RESEARCH

Is There An Association Between Blood Group Types And Chronic Spontaneous Urticaria?

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Abstract: Chronic spontaneous urticaria is accepted as a systemic inflammatory disease. ABO blood groups are useful and valuable resource for researches because the inheritance of blood groups is not affected by any environmental factors. To our knowledge, the assoociation between chronic urticaria and blood groups has not been understood properly. The aim of this study was to investigate the association between ABO blood groups and chronic spontaneous urticaria. It was a retrospective observational study. 139 patients with chronic spontaneous urticaria and 286 healthy control were included in this study. In the study 63 patients had type A (45.3%), 18 patients had type B (12.9%), 2 patients had type AB (1.4%) and 46 patients had type O (40.3%). When the control group is investigated in terms of ABO blood groups, 121 people were type A (42.3%), 49 people were type B (17.1%), 18 people were type AB (6.3%) and 98 people were type O (34.3%). There was no significant relationship between ABO blood group and patient or control group (X2=6.856, p=0.077). However, there was a significant relationship between the Rhesus (Rh) factor and patient and control group (X2 = 4.02, p=0.045). There wasn't an association between blood groups and chronic spontaneous urticaria. Hovewer we established that the number of patients with Rh(-) blood group increased and the number of patients with Rh(+) blood group decreased in chronic spontaneous urticaria group. Further researchs are needed to understand the association.

INTRODUCTION

Chronic urticaria is a disease characterized by urticaria exceeding 6 weeks duration. The disease is divided in two as inducible urticaria and chronic spontaneous urticaria (CSU). Nearly 40% of CSU patients are observed to have accompanying angioedema attacks, while 10% have only angioedema tableau [1]. In most cases, generally it is a self-limiting disease continuing for 2-5 years, though 20% of patients have disease lasting more than 5 years [2]. At any time, CSU is observed in 0.5-1% of the population. The disease has a large effect on quality of life [3]. Though the etiology of chronic urticaria is not fully understood, diseases associated with chronic inflammation, autoimmunity, malignancy, stress, depression, some infectious processes and medications are mentioned [4]. The CU immunopathogenesis is not fully understood. Studies in recent times have shown that many cytokine values like IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17, IL-18, IL-23, IL-31 and tumor necrosis factor-alpha (TNF-α) are increased in CSU, and additionally many coagulation factor, mediator, enzyme, hormone, receptor, complement, peptide, autoantibody, immunoglobulin and chemokine levels were shown to vary 3. A recent study showed the soluble adhesion molecule sICAM-1 and sVCAM-1, a marker of endothelial dysfunction, had higher serum levels in CSU compared to a control group [5]. In parallel to soluble adhesion molecules, endothelial destruction markers like Factor VIII (FVIII) and von Willebrand factor (VWF) were identified in plasma from CSU patients [6]. In the literature there are many publications about the blood coagulation cascade being active in CSU and that may reflect disease activity [6,7]. The disease is accepted as a systemic inflammatory disease [3].

It has been known that the ABO blood type has a profound influence on hemostasis, and is a major determinant of the VWF and, consequently, FVIII plasma levels. VWF levels are approximately 25% higher in individuals who have a blood group other than O [8]. Genomic studies in recent times have revealed a correlation between the ABO gene with important proinflammatory cytokines, intercellular adhesion molecule 1 (ICAM-I) and TNF-α which affect the systemic inflammatory response [9,10]. Since A blood group was defined as a risk factor for stomach cancer, the correlations between ABO blood group and diseases have been a topic of interest and research. ABO blood group antigens (A, B and H antigens) are complex carbohydrate molecules and function as red blood cell surface markers, additionally they are expressed by body fluids, a variety of cell and tissue types and in skin [11]. The presence of antigens in many tissues leads to consideration that blood group antigens may not only determine blood group, but may play roles in a broader area.

All available literature data leads to consideration of a possible correlation between CSU etiopathogenesis with blood groups.

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MATERIALS and METHODS

For the study local ethics committee permission was received. (27.02.2020/KAEK 30). The study was actualized according to the rules expressed in the Declaration of Helsinki.The study was performed retrospectively. The study included 139 CSU patients with ABO-Rh blood group data attending our dermatology clinic from January 2019 to December 2019 and 286 age- and sex-matched healthy controls. Those with systemic inflammatory diseases like diabetes, hypertension, systemic lupus erythematous, rheumatoid arthritis, bullous diseases, and Behçet's disease were excluded from the study. Demographic data like age and sex and angioedema history were recorded. In the control group, only sex and age information were recorded. All individuals were grouped according to A, B, AB, and O blood groups and Rh- and Rh+ according to Rh factor status.

Statistical analyses were completed with SPSS v.17.0 software. Fit of variables in both groups to normal distribution was separately investigated with analytic methods (Kolmogorov-Smirnov/Shapiro-Wilk test). Descriptive statistics are shown as mean ± standard deviation and frequency-percentage. Comparisons between groups used the t test or Mann-Whitney U test. Comparison of categoric variables used the chi-square (Pearson and/or Fisher) test. Situations within the 95% confidence interval or with $p<0.05$ were accepted as the boundary for statistical significance.

