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ABO Blood Groups, Rhesus Factor, and Rheumatoid Arthritis

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Abstract. The ABO and Rhesus blood group systems play critical roles in clinical practice, particularly concerning their associations with autoimmune diseases, including rheumatoid arthritis (RA). This study aimed to investigate the relationship between ABO blood types, Rh factors, and RA in a Georgian population. A total of 157 participants were included, comprising 93 RA patients and 64 healthy controls. Blood samples were analyzed for ABO and Rh D blood group determination, revealing that blood type O was the most prevalent among RA patients (50.5%), followed by type A (35.5%), while the control group exhibited similar distributions (O: 54.7%, A: 34.4%). The Rh factor analysis indicated a slightly higher prevalence of Rh-positive individuals in the RA group (84 patients) compared to Rh-negative individuals (9 patients). The overall distribution of blood types in RA patients closely mirrored that of the general population, indicating no significant link between ABO blood types and RA. Further research is warranted to explore these associations and their implications for RA pathogenesis and potential therapeutic targets.

Keywords: Rheumatoid Arthritis, ABO Blood groups, Rhesus Factor.

1. Introduction

Although numerous blood group systems have been established based on different blood group antigens, ABO and Rhesus are the most significant in clinical practice. The ABO blood type system is divided into four fundamental groups, A, B, AB, and O, based on the presence of the A and B antigens. These antigens are regulated by three allelic A, B, and O genes found on the long arm of chromosome 9[1]. Glycosyltransferases catalyze processes that result in the oligosaccharide antigens associated with blood groups A and B. A and B antigens are synthesized as a result of the A and B glycosyltransferases, which are encoded by functional A and B alleles. The A and B genes encode separate sugar-specific transferases because nucleotide alterations result in amino acid substitutions. Due to their inability to generate functional enzymes, the O genes are inactive. On chromosome 19, the H gene, which forms the H-antigen, is present in Group O individuals. In order to create the A and B antigens, this antigen acts as a precursor oligosaccharide[2].

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The Rhesus system classifies blood groups as Rh− or Rh+ based on the presence of the Rhesus D antigen on red blood cell surfaces. Rh antigens are encoded by three pairs of allele genes on chromosome 1[3].

It is interesting to note that while the entire human population has comparable ABO and Rh blood types, the number and distribution of these blood groups varies by nationality and ethnicity. Based on several articles[4], [5], worldwide, the distribution of ABO blood groups can be described as O>A>B>AB.

It is known that blood groups Rh and ABO are associated with a number of disorders[6] Their relationship with autoimmune diseases has also been described[7]. Firstly, ABO blood type and specific HLA antigens have been consistently linked to a number of human diseases in case-control studies. These mostly included autoimmune conditions such celiac disease, psoriasis, rheumatoid arthritis, multiple sclerosis, pemphigus vulgaris, and type 1 diabetes[8]. With an estimated 0.5% to 1% global prevalence[9], rheumatoid arthritis (RA) is particularly intriguing as it continues to be a significant public health concern. Furthermore, despite intensive research, the specific cause of RA remains unknown, but it is likely to be the result of a complex combination of genetic and environmental factors[9]. Several genetic variables have been linked to RA susceptibility, but the relationship between blood types and rheumatoid arthritis has received more attention in recent years. The hypothesized linkages between blood types and RA are biologically feasible, since blood group antigens have been linked to a variety of immunological activities, including the control of inflammatory responses and the modulation of immune cell interactions. Specific blood group antigens have also been shown to alter the expression and function of immune-related molecules such as cytokines and cell adhesion molecules, both of which play important roles in RA pathogenesis[10]. Also, the complement system serves as the first line of defense in the clearance of infections, dying cells, and immune complexes. Several complement regulating proteins are located in plasma and on cell membranes, preventing complement activation on RBCs. A decrease in the production and/or function of complement regulatory proteins may result in undesired complement activation and rapid RBC elimination[11]. RBCs' immunologic role offers a neglected but potentially rich field of study that could produce fresh perspectives on immune regulatory mechanisms. Since RBCs have been linked in both clinical and experimental settings to thrombosis or bleeding, there is a renewed focus on the role of these cells in rheumatic diseases. This suggests that RBCs may be a potential target for therapy in a variety of conditions.

