 (100)	0.135 <sup>b</sup>
Symptoms related to bleeding				
Echymosis	76 (44.2)	63 (39.9)	13 (92.9)	<0.001 <sup>a</sup>
Epistaxis	67 (39)	59 (37.3)	8 (57.1)	0.145 <sup>b</sup>
Gingival bleeding	31 (18)	26 (16.5)	5 (35.7)	0.137 <sup>b</sup>
Petechiae	100 (58.1)	90 (57)	10 (71.4)	0.293 <sup>b</sup>
Pleural effusion	4 (2.3)	0	4 (28.6)	<0.001 <sup>a</sup>
Hematuria	13 (7.6)	7 (4.4)	6 (42.9)	<0.001 <sup>a</sup>
Hematemesis	2 (1.2)	0	2 (14.3)	0.006 <sup>b</sup>
Melena	2 (1.2)	0	2 (14.3)	0.006 <sup>b</sup>
Vital signs				
Fever (°C)	38.4 (37.5-40)	38.2 (37.5-39)	39.8 (38.2-40)	<0.001 <sup>a</sup>
SBP (mmHg)	120 (90-150)	120 (90-150)	110 (90-120)	0.009 <sup>b</sup>
DBP (mmHg)	60 (40-75)	60 (50-75)	57.5 (40-60)	<0.001 <sup>a</sup>
Pulse rate (bpm)	80 (76-118)	80 (76-98)	110 (78-118)	<0.001 <sup>a</sup>
Laboratory parameters				
WBC (x10 <sup>3</sup> /mm <sup>3</sup> )	15 (13-22)	15 (13-19)	20 (19-22)	<0.001 <sup>a</sup>
Platelet (x10 <sup>3</sup> /mm <sup>3</sup> )	89 (40-98)	89 (75-98)	41.5 (40-45)	<0.001 <sup>a</sup>
INR	1.5 (1.3-4.6)	1.5 (1.3-3.9)	4.05 (3.5-4.6)	<0.001 <sup>a</sup>
AST (IU/L)	160 (90-1255)	156 (90-960)	984 (838-1255)	<0.001 <sup>a</sup>
ALT (IU/L)	133 (63-1204)	126 (63-912)	929 (759-1204)	<0.001 <sup>a</sup>

a: Mann-Whitney U test, b: Fisher's Exact test, c: Chi-Squared test, Others\*: sore throat, backache, weakness, SBP: systolic blood pressure, DBP: diastolic blood pressure, WBC: white blood cell, INR: international normalized ratio, AST: aspartate aminotransferase ALT: alanine aminotransferase

Table 2: Area, cut-off, sensitivity and specificity of vital signs and blood values

Variable (s)	Area	Cut-off		Asymptotic 95% CI	
		Sensitivity	Specificity	Lower Bound	Upper Bound
WBC (x10 <sup>3</sup> /mm <sup>3</sup> )	0.999	18500	100	0.996	1.000
Platelet (x10 <sup>3</sup> /mm <sup>3</sup> )	>0.999	60000	100	1.000	1.000
INR	0.997	2.75	100	0.992	1.000
AST (IU/L)	0.992	682	100	0.982	1.000
ALT (IU/L)	0.993	607.5	100	0.983	1.000
Fever (°C)	0.888	38.7	69.2	0.785	0.991
SBP (mmHg)	0.701	115	78.6	0.579	0.823
DBP (mmHg)	0.855	52.5	78.6	0.758	0.951
Pulse rate (bpm)	0.868	82.5	84.6	0.054	0.257

CI: Confidence Interval, WBC: white blood cell, INR: international normalized ratio, AST: aspartate aminotransferase ALT: alanine aminotransferase, SBP: systolic blood pressure, DBP: diastolic blood pressure

