No Relationship Between Blood Groups and Psoriatic Arthritis

Kan Grupları ile Psoriatik Artrit Arasında Herhangi İlişki Yoktur

Samet KARAHAN¹ Kemal ÖZYURT²

ÖZ

Giriş: Psoriatik artrit (PsA) inflamatuar bir kas-iskelet sistemi hastalığıdır. PsA'nın kesin nedenleri belirlenmemiştir. Halen ABO ve Rh kan grupları birçok hastalık için ilgi alanı olmaya devam etmektedir. Bu çalışmada, PsA'da ABO ve Rh kan gruplarının dağılımında farklılık olup olmadığının araştırılması amaçlandı.

Araçlar ve Yöntemler: Ocak 2019-Haziran 2020 tarihleri arasında Orta Anadolu'da üçüncü basamak bir hastanenin erişkin Romatoloji polikliniğine ardışık olarak başvuran 233 PsA hastası kaydedildi. Hastaların kan grupları, 1 Ocak 2019- 31 Haziran 2020 tarihleri arasında aynı hastanede elektif operasyon öncesi tetkik edilen 6280 kişinin kan grupları ile karşılaştırıldı. Kontrol hastalarından tıbbi kayıtlarında 14'ünde Psoriazis / PsA varlığı nedeniyle çalışma dışı bırakıldı. Ayrıca 1 Ocak 2019 ile 1 Temmuz 2020 tarihleri arasında Türk Kızılayı Kayseri Kan Merkezi'ne gönüllü olarak kan bağışı yapan 38.416 kişinin (donör grubu) kan grupları, kontrol grubundakilerin kan grupları ile karşılaştırıldı.

Bulgular: PsA hastalari ile kontrol grubu arasındaki istatistiki kıyaslamada herhangi bir kan grubunda hem kadınlarda hem erkeklerde hem de kümülatif olarak anlamlı bir fark saptanmadı.

Sonuç: Çalışmanın sonucu, PsA'lı hastalar ile kontrol grubu arasında kan grupları arasında anlamlı bir fark olmadığını göstermektedir.

Anahtar Kelimeler: ABO kan grubu; psoriasis; psoriatik artrit; Rh kan grubu

ABSTRACT

Purpose: Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease. The exact causes of PsA have not been identified. ABO and Rh blood groups continue to be an area of interest for various diseases. In this study, we aimed to evaluate whether there is any difference in the distribution of ABO and Rh blood groups in PsA.

Materials and Methods: 233 PsA patients (PsA group) consecutively referred to the adult rheumatology outpatient clinics of a tertiary care hospital of central Anatolia between January 2019 and June 2020 were enrolled. The blood groups of the PsA group were compared with the blood groups of 6280 individuals who tested before elective operations at the same hospital between 1 January 2019 and 31 June 2020 (Control Group). Fourteen of the control group were excluded due to the presence of psoriasis/PsA in their medical records. In addition, the blood groups of 38.416 people who voluntarily donated blood to the Turkish Red Crescent Kayseri Blood Center between January 1, 2019 and July 1, 2020 (donor group) were compared with the blood groups of the control group.

Results: There was no significant difference between the PsA patients and the control group in any blood group, both in women, men and also cumulatively.

Conclusion: The result of the study shows there is no significant difference in the blood groups between patients with PsA and the control group.

Keywords: ABO blood group; psoriatic arthritis; psoriasis; Rh blood group

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¹Kayseri City Hospital, Department of Internal Medicine, Division of Rheumatology, Kayseri, Türkiye.

²Ahi Evran University, Faculty of Medicine, Department of Dermatology, Kırsehir, Türkiye.

