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Association of *Brucella* Infection with ABO Blood Groups in Children

Çocuklarda Kan Gruplarının *Brusella* Enfeksiyonu ile İlişkisi

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Abstract

Objective: Brucellosis is the most prevalent zoonotic infection worldwide. ABO blood groups have been associated with a number of infectious and non-infectious diseases. However, there is no study that investigated whether blood groups have an effect on the occurrence of *Brucella* infection among children.

Material and Methods: The files of 101 patients with a diagnosis of brucellosis, aged between 1 and 216 months, who applied to the pediatric infectious diseases outpatient clinic of a tertiary education and research hospital between January 2018 and August 2020, were retrospectively analyzed. The control group consisted of 204 pediatric patients who had no findings compatible with brucellosis or chronic disease, and whose blood group was performed for any reason.

Results: In the blood group evaluation, the most common blood group A was observed in the patient and control groups. No statistically significant difference was found in ABO blood groups between the two groups (p= 0.454).

Conclusion: This study showed that there was no difference in blood groups between pediatric patients with brucellosis and the control group.

Keywords: ABO blood types, brucellosis, children, Rh groups, zoonosis

Öz

Giriş: Bruselloz dünya çapında en yaygın zoonotik enfeksiyondur. ABO kan grupları, bir dizi bulaşıcı ve bulaşıcı olmayan hastalıkla ilişkilendirilmiştir. Ancak çocuklarda *Brucella* enfeksiyonu oluşumunda kan gruplarının etkisinin olup olmadığını araştıran bir çalışma bulunmamaktadır.

Gereç ve Yöntemler: Üçüncü basamak bir eğitim ve araştırma hastanesinin çocuk enfeksiyon hastalıkları polikliniğine Ocak 2018-Ağustos 2020 tarihleri arasında başvuran bruselloz tanılı yaşları 1-216 ay arasında değişen toplam 101 hastanın dosyası retrospektif olarak incelendi. Kontrol grubu olarak, bruselloz veya kronik hastalık ile uyumlu bulgusu olmayan, herhangi bir nedenle kan grubu bakılmış 204 çocuk hasta alındı.

Bulgular: Kan grubu değerlendirmesinde hasta ve kontrol grubunda en sık A kan grubu izlendi. ABO kan gruplarında iki grup arasında istatistiksel olarak anlamlı fark bulunmadı (p= 0.454).

Sonuç: Bu çalışma brusellozlu çocuk hastalar ile kontrol grubu arasında kan grupları açısından fark olmadığını göstermiştir.

Anahtar Kelimeler: ABO kan grupları, bruselloz, çocuklar, Rh grupları, zoonoz

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Introduction

Brucellosis is the most common zoonotic infection worldwide and is caused by *Brucella* species which are gram-negative bacteria (1). *Brucella* spp. infection affects more than 500.000 people annually and it is a major public health problem for the countries around the Mediterranean Basin, Asia, Africa, South America, Eastern Europe, Middle East as well as Türkiye. The prevalence of brucellosis depends on various factors such as region, dietary patterns, animal husbandry, and their impact has been shown by studies (2,3).

Differences in blood group antigen expression determine host susceptibility in chronic diseases and some infectious diseases. An association between ABO blood groups and a number of diseases including coronary heart disease, tumors, *Plasmodium falciforum* infection, *Helicobacter pylori* infection and hepatitis has been reported in the literature (4-11). To our best knowledge, there is no study between brucellosis and blood group antigens, except for the study by Mohsenpour et al. in 2015 in which she evaluated the association of brucellosis and blood group antigens in adults (12). The present study aimed to examine blood groups ABO in patients diagnosed with *Brucella* spp. infection in the childhood.

Materials and Methods

Our study included 289 patients who were followed up and treated for *Brucella* spp. infection by the pediatric infection clinic of a tertiary training and research hospital between January 2018 and August 2020. Clinical findings, laboratory, and blood group parameters of the cases were obtained by retrospective analysis of the files. One hundred and one cases whose blood group was checked for any reason were included in the study and 188 cases were excluded from the study because blood group results could not be obtained. The control group included 204 children who did not have clinical and laboratory findings compatible with brucellosis and/or any chronic disease, and whose blood group was checked for any reason in our hospital. Approval for the study was obtained from the institutional review board (Decision no: 2020/6-51).