RESULTS

In this study, among 139 CSU patients, 95 were female (67.9%) and 44 were male (32.1%). Mean age of patients was 41.7±13.4 years. Among 286 healthy controls, 192 were female (67%) and 94 were male (33%). Mean age in the control group was 40.4±14.9 years. When analyzed in terms of age and sex, there were no significant differences between patient and control group ($p>0.05$).

When ABO blood groups are investigated, 63 patients had type A (45.3%), 18 patients had type B (12.9%), 2 patients had type AB (1.4%) and 46 patients had type O (40.3%). When the control group is investigated in terms of ABO blood groups, 121 people were type A (42.3%), 49 people were type B (17.1%), 18 people were type AB (6.3%) and 98 people were type O (34.3%). There was no significant relationship between ABO blood group and patient or control group ($X2=6.856$, $p=0.077$) (Table1). However, there was a significant relationship between the Rhesus factor and patient and control group ($X2 = 4.02$, $p=0.045$). For the patient group, 125 (89.9%) patients were Rh (+) and 14 (10.1%) patients were Rh (-). In the control group, 236 (82.5%) individuals were Rh (+) and 50 (17.5%) were Rh (-). Therefore, there was a significant difference of approximately 7.5% in Rh (-) and Rh (+) ratios between the control and patient groups (Table3). When each blood group in the patient and control groups are assessed in terms of Rh factor, no significant correlation was identified ($X2 =10.313$, $p=0.172$) (Table2). While 75 patients (54%) had history of angioedema, 64 (46%) had no angioedema history. When the patient group was investigated in terms of those with and without angioedema, there was no significant relationship between ABO blood group and Rhesus factor and angioedema ($X2= 8.786$, $p=0.186$) (Table4). Findings in our study are shown in Tables 1, 2, 3 and 4.

Table 1. Compare of ABO blood group distrubition between control and patients

ABO	Control (n=286)		Patients (n=139)		Total		Statistics
	n	%	n	%	N	%	χ^2/P
A	121	42.3	63	45.3	184	43.3	
B	49	17.1	18	12.9	67	15.8	χ^2=6.856
AB	18	6.3	2	1.4	20	4.7	p=0.077
O	98	34.3	56	40.3	154	36.2	
Total	286	100.0	139	99.9	425	100.0	

*p<0.05 was considered significant. Pearson's Chi-Square test was used.

Table 2. Compare of blood group distrubition between control and patients

Blood Groups	Control (n=286)		Patients (n=139)		Total		Statistics
	N	%	n	%	N	%	χ^2/P
A-	17	5.9	6	4.3	23	5.4	
A+	104	36.40	57	41	161	37.9	
B-	10	3.5	3	2.2	13	3.1	
B+	39	13.6	15	10.8	54	12.7	χ^2=10.313
AB-	6	2.1	0	0.0	6	1.4	p=0.172
AB+	12	4.2	2	1.4	14	3.3	
0-	17	5.9	5	3.6	22	5.2	
0+	81	28.3	51	36.7	132	31.1	
Total	286	100.0	139	100.0	425	100.0	

*p<0.05 was considered significant. Pearson's Chi-Square test was used.

*: Statistically significant difference in comparison to the control group, #: Statistically significant difference in comparison to the obese non-diabetic group ($p<0.05$). (By Anova and post-hoc Tukey HSD analyses).

Table 3. Compare of Rh blood group distrubition between control and patients

RhGroups	Control (n=286)		Patients (n=139)		Total		Statistics*
	n	%	n	%	N	%	χ^2/P
(-)	50	17.5	14	10.1	64	15.1	χ^2=4.02
(+)	236	82.5	125	89.9	361	84.9	p=0.045
Total	286	67.3	139	32.7	425	100.0	

*p<0.05 was considered significant. Pearson's Chi-Square test was used.

Table 4. Compare of angioedema between control and patients

Blood Groups	Angioedema (+)		Angioedema (-)		Total		Statistics
	n	%	n	%	N	%	χ^2/P
A-	4	5,3	2	3,1	6	4.3	
A+	30	40.0	27	42.2	57	41.0	
B-	2	2.7	1	1.6	3	2.2	
B+	11	14.7	4	6.3	15	10.8	χ^2=8.786
AB+	1	1.3	1	1.6	2	1.4	p=0.186
0-	0	0.0	5	7.8	5	3.6	
0+	27	36.0	24	37.5	51	36.7	
Total	75	100.0	64	100.0	139	100.0	

*p<0.05 was considered significant. Pearson's Chi-Square test was used.