Table 3: Logistic regression analysis of factors affecting mortality

	B	S.E.	Wald	P-value	Odds ratio
Tick location	-2.475	6830.711	0.000	1.000	0.084
Time to hospital admission (day)	0.126	3774.177	0.000	1.000	1.134
Number of ticks	-0.492	38032.052	0.000	1.000	0.612
Tick removal	-6.024	42157.078	0.000	1.000	0.002
Pleural effusion	1.522	44221.525	0.000	1.000	4.580
Hematemesis	-2.617	68776.325	0.000	1.000	0.073
Fever (°C)	0.634	10838.984	0.000	1.000	1.885
SBP (mmHg)	0.023	414.191	0.000	1.000	1.023
DBP (mmHg)	0.007	908.723	0.000	1.000	1.007
Pulse rate (bpm)	0.052	650.395	0.000	1.000	1.054
WBC (x10 <sup>3</sup> /mm <sup>3</sup> )	0.001	4.271	0.000	1.000	1.001
Platelet (x10 <sup>3</sup> /mm <sup>3</sup> )	-0.001	0.683	0.000	0.999	0.999
INR	2.313	8035.493	0.000	1.000	10.106
AST (IU/L)	0.041	186.557	0.000	1.000	1.042
ALT (IU/L)	-0.040	188.781	0.000	1.000	0.961
Impaired consciousness	-1.430	15969.314	0.000	1.000	0.239
Echymosis	-0.783	10005.927	0.000	1.000	0.457
Melena	5.792	55499.290	0.000	1.000	327.655
Hematuria	-2.575	12429.540	0.000	1.000	0.076
Constant	-14.249	531592.665	0.000	1.000	0.000

B: regression coefficient, S.E.: Standard error of the coefficient, SBP: systolic blood pressure, DBP: diastolic blood pressure, WBC: white blood cell, INR: international normalized ratio, AST: aspartate aminotransferase ALT: alanine aminotransferase

## Discussion

CCHF symptoms are observed only in human hosts. The disease progresses along four stages: incubation, pre-hemorrhagic stage, hemorrhagic stage and healing stage [2]. The increased viral load in the liver and lymphoid tissues gradually leads to coagulopathy, subsequently leading to thrombocytopenia, organ failure and shock [7]. The disease severity is associated with the viral load and severity of bleeding [2,8]. Furthermore, it has been reported that CCHF can lead to organ failure by causing apoptosis in many cell types of endothelial and parenchymal origin [4].

Saksida et al. [9], Hasanoğlu et al. [7] and Yilmaz et al. [10] reported the mortality rate associated with CCHF to be 27.5%, 8.1%, and 5%, respectively. The mortality rate was reported to be lower in countries such as Turkey and Russia, where CCHF is endemic, but the underlying reasons have not yet been elucidated [5,6]. In agreement with findings in the literature, the mortality rate was found to be 8.1% in the present study. We believe that differences in vector, host or pathogen structure and/or administered treatments result in different mortality rates.

Studies have shown that the disease occurs in all age groups and is more common in men [7,11]. The proportion of male patients in the present study was consistent with previous findings, and no relationship was found between age, gender and mortality. We believe that all age groups are at similar risk because although the elderly and children do not actively work in Turkey, they visit rural or forested areas together with their families where they come in close contact with animals that carry ticks. The frequency of tick contact is higher in men because they work in fields and forested lands, whereas women usually perform household chores.

The incubation period begins after viral infection and lasts 3–7 days. Symptoms are not expected to manifest during this period. The pre-hemorrhagic stage begins after the incubation period and lasts 4–5 days, followed by the hemorrhagic stage, during which the patient develops bleeding-related symptoms [2,12]. In the present study, it was found that patients began to exhibit symptoms three days after tick removal, and non-survivors had a delayed admission to the emergency department. We believe that the patients did not present to the emergency department before three days because of the lack of any symptoms during the incubation period, and because they ignored the symptoms that occurred during the pre-hemorrhagic period. We believe that the non-survivors ignored the symptoms prior to the disease entering the hemorrhagic stage and attributed

