

Linkage of ABO blood groups with ischemic stroke

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Abstract

Aim: Like cancer and myocardial infarction, the cerebrovascular accident causes death and morbidity in adults. Ischemic stroke is the most common type of stroke. Predisposing conditions to other cardiovascular diseases similarly play a facilitating role for stroke. The association of ABO blood types with several illnesses as described in previous studies. In this retrospective observational study, our purpose is to show the contribution of ABO blood types in ischemic stroke patients. Our study is important because it is a rare analysis elucidating the link between ABO blood groups with IS risk in the Turkish population.

Materials and Methods: 1,540 cases diagnosed with ischemic stroke and 20,863 healthy subjects determined as the control group was included in this research. Ischemic stroke cases and the healthy subjects were between 45-90 years old. Both these groups were examined for blood group analysis.

Results: When the patients and healthy subjects were examined in terms of blood group distributions, the blood group type distribution within each group had similar characteristics. In terms of Rh status and Blood type distribution, Ischemic stroke cases, and the healthy subjects were not statistically different from each other.

Conclusion: We were not able to show any relation between ischemic stroke and ABO blood type in our study.

Keywords: ABO blood types; cardiovascular diseases; stroke

INTRODUCTION

The cerebrovascular accident causes death and morbidity in adults. Stroke is classified as ischemic and hemorrhagic stroke according to the underlying cause. Among stroke types, the most frequent type of stroke is Ischemic type stroke (1,2). Ischemic stroke is classified as major arterial atherosclerosis, cardio embolism, small artery infarction, infarction with unspecified etiology, and other causes (vasculitides, fibromuscular dysplasia, hypercoagulability) (3).

Diseases and patient characteristics that lead to stroke are age, stroke history in relatives, hypertension, hyperlipidemia, diabetes mellitus, atrial fibrillation, valvular heart disease, coagulation abnormalities, oral contraceptive intake, obesity, and smoking (4).

After Landsteiner discovered the types A, B, AB, and O, the following researchers determined that the ABO system also consists of additional subgroups. The ABO system is not only a blood group system but also a histological grouping system because antigens belonging to the ABO system are located on the surface of erythrocytes and platelets as membrane antigens, as well as in vascular, intestinal, cervical, and breast epithelium cells. They are found dissolved in plasma, saliva, milk, urine, and feces.

Besides, there are strong reactive antibodies in the serum against antigens that are not present on the surface of the erythrocyte (5,6).

Associations between ABO groups and pathogenesis of several diseases have been described in different studies including infectious, neurological, cardiovascular diseases, and malignancies (7-9). The mechanism behind this association is revealed in several researches.

Some mechanisms that explain how infectious agents can cause disease more easily in individuals with certain blood groups have been proposed. One of these mechanisms is to protect infectious agents from the immune system response by imitating host blood group antigens. Another mechanism can be explained by the antigenic similarity of being able to use glycosylated receptors on the host cell surface (10).

The relationship between blood group and malignancy is explained by the following mechanisms: Some adhesion molecules that are related to ABO blood groups contribute to tumorigenesis. Besides, the Willebrand factor (VWF), which transports the blood group markers, is thought to be effective in regulating the mechanisms of tumor angiogenesis and apoptosis (11).

Received: 18.01.2021 **Accepted:** 05.03.2021 **Available online:** 18.10.2021

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VWF & FVIII are the main plasma proteins that play role in thrombosis. These prothrombotic proteins also contribute to a relation with blood group and cardiovascular disease. VWF carry A, B, and H antigens. VWF activity varies from the different degrees of glycosylation on each blood group type. A and B antigens have modulatory effects on VWF activity. These antigens are produced by the enzymes A and B glycosyltransferase. These enzymes are associated with H oligosaccharides on VWF. Hence, the development of arterial-venous thromboembolism, coronary artery infarction, and cerebrovascular disease rise through patients who have blood types other than the O blood group (12,13).

In this retrospective observational study, we purposed to determine the patterns of ABO blood types among ischemic stroke cases and compare these patients with the healthy control group who have similar ages with ischemic stroke patients.

MATERIALS and METHODS

Between January 1, 2008 and December 1, 2019, our study included 1540 cases diagnosed with ischemic stroke and 20,863 healthy subjects as the control group. Ischemic stroke patients and the control group were between the ages of 45-90. Both these groups were examined for blood group analysis. Files were investigated retrospectively. Age, gender, blood group, and Rh status were recorded in to a statistic program. This research was accepted by the local ethical commission (date: 26.02.2020 no: 2081).

Descriptive statistics were shown as frequency or percentage for categorical variables and as mean, standard deviation, median and interquartile range values for continuous variables.

Shapiro Wilk test was used to examine the coherency of continuous variables to normal distribution. Independent sample t-test was performed for comparing variables with normal distribution between two groups, and the Mann Whitney U test was used for comparing variables without normal distribution between 2 groups. A paired t-test was performed for intra-group comparisons of variables with a normal distribution. Wilcoxon test was performed for intra-group comparisons of variables without normal distribution. Statistical significance was regarded as significant if a P-value below 0.05.