DISCUSSION

ABO and Rh blood groups differ by race. Inheritance of blood groups is not affected by environmental factors, providing a useful resource for studies. Following the study conducted at 1953 reporting the relationship between blood group A and gastric carcinoma, relationship shown between a number of disease and blood groups. Although different results are found, the relationship between blood groups and diseases are not yet well understood. Nevertheless the data gathered gave clues about etiopathogenesis [12]. Blood groups ABO were used as a genetic marker in infectious and non-infectious diseases. In case control studies significant relationship shown between HLA antigens and blood groups in some diseases. Psoriasis, romatoid arthritis, juvenile diabetes, multiple sclerosis were among the disease that are studied [13]. Besides red blood cells A, B, H(O) antigens were expresses on the surface of epithelial cell including skin cell. Associations shown between epithelial malignancies and ABO blood groups [14]. On the skin these antigens are expressed at strosum corneum, strosum granulosum and strosum spinosum [15]. In the literature some significant associations shown between blood groups and acne, pemphigous, psoriasis, Betçet's disease, rosacea and skin malignancies. Hovewer no significant relationship found in some studies [12-19].

Though there are different results in the literature, there are studies investigating the correlation between allergic and atopic diseases with blood groups. In one study, significant relationships were shown between respiratory atopy and blood group antigen system. Specific blood group types were reported to vary according to asthma phenotypes. B phenotype was associated with severe asthma and O and A phenotypes were associated with mild to moderate asthma [20]. A review showed the relationship between allergic diseases like atopic dermatitis, allergic rhinitis and asthma with ABO blood groups[11]. Another study demonstrated a significant correlation between O blood group with allergic rhinitis risk [21]. One study showed that grass-pollen hay fever patients with B blood group had high pollen allergy predisposition and this was followed by the O blood group [22]. Atopic diseases like atopic dermatitis, hay fever, allergic rhinitis, asthma and acute urticaria were investigated and A and B blood groups were found to be high compared to the control group. This study additionally included data about 15 genetic blood polymorphism phenotypes and gene distributions like MNSs, Rhesus, P, Kell, Duffy, Kidd and 6-PGD and results supported the hypothesis that specific phenotypes may be associated with atopic predisposition [23].

Possible correlations were shown between some infectious diseases and blood groups. Coronavirus disease 19 (COVID-19) is a disease caused by a novel coronavirus and is currently causing a pandemic. A study of COVID-19 patients in recent times showed that A blood group represented increased risk for disease while O blood group may be protective [24]. Additionally, it was shown that O blood group is protective against Plasmodium falciparum infection with a well-defined mechanism [25]. Blood group antigens may affect the susceptibility of individuals to microorganisms or diseases and may act like potential receptors for materials like toxins or allergens [11]. As is known, the etiology of CSU is not fully understood, but it is reported that infections contribute to the onset, continuation or worsening of CSU [26]. Possible correlations between infections and blood groups lead us to consider possible correlations with CSU.

When the literature is examined, only two studies investigated blood groups in urticaria patients. However, results are incompatible. These studies were performed with lower patient numbers compared to our study [27-28]. Different from these studies, we investigated the correlation between angioedema with blood groups and Rh factor status with disease. A study by Goyal et al. in recent times, investigated the prevalence of blood group types in chronic skin diseases [27]. Among the 1500 patients in the study, 126 were chronic urticaria patients. The patient numbers were 14 patients with type A, 52 patients with type B, 10 patients with type AB and 50 patients with type O. Blood group B was observed most, but there was no statistically significant correlation. Blood group O was found to be statistically significantly more common. Blood group A was identified to be statistically significantly less common. Tanrıverdi et al. investigated 100 chronic urticaria patients in a study without a control

group and identified highest frequency for the O and A groups, in that order. The authors did not show a significant correlation between blood groups with urticaria 28. In our study, there were 63 patients with blood group A, 18 patients with blood group B, 2 patients with blood group AB and 56 patients with blood group O. In our study, the most common was A (45.3%), with O the second most common (40.3%). The group identified least often was AB (1.4%). In the control group again the most common blood group was A (42.3%), followed by O in second place (34.3%). There was no significant relationship between ABO blood group and patients or control group. In terms of Rh factor, each blood group was separately compared with the control group but no statistical relationship was found. However, when all patients are investigated in terms of Rh factor, the patient group had significantly higher Rh(-) patient numbers, while the number of Rh(+) patients was significantly low. Among patients, 75 (54%) had history of angioedema and 64 patients had no history of angioedema (46%). When those in the patient group with and without angioedema are compared in terms of blood group and Rh distribution, again no significant correlation was found. In the study by Goyal et al. most patients were male (58.73%), while in the study by Tanrıverdi et al. most patients were female (56%), similar to our study. In our study, the number of females was dominant at 95 (67.9%).

Study limitations: It is a retrospective study with low number cases.

Conclusion

In this study we did not find any significant results in terms of ABO blood groups among spontaneous urticaria patients. However, in terms of Rh factor, chronic spontaneous urticaria patients had significantly increased Rh (-) frequency and reduced Rh (+) frequency compared to the control group. When we examine the literature, we thought there may be a relationship between CSU and blood groups due to the connection between blood groups with coagulation and inflammation and studies related to infectious diseases, allergic and atopic diseases. More studies involving systemic investigations, larger sample sizes and using case-control design will provide clearer data and blood group type may gain importance for assessment of chronic urticaria risk in the future.

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