Corresponding Author: Samet Karahan, Kayseri City Hospital, Department of Internal Medicine, Division of Rheumatology, Kayseri, Türkiye. e-mail: doktorsamet@yahoo.com

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INTRODUCTION

Red blood cell (RBC) surface is coated with antigens made of proteins or glycoproteins and they bind to internal membrane proteins or lipids. The blood group system, also called as blood type system, is a collection of one or more of these antigens which are under the control of a single gene or a cluster of closely related homologous genes. According to the International Society for Blood Transfusion's 2016 Seoul and London Meetings, 308 different blood group antigens were found in 36 blood group systems.1 ABO blood group system is the most critical factor for blood transfusion and tissue transplantation. Because antigens of the ABO system are not only found on the surface of erythrocytes, but also in platelets, lung, cervix, gastrointestinal and breast glandular epithelium, vascular endothelium and uroepithelium. Apart from this rich antigen repertoire, the serum also contains a high rate of antibodies against the antigen not expressed on the erythrocyte surface.² In some cases, anti-A or anti-B antibodies may appear more than usual such as after pregnancy, recent vaccination, or intake of high doses of live bacteria such as probiotic therapy.³ Previously mentioned isohemagglutinin antigens, or antibodies against them, in particular epithelial cells led to the hypothesize that there may be a predisposition to tumors that develop from these epithelial cells. Indeed, in the cases of gastric cancer that confirms this hypothesis, blood group "A" is more common than blood group 'O'.4

Psoriatic arthritis (PsA) is a chronic, inflammatory musculoskeletal disease in the member of spondyloarthropathy (SpA) associated with psoriasis (PsO). According to the results of a relatively new study, the prevalence of SpA in PsO was significantly higher compared to non-PsO subjects (14.3% vs. 1.5%; p<0.001).⁵ Unlike male dominance in ankylosing spondylitis, the prototype of SpA, males and females are equally affected in PsA. As a result of a meta-analysis published in 2019, it identified the total pooled PsA prevalence of 20 percent in patients with PsO and 25 percent in patients with moderate to severe PsO.⁶ The exact causes of PsO and PsA have not been identified. However, it seems likely that all of the genetic, immunological and environmental factors contribute. In terms of the genetic burden of PsA, human leukocyte antigens (HLA) -B13, HLA-B17, HLA-B57, HLA-B27 and HLA-Cw * 0602 show more positivity in PsA patients compared to the general population.⁷ ABO blood groups continue to be an area of interest for various diseases, including inflammatory diseases since old times. For example, the study designed in Scotland and stated that the distribution of blood groups in rheumatoid arthritis compared with healthy controls is not statistically significant, was designed in 1968.8 Similarly, no statistical difference was found in an old study for ankylosing spondylitis.9 On the other hand, studies investigating whether blood groups are cause for the occurrence of the disease in PsO patients were also designed and according to some of these studies, the dominance of any blood group in PsO patients was not detected.^{10,11} In this study, we aimed to investigate the distribution of blood groups in PsA patients, as a cross sectional study.

MATERIALS and METHODS

This study was carried out in accordance with the Declaration of Helsinki ethical principles and approved by Erciyes University School of Medicine Ethical Committee for Clinical and Laboratory Research (Date: 25.09.2019, Decision Number: 2019/638). All patients gave written informed consent.

Selection and Description of Participants

This study is designed to be single-centered and crosssectional. 233 PsA patients who consecutively referred to the adult rheumatology outpatient clinics of a tertiary hospital in Central Anatolia, Turkey, between January 2019 and June 2020 were enrolled. The blood groups of the patients were compared with the blood groups of 6280 individuals who tested before elective operations, but not cancer surgery, at the same hospital between January 1, 2019 - June 31, 2020 (Control Group). Fourteen of them were excluded due to the presence of PsO/PsA in their medical records. Although PsA is known to affect both genders equally,12 PsA patients and blood donors are also grouped according to their gender to avoid bias in terms of gender. In addition, the blood groups of 38.416 people who voluntarily donated blood to the Turkish Red Crescent Kayseri Blood Center between January 1, 2019 and July 1, 2020 (Donor Group)

were compared with the blood groups of the control group. The rationale for this comparison is to determine whether there is accumulation of any blood groups in the control group selected from the patients who applied to the hospital for preoperative examination.