their non-specific findings to other causes. Therefore, we attribute some of the patients' death to their inability to combat increased viral loads, bleeding, sepsis and shock. Some studies reported that fever observed during the pre-hemorrhagic period was the most common symptom, followed by asthenia, headache, anorexia and myalgia [7,10,12]. During the pre-hemorrhagic period, fever rises suddenly and can reach 40°C [12]. Hasanoğlu et al. [7] reported no relationship between high fever and mortality. Ahmeti et al. [1] reported that non-specific findings did not affect the clinical course of patients. In the present study, the most common symptom was fever, followed by abdominal pain and diarrhea. There was no relationship between non-specific findings and mortality. We found that patients who presented with impaired consciousness had a higher mortality rate. We believe that cytokines and interleukins secreted as a result of inflammation against the virus in the pre-hemorrhagic stage of infection are responsible for these symptoms. We believe that these symptoms are not associated with mortality because of the low viral load in the pre-hemorrhagic stage and no bleeding incidence. Furthermore, the cause of impaired consciousness may be secondary to sepsis or hemorrhagic shock, or it may be caused by minor intracranial hemorrhages that are not observed on imaging findings. Therefore, these patients have a higher mortality rate.

The hemorrhagic stage of CCHF results in either recovery or death. Bradycardia and hypotension may develop during this period because of sepsis, septic shock and hemorrhage [12]. Ahmeti et al. [1] reported that bradycardia and blood pressure played no role in determining the clinical course. In the present study, fever and heart rate were found to be higher and blood pressure was found to be lower in non-survivors. We believe that increases in fever and heart rate and decrease in blood pressure are a result of the elevated inflammation in response to the viral load and occurrence of superinfections and shock caused by sepsis and hemorrhage.

Previous studies reported that tick bites generally occur on the torso and extremities [11,13]. Uluğ et al. [11] reported that 74% of ticks were removed by a doctor and that fragmented tick tissues remained in cases where the ticks were removed by the patient or his/her relatives. They also reported more than one tick in 3% of the cases. Similar to findings in the literature, in the present study, the most frequent bite location was the torso and arms; more than one tick was present in 2.3% of the cases, and the tick was removed by the patient or his/her relatives in 2.3% of the cases. We found that the mortality rate was higher in cases in which the bite was located in the head and neck region, there was more than one bite, and the tick was not removed by a doctor. We believe that the torso and extremities are frequently bitten because of their large surface area, and because some patients are engaged in farm work, resulting in a higher frequency of tick contact, and because some patients use traditional treatment methods instead of visiting a doctor. We believe that mortality is higher in cases of tick bites in the head and neck region owing to higher blood circulation in this region. Additionally, mortality is higher in cases with more than one tick bite owing to higher viral load and a higher risk of contracting CCHF. Mortality is also higher in cases in which the tick is not removed by a healthcare professional because tick tissues may

remain on the skin and tick saliva may enter the body in cases where the tick is squeezed during removal.

The main cause of bleeding in CCHF is endothelial damage, decreased production of coagulation factors in the liver, and destruction of blood cells [4]. The tendency for bleeding increases in patients with CCHF and extensive bleeding occurs especially in subcutaneous tissues; additionally, epistaxis, gingival bleeding, hematuria, hematemesis, vaginal bleeding and bleeding occur in internal organs [3,14,15]. Gök et al. [12] reported that hematuria, hematemesis, hematochezia, melena and vaginal bleeding were common findings in patients with CCHF, and bleeding in the lungs, brain and peritoneum were rarely observed. Saksida et al. [9] reported bleeding in all patients with a severe clinical course or fatal outcome. Hasanoğlu et al. [7] reported that 25% of cases had bleeding and emphasized that bleeding was as important as the viral load for mortality. They also reported that patients who developed petechiae, melena, epistaxis and hematuria had a higher mortality rate. Ahmeti et al. [1] reported that patients with bleeding had a poor clinical picture. In the present study, we found that bleeding occurred in 87.1% of the cases and the risk of mortality increased in cases with bleeding in regions with high blood loss, such as the lungs, intestinal system and bladder. We believe that the frequency of bleeding increases in patients with CCHF because of impairment or decreased production of coagulation factors and thrombocytopenia. We believe that hemorrhagic shock develops as a result of hemorrhage in patients with CCHF and deteriorated hemodynamics increases mortality.