Recent data implies that there may be a blood group association that either increases or decreases the probability of having RA. Numerous investigations have looked into the possible relationships between Rh and ABO blood types and RA severity, clinical outcomes, and susceptibility. For example, it was reported by Nik et al., (2021)[12] that arthritis was more prevalent in the B blood type and Rh-positive group. Additionally, in a 2017 study carried out in Turkey was shown that blood type A was found to be at the highest rate in patients with RA. [13].

However, contradicting findings have been reported by several other researchers, who found no meaningful correlations between blood types and RA. A 2020 study carried out in China found no significant differences in the distribution of blood types among rheumatic disorders[14].

Understanding and establishing a link between blood types and RA could have significant clinical significance. If a substantial correlation is found, blood types could be used as a biomarker to measure RA risk, allowing for earlier diagnosis and more customized treatment options. Furthermore, such studies may provide new insights into the underlying mechanisms of RA, allowing for the creation of targeted therapeutics.

The purpose of this study was to ascertain whether there is a connection between ABO and rheumatoid arthritis in the Georgian population, given that the distribution of ABO genes varies among ethnic and social groups.

2. Materials and Methodology

The study was conducted in Georgia. The total 157 voluntaries took part in the cross-sectional study. 17 male and 140 females are represented among them. The sample included 93 people with rheumatoid

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arthritis and 64 healthy control adult patients (age range ≤20-80). Participants without a Georgian ethnic background, minors, and those without rheumatoid arthritis were automatically excluded from the study. Between April 6, 2023 and July 13, 2024, in Batumi, Georgia, at the N4 Batumi polyclinic, as well as at BAU Batumi International University and Shota Rustaveli State University of Batumi, research data was gathered and processed.

The information for this study was gathered by a survey. The Ethics Committees of School of Medicine and Health Science of the BAU International University Batumi, approved this cross-sectional study with reference number N-MED006. All participants signed the informed consent form to indicate their consent, and their privacy was maintained. Each participant in the study whose biological samples were collected was assigned a unique code/number.

A total of five (5.0) mL of venous blood was taken in sample tubes containing EDTA (dipotassium ethylene diamine tetra-acetic acid), of which 1 mL was used for serological determinations of ABO and Rh D blood groups, while the remaining volume was utilized for the next step of research. Blood samples were examined within 24 to 48 hours of collection. All collected samples were transported from the collecting site to the laboratory for examination by cold chain (ice packs in an airtight).

Determination of ABO and Rh D Blood Group were conducted using Anti-A monoclonal Reagent, Rapid Labs Ltd, Expiry Date: 2025/05/18, Anti-B Monoclonal Reagent, Rapid Labs Ltd, Expiry Date: 2025/05/18, Anti-AB Monoclonal Reagent, Rapid Labs Ltd, Expiry Date: 2025/05/18 Anti-D, Rapid Labs Ltd, Expiry Date: 2025/05/18. The presence or absence of the A, B, and D antigens on human red blood cells can be determined by testing them with the appropriate antisera, specifically Anti-A, Anti-B, Anti-AB, and Anti-D. The process is based on agglutination.

The materials section incorporates data on blood group distribution and the number of blood donors[15]. This inclusion allows for a more robust analysis by providing context and comparative data on donor demographics and blood type frequencies within the studied population.

3. Statistical analysis

All analyses were conducted using GraphPad Prism 8.0 software. The chi-square test was used for investigating the correlation between the types of rheumatic diseases and blood groups. When the p-value was less than 0.05, the results were considered statistically significant.

4. Results

4.1. Comparison of ABO blood groups between patients with Rheumatoid Arthritis and a healthy population

Within the scope of the research, the distribution of blood groups among 93 individuals with rheumatoid arthritis was investigated. The distribution of blood groups was contrasted also with a) control group (total number = 64), b) people in region; which consisted of 1501 people in the region overall, including blood donors.

The distribution of the ABO system blood groups is uneven in both the healthy population and the group of RA patients; specifically, the distribution of blood groups in the 1) RA patient group is as follows: I (O) = 50.5%; II (A) = 35.5%; III (B) = 10.7%; IV (AB) = 3.2%. 2) In the control group: O (I) = 54.7%, A (II) = 34.4%, B (III) = 7.8%, and AB (IV) = 3.1% 3) The following are the ABO group distributions in region: O (I) = 48.4%, A (II) = 37%, B (III) = 10.4%, and AB (IV) = 4.3% 4) The distribution of ABO blood groups among blood donors is as follows: O (I) = 49.9%, A (II) 34.5%, B (III) 10.8%, and AB (IV) 4.7% (Table 1).