Diagnoses of patients with PsO were verified by the dermatologist researcher of the study, K. O., and the examination of the patients who did not have PsO and had PsO in their family was also confirmed by the same researchers. In addition, PsA of patients were classified by S. K., the rheumatologist of the study, according to the CASPAR classification criteria.13 Demographic data, presence of sacroilitis, spondylitis, peripheral arthritis, nail involvement, C-reactive protein (CRP, normal value≤5mg/L), erythrocyte sedimentation rate (ESR, normal range 0-20mm/h), rheumatoid factor (RF) and anti-cyclic citrulline peptide (Anti-CCP) positivity and history of dactilitis, uveitis, inflammatory bowel disease and also medications used were recorded by medical file screening and face to face interview by rheumatologists of the study. PsA patients and controls were grouped separately according to their gender, and cumulative comparison was also performed.

Technical Information: Blood Groups

During the outpatient clinic visit, patients who do not have a blood group result in any official documents such as driver's license and identity card, ABO blood group phenotyping was done by indirect technique and were classified according to blood groups (A, B, AB, O) and Rh status (+/-).

Statistical Analysis

Statistical Package for the Social Sciences (SPSS version 25.0, IBM, New York, USA) was used for analyzes. Demographic tables were generated for percent rate and total percentage frequencies. Kolmogorov-Smirnov test was used to check the normal distribution of data. 95% confidence interval was calculated using the correlation coefficient with the help of the Chi-square test and/or Fisher's exact test. Regression models were created to determine if any blood group was associated with PsA.

Probability values below 0.05 were considered significant. All significance tests were 2-sided.

RESULTS

In our study 114 of 233 (48.9%) PsA patients were female and the median patient age was 48.74 ± 12.52 years. In addition, there were 2787/6266 (44.5%) females in the control group and the median age of control group was 46.00 years (IQR:38.00–56.00) (p=0.180 and p=0.030, respectively).

Mean disease duration of the PsA patients was 3.44 ± 5.63 . PsA was diagnosed in 19 of 233 patients (8.2%) simultaneously with PsO. 175 patients (75.1%) were diagnosed with PsA after the diagnosis of PsO, and the median time between PsO to PsA was 10.00 years (IQR:4.00–20.00). Six patients (2.6%) were diagnosed with PsA first, and after mean 3.00 ± 1.87 years, PsO was diagnosed afterward. Twenty nine of the patients (12.4%) had no personal PsO history, but their family members had PsO. In 4 patients (1.7%), radiographic and laboratory changes were compatible with PsA and neither family history nor personal history was positive. The demographic and clinical characteristics of PsA patients are presented in Table 1.

When the blood groups in the control group were compared with the healthy controls who donated blood to the Red Crescent, there was no significant difference between the two groups in any blood group. No blood group distribution was different between these two groups [For A Rh (+); control group, 38.1%; donor group, 38.4%, p=0.412; A Rh (-); control group, 4.9%; donor group, 5.2%, p=0.246; B Rh (+); control group, 13.8%; donor group, 13.2%, p=0.195; B Rh (-); control group, 13.8%; donor group, 1.9%; donor group, 1.9%, p=0.939; 0 Rh (+); control group, 29.1%; donor group, 29.4%, p=0.626; 0 Rh (-); control group, 3.9%; donor group, 4.1%, p=0.332; AB Rh (+); control group, 7.3%; donor group, 6.8%, p=0.121; AB Rh (-); control group, 1.0%; donor group, 1.0%, p=0.620].

Table 2 shows the gender distribution and cumulative distribution of blood groups in PsA patients and control group in terms of ABO, but not Rh. There was no signifi-

cant difference between patients with PsA and control group in terms of distribution of ABO blood groups (p=0.610). As seen in Table 2, considering the cumulative blood group distribution regardless of gender, the distribution of PsA patients with A, B, O and AB blood groups was 43.8%, 16.3%, 33.9% and 6.0%, respectively, the distribution of the control group was 42.9%, 15.7%, 33.0% and 8.4%, respectively (p values: 0.798, 0.664, 0.770 and 0.198, respectively).

 Table 1. The demographic and clinical characteristics of PsA patients.

