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ORIGINAL ARTICLE

Is blood group associated with mortality in Crimean-Congo Hemorrhagic Fever?

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ABSTRACT

Objectives: In this trial, our purpose was to determine the distribution of blood groups in Tokat region and Crimean-Congo hemorrhagic fever (CCHF) patient group and to investigate the impact of blood groups on fatal prognosis of the disease.

Material and Method: Demographic and laboratory values and blood groups of patients were recorded. In addition, distribution of blood groups among blood donors who referred to the blood center during same time interval was determined.

Results: Distribution of blood groups among CCHF patients and donors in blood center were found to be similar to Turkish data (P>0.05). On the other hand, a discrepancy was determined in blood group distribution of CCHF patients with a fatal outcome, with a significantly high rate of AB Rh negative blood group in this patient group (P<0.001).

Conclusion: We suggest that blood group may be associated with mortality in CCHF patients and AB Rh negative blood group may be an indicator of poor prognosis. *J Microbiol Infect Dis 2011;1(3):118-121*

Key words: Crimean-Congo hemorrhagic fever, blood groups.

Kırım-Kongo Kanamalı Ateşinde kan gruplarının mortalite ile ilişkisi var mı?

ÖZET

Amaç: Bu çalışmada, Tokat Bölgesinde ve Kırım-Kongo kanamalı ateşi (KKKA) hastalarında kan grubu dağılımını belirlemeyi ve kan gruplarının hastalığın fatal seyretmesi ile ilişkisi araştırıldı.

Gereç ve yöntem: Hastaların demografik özellikleri ve kan grubu dağılımları kaydedildi. Kan merkezine aynı dönemde başvuran kan donörlerinin kan grupları da ek olarak kaydedildi.

Bulgular: KKKA hastalarının ve kan merkezinin kan grubu dağılımları Türkiye verileri ile benzerdi (P>0.05). Ancak, fatal seyreden KKKA hastalarında AB Rh negative kan grubunun diğer hastalara göre belirgin yüksek olduğu görüldü (P<0.001).

Sonuç: KKKA hastalarında kan gruplarının mortaliteyle ilişkisinin olabileceğini, AB Rh negatif kan grubunun kötü prognozu gösterebileceğini düşünüyoruz.

INTRODUCTION

Crimean-Congo Hemorrhagic fever (CCHF) is a tick-borne zoonotic disease caused by the Nairovirus and belonging to the genus Bunyavirus of Bunyaviridae family.[1,2] The disease is prevalent in a wide geographic area encompassing Asia, Eastern Europe, Africa, and Russia.[3,4] Since 2002 it has been seen in central, northern, and eastern regions of Turkey.[5] CCHF is transmitted to humans via tick bites and may lead to symptoms of fever, nausea, asthenia, headache, abdominal pain, diarrhea, myalgia, petechia, and bleeding. CCHF may present with various clinical manifestations; extending from acute, self-limited disease to severe, progressive, hemorrhagic fevers which results in death.[4]

In trials investigating factors associated with mortality in CCHF, the criteria for a poor prognosis were shown to be advanced age, leukocytosis, elevated ALT and AST, and a prolonged PT and aPTT.[6]

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The treatment of CCHF is symptomatic. No specific recommendations are available for ribavirin therapy. Blood and blood product transfusions should be performed as required.[6] Currently, more than 600 antigenic structures among 29 blood groups have been described in humans.[7] The relationship between CCHF and certain blood groups identified as significant for a number of diseases is not clear.[8]

In this trial, apart from well-known indicators of poor prognosis, we aimed to investigate the association of blood group with mortality and its relationship to prognosis in CCHF, an acute and potentially fatal disease with no definite treatment.

MATERIALS AND METHODS

Patients and methods

A total of 292 patients with a confirmed diagnosis of CCHF referring to Tokat State Hospital during 2007-2010 were enrolled in this trial. Patients enrolled during 2010 were evaluated prospectively while the remaining patients were evaluated retrospectively. Among patients referring to the hospital, cases with clinical and laboratory findings suggestive of CCHF and/or a history of tick bite were hospitalized.