The Figure 1 shows that there is an uneven distribution in practically all four groups, but the first and second ABO blood groups are especially prevalent. As shown, about 51% of RA patients have the first O (I) blood group. The fact that more than half of RA patients have O (I) suggests the idea that people with this type are more susceptible to RA.

If we compare patients with RA with the control group, we see that the distribution of blood groups is almost the same. It might suggest that the sampling method used for selecting individuals in both

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groups was appropriate and that there was no significant bias introduced in the selection process which leads to the reliable results.

If we compare patients with healthy individuals in region including blood donors, we can see that ABO blood distribution is likely the same, which suggests several key points: 1) The patient group likely reflects the general population of the region, indicating that the selection of patients was not biased by factors related to blood group distribution. This similarity suggests that patients in our study are representative sample of the local population. 2) It may indicate that there is no specific association between blood type and the RA susceptibility. Since the distribution mirrors that of the general population, it suggests that blood group does not play a significant role in the likelihood of developing the condition or Rheumatoid Arthritis.

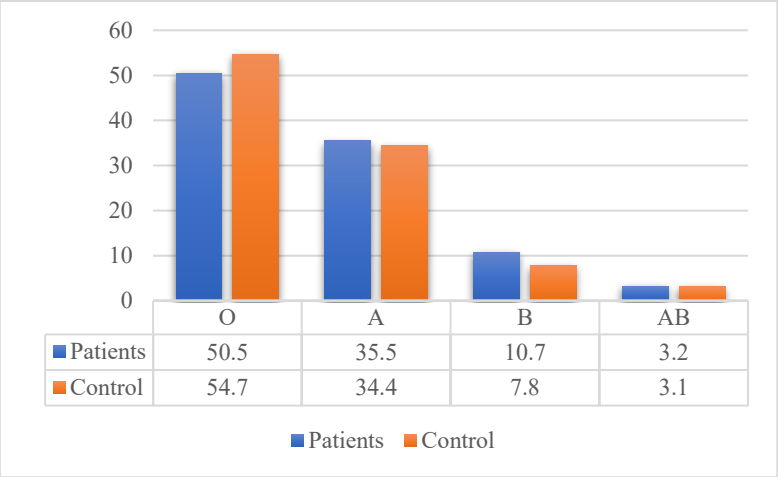

Figure 1. ABO blood system distribution in patients with rheumatoid arthritis and a healthy control group.

Table 1. Distribution of ABO blood group phenotypes across different groups

	Patients		**Control**		**Regional Distribution**		**Blood donors**	
	N	%	N	%	N	%	N	%
O	47	50.5	35	54.7	238	48.4	504	49.9
A	33	35.5	22	34.4	182	37	349	34.5
B	10	10.7	5	7.8	51	10.4	109	10.8
AB	3	3.2	2	3.1	21	4.3	47	4.7
Total	93	100%	64	100%	492	100%	1009	100%
chi-square	2.313							
p-value	0.9854							
the result in significant	$P < 0.05$							

*The chi-square statistic is 2.313. The p-value is 0.9854. The result is not significant at p<.05.

4.2. Comparison of Rh groups between patients with Rheumatoid Arthritis and a healthy control

The study also compared Rh groups in patients with Rheumatoid Arthritis to healthy controls (Table 2). Among individuals with rheumatoid arthritis (RA), those who are Rh-positive (Rh+) are found in slightly higher numbers compared to a control group, while those who are Rh-negative (Rh-) are slightly fewer. Rh+ RA individuals being 2.8% more than the control group suggests that there is a higher prevalence of Rh+ individuals in the RA group compared to a control group. This might imply a potential association between Rh+ status and the likelihood of developing RA. Rh- RA individuals being 2.8% less than the control group means that Rh- individuals with RA are less common than those in the control group. This might suggest that being Rh- could be associated with a lower likelihood of developing RA.

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In summary, these statistics suggest a potential relationship between Rh blood type and rheumatoid arthritis.

Table 2. Distribution of the Rhesus factor in individuals with Rheumatoid Arthritis compared to a healthy control group

	Patients		**Control**	
	N	%	N	%
Rh+	84	90.3	56	87.5
Rh-	9	9.7	8	12.5
Total	93	100%	64	100%
chi-square		0.3128		
p-value		0.5759		
the result in significant		P < 0.05		

*The chi-square statistic is 0.3128. The p-value is 0.5759. The result is not significant at p < .05.