Because there is no effective vaccine or treatment for CCHF, Bartolini et al. [16] emphasized the importance of laboratory analysis in the detection of CCHF outbreaks, in monitoring patients with fever of unknown causes and in the evaluation of the clinical status of patients.

Yılmaz et al. [10] reported that thrombocytopenia and leukopenia are among the primary laboratory findings of CCHF and that thrombocytopenia developed in 93.2% of cases and leukopenia developed in 88.9% of cases. Hasanoğlu et al. [7] found that platelet and leukocyte counts were significantly lower in non-survivors but the WBC count was not significant in predicting mortality. Ahmeti et al. [1] reported that patients with a leukocyte count higher than 7700/ $\mu$ L had a poor clinical status and thrombocyte count was not associated with the clinical status. Swanepoel et al. [17] reported that WBC counts higher than 10,000/mm<sup>3</sup> and/or platelet counts lower than 20000/mm<sup>3</sup> were associated with poor prognosis. In the present study, thrombocytopenia and elevation in WBC counts were observed in non-survivors. We believe that decreased platelet counts occur due to deterioration of cell structure. We believe that sepsis and increased viral load leads to increased WBC counts, increased platelet destructions and decreased platelet production due to organ failure.

Yılmaz et al. [10] reported elevated transaminase levels in 85.9% of patients with CCHF. Hasanoğlu et al. [7] reported that transaminase levels and INR values were increased further in non-survivors. Ahmeti et al. [1] reported that AST, ALT and thrombocytopenia played no role in determining the clinical status; however, they used low cut-off values for AST and ALT (168 U/mL and 147 U/mL, respectively). Saksida et al. [9]

reported that transaminase levels of non-survivors were higher and their partial thromboplastin time was longer. Swanepoel et al. [17] reported that AST and ALT levels above 200 U/L and 150 U/L, respectively, indicated poor prognosis. Consistent with findings in the literature, in our study, INR was prolonged and AST and ALT levels were high. We believe that excessive viral loads and sepsis cause more cell damage and apoptosis in the liver, and therefore, INR and AST and ALT levels are higher in non-survivors.

Hasanoğlu et al. [7] found that AST had a specificity of 87% and sensitivity of 79%, ALT had a specificity of 91% and sensitivity of 71%, platelet count had a specificity of 61% and sensitivity of 86% and INR had a specificity of 81% and sensitivity of 93% for predicting prognosis. In our study, the sensitivity was 100% and specificity was 98.1%–100% for the determined cut-off values. The high sensitivity and specificity of AST, ALT and INR levels above the determined cut-off values in the blood tests and platelet count below the determined cut-off value may be indicative of mortality in these patients.

To our knowledge, there is no study in the literature evaluating the sensitivity and specificity of vital parameters for CCHF. For vital parameters, the sensitivity was 69.2%–84.6% and specificity was 56.3%–96.2%. We believe that vital parameters can be used to predict mortality in patients with CCHF.

Our study has several limitations. First, this study is a single-center, retrospective study. Second, the number of patients in study groups is small at some level. Further large-scale, multicenter studies are needed.

### Conclusion

The occurrence of bleeding in some regions is one of the main factors for mortality. Factors such as the number of ticks, the number of people removing the ticks and location of the bite were found to affect mortality. We believe that blood tests and vital parameters can be used to predict mortality in patients with CCHF.

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