Sera from children in the patient group were screened for *Brucella* using the Rose Bengal test (Biomedica Diagnostics, Canada). For the test, 50 µL of the patient serum was mixed with 50 µL of Rose Bengal antigen on a glass slide with white background using circular motion for four minutes to see whether an agglutination reaction has occurred. Samples with a visible agglutination were considered as positive. Next, all positive samples along with samples tested positive on the Rose Bengal test despite clinical findings were assessed for the presence of blocking antibodies using the *Brucella* capt test (Vircell, S.L., Granada, Spain). There is no *Brucella* tube agglutination test as a *Brucella* spp. infectious test in our hospital, and *Brucella*capt test was applied to all cases with suspected brucellosis. For the *Brucella*capt test, serial dilutions of the patient sera were performed from 1/20 to 1/5120 and incubated with antigens at 37°C for 24 hours. Homogeneous adhesion of the antigens on the wall of the well was considered as positive, and the precipitation of the antigens at the bottom of the well as a blue spot was evaluated as negative. Together with clinical findings, agglutination at a titer of ≥1/160 indicated the presence of brucellosis.

The blood groups of the patients were tested on an automated blood group analyzer (Ortho AutoVue Innova, Ortho Clinical Diagnostics, Raritan, NJ, USA) which uses the column agglutination technique. The patient and control groups were divided into four groups according to their blood groups as A, B, AB and O blood groups.

Statistical Analysis

Data obtained from the study were analyzed using the SPSS (IBM, Version 21.0, Chiago, IL) software package. Categorical variables were presented as number and percentage and compared using the Chi-square and Fisher's exact tests. Kolmogorov-Smirnov test was used to check whether data followed normal distribution. Continuous variables without normal distribution were presented as median (minimum and maximum) and compared using the Mann-Whitney U test. Statistical significance level was set at $p< 0.05$. In addition, Oneway Anova test was used to compare more than two groups in the evaluation of parametric data.

Results

In our study, there were a total of 101 pediatric cases, 57 (56.4%) boys and 44 (43.6%) girls, whose blood group results could be reached with clinical and laboratory findings compatible with brucellosis in the patient group. The control group included 204 children, 108 (52.9%) boys and 96 (47.1%) girls, whose blood group was checked, without clinical or laboratory findings suggestive of *Brucella* spp. infection or any chronic disease. There was no significant difference between the patient and control groups in terms of sex distribution ($p= 0.325$). Mean age of the patient group was 156 (19-216) months, and mean age of the control group was 141.5 (4-216) months, and no statistically significant age difference was observed between the groups ($p= 0.093$).

Blood group examination in the patient and control groups showed that a total of 123 (40.3%) study subjects were of blood group A, and blood group A was the most prevalent. No significant difference was found between patient and control groups with respect to *Brucella* spp. infection and ABO blood groups ($p= 0.454$) (Table 1).

Table 1. Relations between ABO blood groups and number of subjects in the patient and control groups

ABO n (%)	Patient Group n (%)	Control Group n (%)	Total n (%)	p
O	35 (34.7%)	60 (29.4%)	95 (31.1%)	p= 0.454
A	38 (37.6%)	85 (41%.7)	123 (40.3%)	
B	17 (16.8%)	44 (21.6%)	61 (20.0%)	
AB	11 (10.9%)	15 (7.4%)	26 (8.5%)	

Table 2. Relations between ABO blood groups and symptom-examination findings

Syptom-Examination Findings	Blood Groups				Total	p
	O	A	B	AB		
Fever	19	19	8	2	55 (54.4%)	0.261
Arthritis	12	12	8	6	38 (37.6%)	0.433
Hepatosplenomegaly	10	13	4	4	31 (30.7%)	0.832
Weight loss	25	14	8	9	66 (65.3%)	0.214
Myalgia	30	32	12	9	83 (82.1%)	0.579

The most common symptoms in the patient group were fever, myalgia, weight loss, and the most common physical examination findings were arthritis and hepatosplenomegaly. The relationship between blood groups and symptom-examination findings were investigated. There was no statistically significant relationship between ABO blood groups and symptom-examination findings (p> 0.005) (Table 2).