Venous blood samples of patients were transferred to Refik Saydam National Hygiene Center Laboratory for confirmation of diagnosis. IgM positive cases with confirmed CCHF virus PCR were enrolled in the trial. Epidemiological and demographic characteristics, clinical and laboratory values and blood groups of each patient were recorded. Since leukocyte and platelet counts varied between initial referral and follow-up examinations, initial value and the minimum value during follow-up were recorded. In addition, blood group recordings of 28,154 blood donors who were referred to Tokat State Hospital during 2007-2010 were also evaluated.

Statistical Analysis

Statistical analysis was performed by SPSS software 15.0 for Windows (Chicago, IL, USA). Kolmogorov-Smirnov test was utilized to evaluate normal distribution among variables. The correlation between blood groups and mortality was assessed by Fisher's exact test. The two independent sample t test or Mann Whitney U test was used to compare continuous variables between the two groups. Continuous variables were presented as means (standard deviation [SD]) or as medians (interquartile range [IQR]). A P value of less than 0.05 was considered to be statistically significant.

RESULTS

A total of 292 patients with a confirmed diagnosis of CCHF referring to Tokat State Hospital during 2007-2010 were included into this study. Demographic characteristics and laboratory findings of the patients with a diagnosis of CCHF are shown in Table 1.

Table 1. Demographic Characteristics and Laboratory Findings of Patients

	Patient (n=292)
Age, mean (SD)	46.6 ± 17.9
Male patients (%)	156 (53.4)
ALT, median (IQR)	45 (27-92)
AST, median (IQR)	84 (42-171)
WBC median (IQR)	2700 (2000-3775)
Hemoglobin, median (IQR)	13.95 (12.6-15)
Platelet, mean (SD)	92.83±49.56
PT, median (IQR)	13.45 (10.5-35)
aPTT, median (IQR)	37 (30-43.65)

WBC: Leukocytes; WBC: Least value of leukocytes; ALT: Alanine transaminase; AST: Aspartate transaminase; PT: Prothrombin time; aPTT: Active partial thromboplastin time

Table 2. Comparison of blood groups in Tokat Region and among CCHF patients

Blood Groups	Blood Center N (%)	All Patients n (%)
0 Rh Negative	1185 (4.20)	29 (9.93)
0 Rh Positive	7624 (27.07)	71 (24.31)
A Rh Negative	1705 (6.05)	13 (4.45)
A Rh Positive	11043 (39.22)	104 (35.61)
B Rh Negative	532 (1.88)	6 (2.05)
B Rh Positive	3926 (13.94)	41 (14.04)
AB Rh Negative	291 (1.03)	7 (2.39)
AB Rh Positive	1848 (6.56)	21 (7.19)

Table 3. Comparison of blood groups in recovered cases and fatal case

Blood Group	Recovered N (%)	Died N (%)	*P*
0 Rh Negative	29 (10.4)	0	0.221
0 Rh Positive	69 (24.7)	2 (15.38)	0.443
A Rh Negative	13 (4.7)	0	0.427
A Rh Positive	98 (35.1)	6 (46.15)	0.418
B Rh Negative	6 (2.2)	0	0.594
B Rh Positive	40 (14.3)	1 (7.69)	0.501
AB Rh Negative	4 (1.4)	3 (23.07)	<0.001
AB Rh Positive	20 (7.2)	1 (7.69)	0.943

Upon comparison of age, gender and laboratory values (ALT, AST, WBC, hemoglobin, platelet count, PT and PTT) of the 292 patients in terms of blood groups, the platelet counts of cases with 0 Rh positive blood group was found to be higher than patients of the B Rh positive blood group (P=0.003). No difference was seen between other blood groups in terms of age, gender and laboratory values (P>0.05).

Among 292 patients, 279 (95.5%) were recovered and a fatal outcome was observed in 13 patients (4.45%). Distribution of blood groups among patients with a fatal outcome was different from recovered cases. A high rate of AB blood group was observed among fatal patients as compared to the normal population and study group. The AB Rh negative blood group was found to have a rate of 1.03% and 2.9% in blood center samples and in overall CCHF patients, respectively while the rate was 23.07% in CCHF patients with a fatal outcome. The difference was statistically significant (p<0.001).

