Procalcitonin Level and Its Predictive Effect on Mortality in Crimean-Congo Hemorrhagic Fever Patients

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SUMMARY: Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal disease which is endemic to Turkey. We aimed to investigate the procalcitonin levels and their prognostic value over fatality in CCHF patients. The sera were harvested from patients who were diagnosed with CCHF within the first 2 days of the onset of their symptoms. The patients were divided into 2 groups according to their survival status: fatal or non-fatal. The biochemical and hematological parameters were studied in the Biochemistry Laboratory of Sorgun City Hospital. The sera were stored at −80°C until testing for procalcitonin, and the procalcitonin levels were assayed by ELISA at the Biochemistry Laboratory of Kirikkale University. Forty-eight patients were included in the study, with 8 and 40 patients in the fatal and non-fatal groups, respectively. While the procalcitonin level was high in all patients in the fatal group, the same was observed in 30 patients in the non-fatal group (75%). The mean value of procalcitonin was 1.12 ng/ml in the fatal group and was 0.21 ng/ml in the non-fatal group (P = 0.003). According to the results of our study, the procalcitonin levels in the first 2 days of the onset of the symptoms might be helpful for predicting fatality in CCHF patients.

INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal viral disease which is endemic to Turkey, with a fatality rate of 5% (1,2). Although the pathogenesis of the disease is yet to be fully understood, vascular endothelial damage is the most serious pathological sign. Additionally, usually there is deterioration in the biochemical and hematological parameters of the patients (3). The procalcitonin level usually increases in bacterial infections and is more likely to increase to very high levels in sepsis (4). However, the procalcitonin level is usually normal in viral diseases (5). Despite CCHF being a viral disease, many studies have reported the elevation of cytokines and adhesion molecules during the course of this disease (6–10), and multiple organ failure. This result in disseminated intravascular coagulation, which is common in fatal cases (6). In the present study, we aimed to evaluate the procalcitonin level and its predictive effect on mortality in CCHF patients.

MATERIALS AND METHODS

This study was conducted in the Sorgun District in the Yozgat province in Turkey. Ethical approval was obtained from the Kirikkale University Clinical Research Ethical Committee. After receiving written consent from the patients, the sera were harvested from those diagnosed with CCHF using the positive IgM or polymerase chain reaction results tested in the reference laboratory of Turkey. All the serum samples were obtained within the first 2 days of the onset of their symptoms. Further, the patients’ biochemical and hematological parameters were tested on admission, in the Laboratory of the Sorgun City Hospital. The remaining sera were stored at −80°C until testing for procalcitonin and they were tested with commercial ELISA kits (Elecys BRAHMS PCT, Roche, Mannheim, Germany), according to the manufacturer’s recommendations, at the Biochemistry Laboratory in Kirikkale University. The demographics of the patients and the course of their disease were recorded. The patients were divided into 2 groups according to their survival status: fatal or non-fatal. A procalcitonin level of >0.05 ng/ml was accepted as high.

The Statistical Package for the Social Sciences (SPSS version 15.0) was used for the statistical analyses and the Mann-Whitney U and chi square tests were used to compare the groups. Additionally, a Spearman test was used for correlation analysis, P < 0.05 was accepted as statistically significant.

RESULTS

A total of 48 patients were included in the study. Thirty-one of the patients (64.5%) were male and 17 of them (35.5%) female. The average age of the patients was 37.7 years (minimum: 3 years, and maximum: 81 years). Eight of the patients (16.6%) were fatal and 40 of them (83.4%) were non-fatal. While the mean aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP), and procalcitonin...
levels were higher, the albumin, hemoglobin, and platelet levels were lower in the fatal group than in those in the non-fatal group. Additionally, the activated partial thromboplastin time (aPTT) was greater in the fatal group than in the non-fatal one (Table 1). Further, the differences in AST, ALT, CRP, albumin, platelet levels, and aPTT were statistically significant.

Overall, the procalcitonin level was high in 38 patients (79.2%). They were also high in all of the 8 fatal cases and 30 of the non-fatal cases (75%), but the differences were not significant ($P = 0.112$). While the average procalcitonin level was 1.12 ng/ml in the fatal group, it was 0.21 ng/ml in the non-fatal group, and the differences was statistically significant ($P = 0.003$).