4.3. Comparison of ABO and Rh groups between patients with Rheumatoid Arthritis and a healthy control

The analysis of patients with rheumatoid arthritis (RA) reveals intriguing associations between blood type and Rh factor. Among the 93 RA patients studied, blood type O (Rh+) is the most prevalent, with 42 individuals, followed by blood type A (Rh+) with 30 patients. Blood type O (Rh-) has 5 patients, while blood type A (Rh-) accounts for 3 patients. The representation of blood type B is smaller, with 9 Rh+ and 1 Rh- patient, while blood type AB is the least common, featuring only 3 Rh+ patients and no Rh- individuals. Overall, the data shows a striking dominance of Rh+ individuals, totaling 84 patients, compared to just 9 Rh- patients. This suggests a potential correlation between being Rh+ and the likelihood of developing RA, particularly for blood types O and A. These findings highlight the need for further investigation into the relationship between blood groups, Rh factors, and the risk of rheumatoid arthritis, as understanding these associations could offer insights into the underlying mechanisms of the disease.

Table 3. ABO blood group and Rh factor distribution in individuals with rheumatoid arthritis compared to a healthy control group.

	Patients		**Control**	
	N	%	N	%
O (Rh+)	42	45.2	32	50.0
O (Rh-)	5	5.4	3	4.7
A (Rh+)	30	32.3	18	28.1
A (Rh-)	3	3.2	4	6.3
B (Rh+)	9	9.7	5	7.8
B (Rh-)	1	1.1	0	0.0
AB (Rh+)	3	3.2	1	1.6
AB (Rh-)	0	0	1	1.6
Total	93	100	64	100%
chi-square		3.914		
p-value		0.0732		

5. Discussion

Our study investigates the distribution of ABO blood groups and Rh factor in individuals with Rheumatoid Arthritis (RA) compared to a control group and the broader regional population. The

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findings reveal predominance of blood group O (50.5%) among RA patients, similar to the scientific paper published in 2024, in which group O prevails[16]. The picture is quite intriguing, as previous research has shown that the A blood group is more commonly observed in patients with rheumatic diseases [13] [8] , which may indicate an increased risk for certain autoimmune conditions, particularly Rheumatoid Arthritis.

When comparing the blood group distribution of RA patients to that of healthy controls and the general population, we find that the distributions are largely similar. This raises important considerations regarding the role of blood type in RA susceptibility. The lack of significant variation suggests that, while blood group O is the most prevalent among RA patients, it does not necessarily indicate a direct causal relationship between blood type and the development of RA.

Additionally, recent studies[12] [16] [1] [17]show that the distribution of the Rh factor indicates a higher prevalence of Rh-positive individuals among RA patients. Our findings align with this observation, as we found that Rh-positive individuals are more common among RA patients compared to the control group, with a difference of 2.8%. This observation may suggest a potential association between Rh-positive status and an increased likelihood of developing RA. Conversely, the lower prevalence of Rh-negative individuals in the RA group indicates that being Rh-negative might be associated with a reduced risk of developing the disease. This intriguing finding warrants further exploration, as the biological mechanisms linking Rh status and RA are not well understood.

The representation of blood types within the RA cohort further emphasizes the dominance of Rh-positive individuals, particularly those with blood types O and A. This prevalence underscores the need for additional studies to elucidate the potential mechanisms behind these associations, particularly considering genetic, environmental, and immunological factors that may contribute to RA pathogenesis.

Importantly, the study's robust methodology—including the similarity in blood group distribution between the RA patients and the control group—suggests that the sampling process was sound, minimizing potential biases. This strengthens the reliability of our findings and reinforces the idea that the RA patient group is representative of the local population regarding blood type distribution. However, it is important to note that the sample size in this study, while providing preliminary insights, was relatively small, with only 93 RA patients and 64 controls. This limitation may impact the generalizability of our findings, highlighting the need for larger-scale studies to confirm these associations and better understand the complex interactions between blood type, Rh factor, and RA susceptibility.

6. Conclusion

While the data points to a potential correlation between Rh-positive status and the likelihood of developing rheumatoid arthritis, the lack of significant divergence in ABO blood group distribution between RA patients and healthy controls suggests that blood type may not be a major risk factor for RA. Future research should delve deeper into the interplay between blood group types, Rh factors, and autoimmune diseases, potentially guiding the development of targeted prevention and treatment strategies. Understanding these associations could provide valuable insights into the underlying mechanisms of RA and enhance our overall comprehension of autoimmune disorders.

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