PsA patients		
Variables	(n=233)	
Age, years, mean \pm S.D.	48.74±12.52	
Female, no. (%)	114 (48.9)	
CRP (mg/L), mean \pm S.E.M.	12.98±12.60	
ESH (mm/h), mean \pm S.E.M.	16.41 ± 12.81	
Co-morbidities	No (%)	
Steatosis	72 (30.9)	
Hypertension	68 (29.2)	
DM, Insulin resistance	43 (18.5)	
Hyperlipidemia	36 (15.5)	
ASHD	19 (8.2)	
COPD	12 (5.2)	
Asthma	10 (4.3)	
BAD, Depression	10 (4.3)	
Others	33 (14.2)	
No comorbidity	124 (53.2)	
Presence/History of	No (%)	
Sacroiliitis	105 (45.1)	
Spondylitis	92 (39.5)	
Peripheral arthritis	129 (55.4)	
Dactilitis	60 (25.8)	
Uveitis	16 (6.9)	
IBD	0	
Nail Involvement	No (%)	
Pitting	130 (55.8)	
Onycholysis	71 (30.5)	
Hyperkeratosis	52 (22.3)	
RF; n (%)	10 (4.3)	
Anti-CCP; n (%)	3 (1.3)	
HLA-B27; n (%)	9 (3.9)	
Medication (csDMARD)	No (%)	
NSIAD	179 (76.8)	
Methotrexate	132 (56.7)	
Leflunomide	26 (11.2)	
Sulfasalazine	69 (29.6)	
Steroid	7 (3.0)	
Cyclosporine	1 (0.4)	
Local treatment	59 (25.3)	
Isotretinoin	1 (0.4)	
Medication (bDMARD)		
Anti-TNF	41 (17.6)	
Secukinumab (Anti-IL17)	3 (1.37/)	
Ustekinumab (Anti-IL12/23)	8 (3.4)	

Values are presented as mean±standart deviation (S.D.), mean±standart error of the mean (S.E.M.), number (%), or median (interquartile range) Abbreviations: PsA: psoriatic arthritis; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; ASHD: Atherosclerotic heart disease; COPD: Chronic obstructive pulmonary disease; BAD: Bipolar affective disorder; IBD: Inflammatory bowel disease; RF: Rheumatoid factor; Anti-CCP: Anti cyclic citrulline peptide; HLA: Human leukocyte antigen; csDMARD: Conven-tional synthetic disease modifying drug; NSAID; Non-steroidal anti-inflammatory drug; bDMARD: biological disease modif-ying drug; Anti-TNF; Anti tumor necrosis factor; Anti-IL17: Antiinterleukin 17; Anti-12/23: Anti-interleukin12/23 Table 3 shows the gender distribution and cumulative distribution of blood groups in PsA patients and control group in terms of ABO, and also Rh. There was no significant difference between patients with PsA and control group in terms of distribution of ABO and Rh blood groups (p=0.909).

Table 2. Distribution of blo	ood group in PsA patients and healthy
donors (Only ABO).	

Variables	PsA Group (n,%)	Control (n,%)	p value
Male			
А	58 (48.7)	1.484 (42.7)	0.187
В	14 (11.8)	549 (15.8)	0.236
0	42 (35.3)	1.158 (33.3)	0.648
AB	5 (4.2)	288 (8.3)	0.110
Total	119	3479	
Female			
А	44 (38.6)	1.206 (43.3)	0.323
В	24 (21.1)	435 (15.6)	0.118
0	37 (32.5)	909 (32.6)	0.972
AB	9 (7.9)	237 (8.5)	0.819
Total	114	2787	
Cumulative			
А	102 (43.8)	2.690 (42.9)	0.798
В	38 (16.3)	984 (15.7)	0.664
0	79 (33.9)	2.067 (33.0)	0.770
AB	14 (6.0)	525 (8.4)	0.198
Total	233	6266	

Values are presented as number (%).

Abbreviations: PsA: Psoriatic arthritis

Table 3. Distribution of blood group in PsA patients and healthy donors (ABO and Rh).