*Brucella*capt test titer was 1/160 in 50 (49.5 %) of the cases, 1/320 in 12 (11.9 %) cases, 1/640 in 15 (14.9%) cases, 1/1280 in 13 (12.9%) cases, 1/2560 in 4 (3.9%) cases and 1/5120 in 7 (6.9%) cases. *Brucella*capt test titer and ABO blood groups were compared and no statistically significant difference was found between the groups (p= 0.132).

Discussion

Brucella spp. are small, non-spore forming, facultative gram-negative *coccobacilli*. Major *Brucella* species include *Brucella melitensis, Brucella suis, Brucella abortus and Brucella canis*, with *Brucella melitensis* accounting mostly for infection in humans (2,13). Brucellosis is the most common zoonotic infection across the world (1). Türkiye is one of the countries with the highest incidence of *Brucella* spp. infection, with a varying distribution among different regions (16). Previously, the sporadic distribution of brucellosis was attributed only to the dietary habits of the regions. When the literature is examined, factors that predispose to infection, such as genetic susceptibility, have been discussed in a few studies (6,10,17).

ABO antigens are mainly expressed on the surface of Red blood cells but can be detected on most epithelial and endothelial cells, T cells, B cells, platelets, and most body fluids and are associated with many infectious or non-infectious diseases (18).

In 2005, Kanbay M, et al. reported the association between *Helicobacter pylori* and ABO blood groups (19). In 2009, Rowe JA et al. showed that blood group O protects against severe *Plasmodium falciparum* malaria through the mechanism of reduced rosetting (20). In 2005, Harris JB et al. demonstrated that individuals with blood group O are more susceptible to cholera infection and display a more severe disease course (21). In a meta-analysis published in 2020, Wenzhan Jing et al. investigated whether ABO blood groups were associated with hepatitis B virus infection and reported that the blood group B was associated with a lower risk of hepatitis B virus infection (9).

Apart from infectious diseases, the role of ABO blood groups in non-infectious diseases has also been explored. In the last 50 years, several studies have shown the relationship between ABO blood groups and cardiovascular disease (22-24). In 2012, Dentali F et al. documented that non-O blood group carried a two-fold increased risk of venous thromboembolism (22). The same year, Franchini M, et al. identified the role of ABO blood groups in pancreatic and gastric cancers (25) and later, in 2014, Liumbruno, et al. showed the high prevalence of blood group A in patients with gastric cancer (26). While it is known that infectious diseases invariably arise following exposure to infection, the possibility that genetic makeup of an individual might be a predisposing factor for the development of these diseases led us to explore the relationship between ABO blood groups and brucellosis (27).

Studies have shown that T cells and some interleukins (IL) are higher or lower in individuals with certain blood types, and this is associated with a number of infectious and non-infectious diseases and is associated with an increased or

decreased risk for some diseases (28-30). Keramat F et al. in their study, have shown that there is a relation between brucellosis and IL-17 gene polymorphism and that individuals with some genotypes are more resistant to infection (31). Jin X et al. have investigated the relation between IL-6 and IL-10 and brucellosis in their study and shown that IL-10 may be associated with a reduced risk of infection in some populations (32). Rodríguez-Zapata M et al. have shown the relation between T helper 1 (Th1) and related interleukins and brucellosis (33). We aimed to investigate the relation between brucellosis and blood types based on the knowledge that Th1, IL levels may be effective in brucellosis and that people with different blood types have different T cell and IL levels.

In 2015, Mohsenpour et al., in their study investigating the relation between *Brucella* spp. infection and blood groups in the adult age group, showed that the probability of *Brucella* spp. infection in people with AB blood group is 6.26 times higher than those with O blood group. When the literature is examined, no study examining the relationship between *Brucella* spp. infection and blood groups has been found, except for the study by Mohsenpour et al. in the adult age group. Our study is the first to examine the relationship between *Brucella* spp. infection and blood types in children. In this study, we tried to explain the role of blood types in the development of brucellosis, a zoonotic disease, in addition to existing risk factors such as diet patterns and lifestyle. However, based on our findings, we did not identify ABO blood groups as a risk factor for *Brucella* spp. infection in children.

Conclusion

The present study is the first to show the lack of any relation between Brucella spp. infection and blood groups. Further studies are warranted to corroborate our results.

Ethics Committe Approval: This study was approved by Adıyaman University Non-Invasive Clinical Research Ethics Committee (Decision no: 2020/6-51, Date: 23.06.2020).

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

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