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Frequency of ABO and Rh Blood Groups in Patients with Celiac Disease and Its Relationship with Disease Severity

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ABSTRACT

Background and Objective: As an autoimmune disease, celiac is often caused by the environmental factor of gluten and the genetic factor of HLA. Considering the immunological role of blood groups, this study was designed to evaluate the distribution of ABO and Rh blood groups in patients with celiac disease in West Azerbaijan Province, Iran.

Methods: In this cross-sectional study, all 199 cases recorded in the registry system of celiac patients of West Azerbaijan Province between 2015 and 2021 were included in the study. Demographic variables, disease duration, blood group, disease status, and disease complications were extracted from the electronic file of patients. According to the severity of the disease, the patients were classified into three groups: mild (no symptoms), moderate (subclinical) and severe (classic celiac symptoms).

Findings: In this study, 125 patients (62.8%) were women and the mean age of the patients was 37.15±15.65 years. 71 people (35.7%) had blood type O and 171 people (58.9%) had Rh^+. Patients with blood type O and A most commonly suffered from mild (80.8%) and moderate (50.9%) types of disease, respectively ($p<0.001$). There was no significant difference between the severity of the disease and blood groups and Rh positive and Rh negative.

Conclusion: According to the results of the present study, blood group O is the most frequent among celiac patients. In addition, the severity of the disease in people with blood group O is less than other blood groups.

Keywords: *Celiac Disease, ABO and Rh Blood Groups, Disease Registration System*.

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Introduction

Celiac disease is a type of enteropathy which is caused by mucosal changes in the small intestine due to the presence of gluten. This autoimmune disease manifests in susceptible people in the form of chronic diarrhea and sensitivity to gluten (combination of different proteins in wheat, barley and rye) (1). After absorption, gliadin is metabolized in the intestinal wall by tissue transglutaminase enzyme. In this process, glutamine roots give way to glutamic acid roots. In certain genetically predisposed individuals, altered fragments of gliadin are presented to surface molecules of antigen-presenting cells such as HLA-DQ2 bound to T-lymphocytes, an extensive immune response is triggered, and tissue damage occurs, especially in the small intestine. The components of this immune reaction are antibodies against endomysium and tissue transglutaminase (tTG) and modified gliadins (2, 3).

According to a review article, the overall prevalence of the disease is estimated to be 3% based on serological findings and 2% in studies based on biopsy findings (4). This disease is usually observed along with other autoimmune diseases such as type 1 diabetes, autoimmune thyroid disease and psoriasis (5). Definitive diagnosis of the disease is based on a biopsy of the small intestine. Celiac disease has a strong genetic association with HLA-DQ2 and HLA-DQ8. If both HLAs are negative, the disease can almost be ruled out (6).

According to the findings of a review article based on a screening in the general population, the risk of celiac disease in women is 1.42 times higher than in men, and the sex ratio of this disease is reported to be 1.8:1 to 3:1 (7, 8). Autoimmunity is also influenced by sex hormones. Gender is associated with differences in the clinical presentation, onset, progression and outcome of autoimmune diseases (9). Sex hormones may affect the target organ's vulnerability to an autoimmune response (10). There are also gender-based differences in organ-specific autoimmune diseases such as multiple sclerosis, Guillain-Barré syndrome, Crohn's disease, and celiac disease. Sex hormones have immunomodulatory properties and also perform cell protection following tissue damage in certain conditions. Sex hormones also affect innate and adaptive immune cells, B and T cells, antigen presentation, and cytokine secretion. It appears that sex hormones may also have therapeutic potential in several autoimmune diseases, however, more research is needed before therapeutic recommendations can be made (11, 12).

For examining the relationship between autoimmune disease and blood group antigens and the Rh factor, it has been evaluated as a hematological and genetic marker like other diseases in numerous studies (13, 14). Investigating the existence of a relationship between blood groups and their antigens and diseases, especially autoimmune diseases, requires more studies regarding their pathogenic mechanism. People with blood group O have a strong immune system, and the good and strong immune system of this group makes them more prone to autoimmune diseases, and the rate of allergy is also higher in them for this reason (15-17).

The relationship between blood groups and various diseases, including malignancies, stomach ulcers, infections, diabetes, skin diseases, heart diseases, tooth decay and infectious diseases, has been studied with diverse results, and in some studies, the relationship between blood groups and the prevalence and severity of the disease has been reported (18-21).

According to literature review, there was no study on the distribution of blood groups in patients with celiac disease. For this reason, the present study was conducted to investigate the prevalence of ABO and Rh blood groups and the relationship between blood group and Rh factor and disease severity in patients with celiac disease based on celiac disease registration in West Azerbaijan province.

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Methods

This cross-sectional study was approved by the Ethics Committee of Urmia University of Medical Sciences with the code IR.UMSU.REC.1398.521 and conducted on all patients with celiac disease with a definite diagnosis based on the biopsy report registered in the registration system program of Urmia University of Medical Sciences from March 2015 until February 2022 using complete enumeration method. In the current registry, the patient's profile as well as relevant information is collected directly through patient interviews and medical records. The required information of the patients was extracted from the file of the celiac patient registration system of Urmia University of Medical Sciences. The required information includes demographic data, anthropometric and clinical data, disease duration, blood group (ABO and Rh), disease status and disease complications.