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Variables	PsA patients n,%)	Control n,%)	p value			
Male	, ,					
A Rh (+)	51 (42.9)	1.313 (37.7)	0.290			
A Rh (-)	7 (5.9)	171 (4.9)	0.290			
B Rh (+)	13 (10.9)	485 (13.9)	0.418			
B Rh (-)	1 (0.8)	64 (1.8)	0.724			
O Rh (+)	34 (28.6)	1.027 (29.5)	0.823			
O Rh (-)	8 (6.7)	131 (3.8)	0.138			
AB Rh (+)	5 (4.2)	252 (7.2)	0.205			
AB Rh (-)	0 (0)	36 (1.0)	0.632			
Rh (+)	103 (86.6)	3077 (88.4)	0.527			
Total	119	3479				
Female						
A Rh (+)	40 (35.1)	1073 (38.5)	0.463			
A Rh (-)	4 (3.5)	133 (4.8)	0.533			
B Rh (+)	19 (16.7)	380 (13.6)	0.357			
B Rh (-)	4 (3.5)	55 (2.0)	0.292			
O Rh (+)	34 (29.8)	798 (28.6)	0.783			
O Rh (-)	4 (3.5)	111 (4.0)	1.000			
AB Rh (+)	78 (6.1)	208 (7.5)	0.597			
AB Rh (-)	24 (1.8)	29 (1.0)	0.346			
Rh (+)	100 (87.7)	2479 (88.9)	0.868			
Total	114	2787				
Cumulative						
A Rh (+)	91 (39.1)	2386 (38.)	0.763			
A Rh (-)	11 (4.7)	304 (4.9)	0.927			
B Rh (+)	32 (13.7)	865 (13.8)	0.975			
B Rh (-)	5 (2.1)	119 (1.9)	0.805			
O Rh (+)	68 (29.2)	1825 (29.1)	0.984			
O Rh (-)	12 (5.2)	242 (3.9)	0.319			
AB Rh (+)	12 (5.2)	460 (7.3)	0.206			
AB Rh (-)	2 (0.9)	65 (1.0)	1.000			
Rh (+)	224 (87.1)	5536 (88.3)	0.568			
Total	233	6266				

Values are presented as number (%).

Abbreviations: PsA: Psoriatic arthritis

In referring to Rh blood groups, while 103 (86.6%) of 119 male PsA patients were Rh (+), 3077 (88.4%) of the 3479 controls were Rh (+) (p=0.527). The ratio of female patients with Rh (+) was 100/114 (87.7%) in the PsA group, while it was 2479/2787 (88.9%) in the controls (p=0.868). It was also observed that there was no statistically significant difference in total patient groups [224/233 (87.1%) vs 5536/6266 (88.3%); p=0.568].

DISCUSSION

The most important finding of our study; the distribution of ABO and Rh blood groups is not different for PsA when evaluated separately in males and females and evaluated cumulatively regardless of gender. In the studies carried out in PsO, regardless of the presence of PsA, studies have shown that the distribution of blood groups in PsO is not different with the general population. In a study conducted by Hargreaves et al. about 60 years ago, 200 PsO patients were compared with the control group consisting of non-PsO disease groups of a different study from the same geographical area. As a result, there were 98 (49%) O, 81 (40.5%) A, 18 (9%) B and 3 (1.5%) AB blood group in 200 PsO patients. In contrast, in 2056 control cases, 983 (47.6%) O, 851 (41.5%) A, 161 (7.8%) B and 61 (3%) AB blood groups were present. They showed a striking similarity between the blood groups in comparison with the PsO patients and the control group and it clearly showed that there was no significant relationship between PsO and any specific blood group.¹⁰ In another study involving a limited number of cases in Iran and including pemphigus patients with PsO, the blood group frequencies of PsO patients and control cases were similar and there was no statistically significant difference between PsO and controls.11 One of the limitations of our study may be that the preoperative control group was selected from the patients admitted to the hospital. For this reason, there may be an accumulation of rare blood groups. We think that, we have eliminated this problem somewhat by comparing the blood group of the blood donors selected from patients in the general population with the control group. As a result of the evaluations made between the donor group and control group, it was determined that any blood group in control group did not have a certain accumulation. The question may come to mind why the blood groups of patients in the PsA group are not compared with the donor group. Because rheumatological diseases such as PsO or PsA do not prevent blood donation. So, there may be PsO or PsA patients in the donor group and this selection could lead to bias.

