The early prediction of fatality in Crimean Congo hemorrhagic fever patients

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Crimean-Congo hemorrhagic fever (CCHF) is an important viral hemorrhagic fever from *bunya viridea* family that can cause fatality. The pathogenesis of the disease is not completely known, and its vascular endothelial damage is considered as the basic pathology. Fatality rates of the disease vary between 3-30%.[1] In Turkey, between 2002-2009 there were 4553 affected patients recorded, and 218 deaths (4.89%) were observed.[2] Thrombocytopenia, anemia, and elevated liver transaminase levels can be observed, since the reticuloendothelial system is affected in patients. The present study has been carried out in Yozgat region, which is endemic of the disease.[1] Patients with progressive course are generally transferred to the tertiary care hospitals, since intensive care conditions, and supply of blood products are not adequate in this region. The objective of this study is to evaluate patients with biochemical and hematological values within the first 2 days of the disease, and to be able to carry out an early prediction on patients, whether they should be transferred to tertiary care hospitals.

The current study was carried out retrospectively with CCHF patients in Yozgat region, which is located at the middle part of Turkey, on September 2008 to September 2010. The study was carried out at Sorgun State Hospital, Yozgat, Turkey. The diagnosis was established in the reference laboratory by polymerase chain reaction (PCR), and enzyme linked immunosorbent assay (ELISA) methods. Patients were included in the study if they had any biochemical, or hematological laboratory results within the first 2 days after the onset of symptoms. The exclusion criteria were: history of chronic liver diseases, which can increase aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels, hematologic diseases, and drug usage that can affect hematologic values. Demographic information was noted in the first section of the form prepared for record and follow-up, and the second part was used for laboratory values. Patients were divided into 2 groups: Group 1 - fatal patients; and Group 2 - nonfatal patients.

Data were analyzed using the Statistical Package for Social Sciences version 15 (SPSS Inc., Chicago, IL, USA). Chi-square and Mann-Whitney U tests were used for comparisons. Results of analysis was accepted as significant if $p<0.05$.

In Yozgat region, 352 patients were diagnosed with CCHF, and 17 (4.8%) of them died in 2008-2010. A total of 244 patients (15 of them died) were included in the present study. The average age of nonfatal patients was found to be 38.46 ± 19.07, while that of the fatal patients was 45.47 ± 19.67, and the difference was not statistically significant ($p=0.234$). Fatigue (97.4%) was the most common complaint among patients, and fever (86.9%), headache (79.4%), myalgia (78.4%), nausea-vomiting (68.1%), and diarrhea (27.4%) were observed in reducing frequencies. When the laboratory values of patients were examined, an elevation in white blood cell count (WBC), AST, ALT, lactate dehydrogenase (LDH) and creatine kinase (CK), and a decline in thrombocyte values, and a prolonging in prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR) values were observed in dead patients. The difference between the 2 groups for these laboratory values (except CK values) was found to be statistically significant (**Table 1**).

In our country, the number of CCHF cases increases every year.[2] Precautions to be taken in endemic regions such as Yozgat are important in terms of public health. Hospitals with advanced intensive care conditions and blood products transfusion facilities in Yozgat region are limited. For that reason, patients are transferred to tertiary care hospitals. While transfers can be late for some patients, unnecessary transfers are made for many patients. In CCHF patients, many studies have been conducted to predict fatality.[3-5] Many of those studies were reported from Turkey. However, all of those studies were conducted in tertiary care hospitals and laboratory values of patients within the first 5 days of the disease were used for analysis. In our study, patients were evaluated according to laboratory values within the first 2 days of the disease.

In the present study, exhaustion, fever, headache, and myalgia were most commonly observed complaints in patients, perfectly agreeing with the literature.[3-5] Additionally, a similar relationship with fatality was observed in other studies conducted with elevated ALT, AST, and LDH. However, laboratory values in our study were closer to normal ranges than that reported in other studies from Turkey.[3-5] The reason for this findings may be the early onset of laboratory tests. The CK was not statistically significant in our study. In the literature, there are similar studies where CK is not significant,[4] as well as ones where it is significant.[3,5] In the studies where prolonged PT and aPTT values were examined, it was observed to be related with fatality as in our study.[4,5]

Table 1 - Comparison of laboratory values of fatal and non-fatal patients.

Laboratory tests	Non-fatal patients n=229	Fatal patients n=15	*P*-value
	Average (standard deviation)		
White blood cell count	3422.52 (1894.37)	8043.63 (6247.63)	0.002
Thrombocyte	105614.30 (49404.50)	55461.54 (51973.7)	0.001
Aspartate aminotransferase	139.00 (196.94)	1017.69 (1794.96)	<0.001
Alanine aminotransferase levels	71.74 (81.78)	344.07 (518.28)	0.011
Lactate dehydrogenase	431.23 (438.34)	2957.91 (3614.30)	<0.001
Creatine kinase	409.65 (504.06)	474.71 (615.40)	0.532
Prothrombin time	14.92 (2.54)	22.48 (4.62)	<0.001
International normalized ratio	1.07 (0.21)	1.74 (0.41)	<0.001
Activated partial thromboplastin time	40.65 (9.99)	65.94 (30.88)	0.004

In conclusion, in this study, AST, ALT LDH, PT, aPTT, INR, WBC, and thrombocyte values were determined as predictive values of fatality in line with previous studies. In this study, the laboratory findings of the patients only from our region were evaluated. Furthermore, we could not reach all the laboratory values of some patients. Hence, these are the limitations of this study. However, we believe that those laboratory values in the first 2 days are important, especially that the values in this study are closer to normal ranges than other studies reported from Turkey. The medical equipments of hospitals in endemic regions are limited. In that case, which patients should be transferred to more equipped hospital becomes more important. We believe that being able to predict, which patients will have a fatal course at the very beginning is important, and thus, particularly in the determination of transfers, and more comprehensive studies are needed in this context.

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