The distribution and comparison of blood groups in blood donors and patients are shown in Table 2. In a total of 7 patients of the AB Rh negative blood group, a fatal outcome was observed in 3 patients (23%). The two-tailed P value equals 0.002.

DISCUSSION

This study indicated that the AB Rh negative blood group is associated with mortality in CCHF, a potentially fatal disease leading to hemorrhagic fever. But the small number of fatal outcomes is so low that new studies with larger groups are necessary to investigate and derive better results. Pathogenesis is not clearly defined in CCHF but clinical evaluations and biochemical tests were shown to be utilized in assessment of prognosis. Nevertheless, this is the first trial indicating the significance of blood groups in CCHF.

CCHF is seen in more than 30 countries around the world and it was first reported in 2002 in Turkey. In Turkey, it's most frequently seen in Tokat, Sivas, Gumushane, Amasya, Yozgat and Corum.[9] The current trial was conducted in Tokat, which is an endemic area for CCHF.

CCHF, a viral zoonotic disease, progresses with coagulopathy and may lead to mortality in two weeks with a rate of 5-30%.10 Main laboratory findings are leucopenia, thrombocytopenia and prolonged PT and aPTT.[6] In trials conducted on CCHF, leukocytosis, elevated ALT and AST, PT and aPTT and LDH (lactate dehydrogenase) values were used in assessing prognosis.[4,11,12] No information is available in the literature indicating the role of blood groups in the prognosis of CCHF. In the current trial, high ALT and AST levels and low leukocyte and platelet values were observed, in accordance with the results of other trials.

In addition, no trial was conducted on blood groups in the Tokat region. In this trial, the record of the leading blood center of our region, which is an endemic area for CCHF, was evaluated. In a trial assessing blood groups from various centers in Turkey, the rate of group 0 was found to be 32.7%, group A was 42.8%, group B was 16.5%, and group AB was 8.0%13; no significant difference was seen between distribution of blood groups among CCHF patients and values of the Tokat region and Turkey overall.

Though more than 600 antigenic structures are present in 29 different blood groups in humans, only ABO and Rh antigenic structures are utilized in transfusion medicine. Available information on blood group distribution in a certain city is extremely beneficial for individuals requiring blood transfusions and for healthcare employees of blood centers.[14]

Association of blood groups with a disease is mainly shown in venous thromboembolism. Patients with the 0 blood group were reported to carry a higher risk than cases with a non-0 (group A, B, or AB) blood groups and this finding was postulated to be associated with von Willebrand factor present in 0 blood group.[15,16,17]

In studies conducted on patients with Vibrio cholera infection, mortality was shown to be significantly increased in patients with 0 blood groups, as compared to non-0 groups.[18,19] In a study performed on children infected with Plasmodium falciparum, rosette formation in erythrocytes was decreased in children with 0 blood groups, as compared to children with non-0 blood groups; in addition, vaso-occlusion and severe disease were found to be associated with blood groups.[20,21] The presence of valid information on the distribution of blood groups among patients and in this region, which is an endemic area for CCHF, and available data on specific blood groups in the patient population, is of critical importance.

In this study, the AB blood group was determined in 30.8% of patients with a fatal outcome and 23.07% of these cases were AB Rh negative. This blood group is observed less frequently in the population. The number of the people who died is so low that an exact result is difficult to achieve. In patients progressing with bleeding symptoms, accessing the required blood and blood products for this group may be problematic. Our study is retrospective, so we were unable to prove if the blood transfusion was enough to combat the disease, or if the transfusion was given at the appropriate time to help the patient.

In conclusion, a poor prognosis was observed among CCHF patients of the AB Rh negative blood group and hence, this specific blood group was indicated as an independent risk factor with an unfavorable contribution to mortality in CCHF. The number of patients that died is small and the data about the blood transfusion cannot be proven; thus, we cannot obtain absolute results. Further trials conducted on larger patient groups are required to confirm these results.

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