Our results have shown that the most common comorbidities in PsA patients were hepatic steatosis, hypertension and diabetes mellitus. Also, our data shows that approximately half of the patients had one or more comorbid diseases. According to the results of an epidemiological study conducted by Husted J et al., 2 out of 5 patients with PsA had three or more comorbid diseases and hypertension, hyperlipidemia, type II diabetes and obesity, which are the most common comorbid conditions, cause an increased risk of cardiovascular disease.¹⁴

Although axial involvement in the form of sacroiliitis and/or spondyloarthritis has been reported in PsA at different rates in the literature, it is still important in the diagnosis of PsA. In our study, involvement in the form of sacroiliac joint and spondylitis was observed as 45.1% and 39.5%, respectively, and this data is consistent with the literature.^{15,16} Even though it is no longer used, Moll and Wrigt subtyping PsA joint involvement in 1973, because of involvements such as arthritis mutilans are not common and other subtypes may also be intertwined, the most common subtype of our study is the peripheral articular type observed in 55.4%.¹⁷ Dactylitis or sausage finger, which is defined as a combination of synovitis, enthesitis, tenosynovitis and soft tissue swelling, is a different entity than synovitis. Dactylitis holds joint and periarticular space in the finger and/or toe, can give information about the serious course of the disease in PsA.¹⁸ In our study, dactylitis was observed in 25.8% of patients, and this data is also coherent with the literature. According to the results of a 2012 review, the frequency of uveitis/iritis ranges from 0.7% to 2.7% in PsA patients.¹⁹ The frequency of this extraarticular involvement was found higher in our patients (6.9%) and we think that the reason for this may be that our hospital and uvea clinic is a reference center in our region and that uveitis patients are frequently referred us from this uvea center. On the other hand, inflammatory bowel diseases,

another extraarticular finding of PsA, were never been encountered in our patients.

According to our results, the frequency of any blood group in PsA does not change compared to the general population, as seen in Table 2 and Table 3. Blood group antigens are structures associated with the cell surface and provide the formation of more than 30 blood group systems that can be fatal after blood transfusions and cause rejection of organs or tissues after their transplantations. The best known blood group antigens are ABO and Rh blood group antigens, which are found not only in RBCs and platelets, but also on the surface of most endothelial and epithelial cells, and in 80% of body fluids and secretions. In addition the term "histo-blood group antigens" is used based on the fact that these antigens are not only found in RBCs, but also the antigens are found in "histological tissues", including histological tissue of the gastrointestinal tract.³

ABO blood groups also have been studied as a risk factor for the development and/or severity of most diseases, especially cancers.^{4,22-24} Also, there are various articles about whether blood groups pose risk for disease development and severity in autoimmune/inflammatory diseases.²³⁻²⁵

The ABO gene contains 7 exons, located on chromosome 9 in the 9q34.2 band and encodes a glycosyltransferase that catalyzes the transfer of carbohydrates to the H antigen, forming the antigenic structure of the ABO blood groups.²⁶ According to the results of a study performed by Melzer et al. in 2008, genetic variations in the first intron of the ABO gene were associated with increased serum circulating tumor necrosis factor-alpha (TNF-a) levels.²⁷ As it is well known, the most common genetic variation among humans is single nucleotide polymorphisms (SNPs). Some SNPs in the TNF- α gene promoter region are known to alter serum TNF- α levels and have also been shown to increase the risk of PsA.²⁸ Theoretically, considering the contribution of TNF- α , which can be altered due to genetic variations of SNPs in the ABO gene, it would not be surprising that ABO blood groups facilitate or increase the severity of PsA and other inflammatory diseases. However, our study demonstrated that no blood group increases the development of PsA in clinical practice. However, it can be thought that the effect of blood groups on PsA severity will be a topic of research in the coming years.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

Approval for this study was obtained from the Erciyes University Faculty of Medicine Clinical and Laboratory Research Ethics Committee (25.09.2019 dated and 2019/638 numbered).

Authors' Contributions

Concept/Design: SK. Data Collection and/or Processing: SK. Data analysis and interpretation: SK. Literature Search: SK, KÖ. Drafting manuscript: SK, KÖ. Critical revision of the manuscript: SK, KÖ. Supervisor: SK, KÖ.

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