RESULTS

The mean age of stroke patients was over the control group; 77 ± 9.4 , 63 ± 5.6 years ($p < 0.0001$) respectively. When the patient and healthy subjects were compared in terms of gender, a significant difference was observed between the groups ($p < 0.0001$) (Table 1). The highest frequent blood type in ischemic stroke and control groups was A Rh +. However, when the patients and healthy subjects were examined in terms of blood group distributions, the blood group type distribution within each group had similar characteristics. ($p = 0.3$) (Table 2). Additionally, in terms

of Rh status and Blood type distribution Ischemic stroke cases, and the healthy subjects were not statistically different from each other ($p = 0.234$, ($p = 0.652$) respectively) (Table 3),(Table 4).

Table 1. Distribution of patients and control groups according to gender

	Female	Male	Total	
Ischemic Stroke	814 (52.9%)	726 (47.1%)	1.540 (100%)	$p < 0.0001$
Control	12.131 (58.1%)	8.732 (41.9%)	20.863 (100%)	$p < 0.0001$

Table 2. Blood group distribution of Patients

Blood Group	Ischemic Stroke	Control	Total	
A Rh ⁺	593 (38.5%)	8.129 (39%)	8.722 (38.9%)	$P > 0.05$
A Rh ⁻	82 (5.3%)	1.013 (4.8%)	1.095 (4.9%)	$P > 0.05$
B Rh ⁺	240 (15.6%)	3.099 (14.9%)	3.339 (14.9%)	$P > 0.05$
B Rh ⁻	33 (2.1%)	370 (1.8%)	403 (1.8%)	$P > 0.05$
O Rh ⁺	411 (26.7%)	5.825 (27.9%)	6.236 (27.8%)	$P > 0.05$
O Rh ⁻	59 (3.8%)	671 (3.2%)	730 (3.3%)	$P > 0.05$
AB Rh ⁺	115 (7.5%)	1.562 (7.5%)	1.677 (7.5%)	$P > 0.05$
AB Rh ⁻	7 (0.5%)	194 (0.9%)	201 (0.9%)	$P > 0.05$

Table 3. ABO blood distribution

Blood Group	Ischemic Stroke	Control	
A	675 (43.83%)	9.142 (43.82%)	$P > 0.05$
O	470 (30.52%)	6.496 (31.13%)	$P > 0.05$
B	273 (17.73%)	3.469 (16.63%)	$P > 0.05$
AB	122 (7.92%)	1.756 (8.42%)	$P > 0.05$

Table 4. Comparison of the groups according to Rh status

Blood Group	Ischemic Stroke	Control	
Rh positive	1.359 (88.2%)	18.615 (89.2%)	$P > 0.05$
Rh negative	181 (11.8%)	2.248 (10.8%)	$P > 0.05$

DISCUSSION

Ischemic stroke-associated risk factors and interactions are still not adequately defined. Advanced age, gender, hypertension, hyperlipidemia, diabetes mellitus, and smoking are conditions that predispose to stroke (14). In addition to these possible risk factors, ABO blood groups are also thought to play a role in the occurrence of ischemic stroke. The structural similarity of ABO antigens to VWF and FVIII is the basis for making this proposition. VWF or FVIII molecules are involved in both thromboembolism and IS pathogenesis (15). Recent genome-based and observational researches have examined the linkage with ischemic stroke and blood groups.

This study is one of the rare analyze to determine the relation of ABO blood types and IS risk in Turkey. In contrast to some studies suggesting an association between ABO blood types and ischemic stroke, this retrospective cohort study did not find an association between ABO blood types and ischemic stroke (IS). As in the pathogenesis of other cardiovascular diseases, a significant difference was observed between ischemic stroke patients and healthy control groups in terms of age and gender.

Contrary to our finding, the REGARDS study found that the risk of stroke in people with AB blood type is a risk factor independent of other facilitating conditions. It is claimed that high factor VIII levels in individuals with this blood group are the main responsible for this risk increase (16). In a study on the Chinese population investigating the relationship of blood group polymorphisms in the ABO gene with stroke, they concluded that gene interactions and single nucleotide polymorphisms (SNP) are associated with Ischemic stroke (17). Another study revealed that some stroke scales are related to ABO types and subtypes in patients with acute ischemic stroke. According to this study, AB blood type and serum white blood cell (WBC) are important factors for stroke severity (18). Wiggins et al. found that IS risk increased within patients who have A and B blood groups (19). Similar to this study, Sabino and friends found A and B blood types were related to IS, additionally, the O blood group had protective effects against IS (20). In similar research, it was concluded A and AB blood groups were related to cardiovascular diseases as a coronary, cerebrovascular, or peripheral vascular disease (21).

Some articles investigating the relationship between blood type and ischemic stroke have concluded similar conclusions to the study. In two genome-based researches; Ling et al. found no linkage between IS and blood groups (22), and E.Hanson et al. concluded that neither ABO phenotype nor genotype makes a major contribution to the pathogenesis of ischemic stroke (23).

CONCLUSION

There are several limitations to this study. We did not separate cases in line with the TOAST Stroke classification. As VWF and FVIII kits are expensive, the routine measurement of the VWF and FVIII levels could not be performed in our hospital. So, VWF and FVIII levels could not be elucidated.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical Approval: This research was accepted by the Kecioren Teaching and Research Hospital local ethical commission (date: 26.02.2020 no: 2081).

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