Patients were divided into three groups based on the severity of the disease: mild, moderate and severe. In the severe or typical form, the patient suffers from classic celiac symptoms such as abdominal pain, diarrhea and weight loss (mainly gastrointestinal), in the moderate or subclinical form, symptoms such as chronic anemia, increased liver enzymes, obesity, infertility, etc. appear and in the mild or asymptomatic form of the disease, the patient does not have any symptoms, and anti-glutaminase antibody is detected during laboratory tests (22).

The basis of diagnosis of celiac disease is based on tissue transglutaminase antibody titer, endoscopy report and pathology of samples taken from duodenum and the evidence in the patients' files, which were either performed in this center or received along with the attached documents of the patients. The patients who were diagnosed with celiac disease based on the biopsy report were included in the study, and if the information was incomplete, the information was completed by referring to the archive, reviewing the patient's file and calling, and eventually, the people who had more than 20% defects in their files were excluded from the study. The process of extracting data from patients' files and entering them into the celiac registration system program was done by specially trained experts.

Data analysis method: Data were analyzed using SPSS software and Chi-square statistical tests, one-way analysis of variance, independent t-test and Kolmogorov-Smirnov, and $p<0.05$ was considered significant.

Results

Out of 199 patients, 125 (62.8%) were women and 74 (37.2%) were men. The mean age of all patients, women and men were 37.15±15.65, 36.04±14.70, and 39.02±17.07 years in a range of 5 to 81 years, respectively. No statistically significant difference was observed between the mean age of men and women. In terms of disease severity, 78 patients (39.2%) were mild, 108 patients (54.3%) were moderate, and 13 patients (6.5%) were severe. No significant difference was observed between gender and severity of disease. Most of the patients were from blood group O (71 people (35.7%)) and blood group A (69 people (34.7%)), respectively. 171 patients (58.9%) were Rh^+. The results showed that there was no significant difference in terms of gender between different blood groups and Rh factor. There was no significant difference between the mean age and different blood groups and Rh factor (Table 1).

Most of the mild patients (80.8%) had blood type O, and moderate patients (50.9%) were among people with blood type A. This difference was statistically significant ($p<0.001$). In all three groups of patients, more than 80% were Rh positive (Table 2).

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Table 1. Comparison of gender and age by blood groups and Rh factor

	Man Number(%)	Woman Number(%)	Total Number(%)	p-value	Mean±SD	p-value
Blood group						
A	25(33.8)	44(35.2)	69(34.7)	0.16	35.69±16.75	0.22
B	9(12.2)	27(21.6)	36(18.1)		37.33±14.59	
AB	7(9.5)	16(12.8)	23(11.6)		32.95±15.21	
O	33(44.5)	38(30.4)	71(35.6)		39.84±15.03	
Rh						
Positive	68(91.9)	103(82.4)	171(85.9)	0.09	36.91±15.35	0.58
Negative	6(8.1)	22(17.6)	28(14.1)		36.91±15.35	

Table 2. Comparison of disease severity in different blood groups and Rh factor

	Mild Number(%)	Moderate Number(%)	Severe Number(%)	p-value
Blood group				
A	9(11.5)	55(50.9)	5(38.5)	<0.001
B	5(6.4)	28(25.9)	3(23.1)	
AB	1(1.3)	17(15.8)	5(38.4)	
O	63(80.8)	8(7.4)	0(0)	
Rh				
Positive	64(82.1)	95(88)	12(92.3)	0.11
Negative	14(17.9)	13(12)	1(7.7)	

Discussion

In this study, the prevalence of celiac disease was higher in women, and blood group O^+ was the most frequent in celiac patients, and then blood group A^- was the most common among these patients compared to other blood groups. In people with blood group O, the frequency of mild cases of the disease was much higher than in other blood groups, and the frequency of severe cases in people with blood group AB was higher than other blood groups ($p<0.001$).

In the present study, among the 199 examined patients, 62.8% were women and 37.2% were men, which indicates that this disease is more common in women. In the study of Jansson-Knodell et al., which was conducted in order to investigate the effect of gender on the clinical manifestations of celiac disease in Pakistani adults, the frequency of female gender was more than male, and female to male ratio in their study was equal to 3.01 (23). Furthermore, in the reviews and reports of the American Gastroenterological Association, the predominance of the female population in celiac disease has been emphasized, so that women to men ratio has been reported as 2:1 (24).

The mean age of the patients in this study was 37.15±15.65 years. In addition, there was no significant difference between the two gender groups in terms of age. In the study by Bai et al., which was conducted with the aim of investigating the effect of gender on the manifestations of celiac disease, the mean age of the patients was higher than our study (more than 45 years). This difference can be due to the regional differences of the two studies. However, in this study, consistent with our study, there was no significant difference between men and women in terms of age (25).

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In evaluating the relationship between blood groups and specific diseases, evidence has shown that the type of blood group may play an important role in contracting diseases, including gastric ulcers and stomach cancer (26). The present study also showed that, like many diseases, the most common blood type among celiac patients is blood type O. Moreover, in this study, it was found that in terms of the severity of the disease, patients with blood group O experienced a less severe form of disease despite the fact that it constituted a higher percentage of patients; about 80% of the patients experienced a mild disease and no patient with this blood type had severe type of the disease.

The results of this study showed that, consistent with previous studies, women made up a higher percentage of the population with celiac disease. Furthermore, the mean age of the patients in this study was 37.15±15.65 years. The results of the study indicated a higher frequency of blood group O among celiac patients. In addition, the severity of the disease in people with blood group O was less than other blood groups.

Conflict of interest: The authors declare that there is no conflict of interest.

Ethical considerations: All patient information was coded and strictly confidential. No additional costs were imposed on the patients and a written informed consent form was obtained from all patients.

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