The procalcitonin level showed a positive correlation with CRP ($r = 0.489, P = 0.008$) (Fig. 1) Study patients had had no bacterial co-infections during their course of the disease.

Table 1. The biochemical and hematological parameters of patients

|                  | Non-fatal mean (SD) | Fatal mean (SD) | $P$ value |
|------------------|---------------------|-----------------|-----------|
| AST (U/l)        | 91.8 (230.6)        | 415.7 (220.5)   | $<0.001$  |
| ALT (U/l)        | 52.7 (81.3)         | 130.0 (88.9)    | 0.002     |
| CRP (mg/l)       | 25.9 (20.6)         | 61.1 (35.4)     | 0.020     |
| Procalcitonin (ng/ml) | 0.21 (0.28)     | 1.12 (1.24)     | 0.003     |
| Albumin (g/dl)   | 4.2 (0.5)           | 3.6 (0.5)       | 0.017     |
| Globulin (g/dl)  | 3.2 (0.5)           | 3.3 (0.6)       | 0.352     |
| Hemoglobin (g/dl)| 13.3 (1.7)          | 12.3 (1.9)      | 0.183     |
| Platelets ($\times 10^9$/l) | 132.075 (38.697) | 25.875 (23.648) | $<0.001$  |
| aPTT (second)    | 40.9 (8.1)          | 77.0 (29.7)     | 0.034     |

AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; aPTT, activated partial thromboplastin time; SD, standard deviation.

Fig. 1. The positive correlation between procalcitonin and C-reactive protein levels.

DISCUSSION

CCHF is still a serious public health issue in Turkey. Although the pathogenesis of the disease is yet to be fully explained, vascular endothelial damage due to the excessive secretion of cytokines and adhesion molecules is thought to be the most likely mechanism (6).

Additionally, the biochemical and hematological parameters are usually affected in CCHF patients. Elevated liver enzymes, prolonged bleeding time, and decreased platelet and leukocyte levels have been observed in many studies (11–15). In most of these studies, majority of these parameters were found to be related to the prognosis. Similarly, in our study, the AST and ALT levels were higher; albumin, hemoglobin, and platelet levels were lower; and aPTT was greater in the fatal than the non-fatal group. Further, all these differences were significant, except for the hemoglobin level.

CRP, which is an acute phase reactant, increases depending on the secreted cytokines due to surgery, tissue damage, or sepsis (16). Even though the CRP level is not usually elevated in viral diseases, an elevated CRP level has been reported in some viral diseases (17). It has also been reported that the CRP level is higher in fatal cases than in non-fatal ones in CCHF (15,18). Similarly, in our study, the CRP level was high in all patients, but it was higher in fatal than in non-fatal patients.

The procalcitonin molecule is primarily synthesized from the C cells of the thyroid gland. In cannot be detected in the sera of healthy persons, but rapidly increases with the onset of an infection (19).

It usually increases in bacterial infections rather than viral ones (5). It is thought that the increase in the procalcitonin level is related to the increase in the cytokine level (16,20).

We could find only one study regarding the relation-
ship between hemorrhagic fever diseases and the procalcitonin level in the literature published in English. In this study, Jereb et al. found high a procalcitonin level in patients with the Hanta virus infection (16). Although several studies have reported high levels of cytokines and adhesion molecules in CCHF patients, to the best of our knowledge, no study has evaluated the level of procalcitonin in such patients (6–10). In our study, the average procalcitonin level was high in both fatal and non-fatal groups, but it was significantly higher in the fatal rather than non-fatal patients. The procalcitonin level was high in all the fatal patients and in 75% of the non-fatal patients. Further, there was a positive correlation between procalcitonin and CRP levels.

Although CCHF is a viral disease, the procalcitonin level increased in correlation with the CRP level in patients. Thus, as the procalcitonin level was higher in fatal rather than non-fatal patients, and all those with a normal procalcitonin level within the first 2 days of the disease survived, procalcitonin level in the early stages of the disease might be helpful for predicting fatality in CCHF patients. However, more detailed investigations are needed because of the limited number of patients in this study.

Conflict of interest None to declare.

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