

# The Relationship Between ABO Blood Groups and Retinal Venous Occlusion

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## Research Article

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# Abstract

*Purpose* The aim of this study is to investigate the relationship between retinal vein occlusions (RVO) and blood groups.

*Methods* Detailed ophthalmological examinations, systemic diseases and blood groups of patients who applied to Balikesir University Faculty of Medicine, Ophthalmology Outpatient Clinic between February 2019 and May 2020 with retinal vein occlusion were retrospectively analyzed. The blood groups of the patients were divided into 2 groups as O and non-O. The results were compared with a normal group matched in terms of age and gender. Regression analysis was performed to determine the relationship between blood group types and vein occlusions.

*Results* A total of 116 people were included in the study. The mean age of 38 patients with vein occlusion was  $61.8 \pm 11.3$ , while the mean age of 78 patients without vein occlusion was  $62.6 \pm 11.1$  ( $p=0.696$ ). In the RVO patients group, 14 (36.8%) were female, 30 (78.9%) had non-O blood group, 20 (52.6%) had hypertension (HT), 19 (50%) had diabetes mellitus (DM). According to the results of simple logistic regression analysis, non-O blood group and HT have statistically significant effects on RVO formation (Simple Regression Analysis results: OR 2.47, 95% CI 1.00-6.09,  $p=0.049$ ; OR 2.22, 95% CI 1.00-4.90,  $p=0.048$ ; respectively). Non-O blood group and HT significance remained limited as a result of multiple regression analysis (OR 2.47, 95% CI 0.97-6.06,  $p=0.057$ ; OR 2.18, 95% CI 0.97-4.88,  $p=0.057$ , respectively).

*Conclusion* Non-O blood type can be considered as a risk factor for retinal vein occlusion.

## Introduction

Retinal vascular occlusion is a serious condition with severe vision loss in adults. Retinal vein occlusions (RVO) are the most common condition among retinal vascular occlusions [1, 2]. In addition, RVO is the most common retinal vascular disease after diabetic retinopathy [3]. Annual prevalence of RVO was found between 0.52% and 1.1% in large-scale studies [4, 5]. As a result of studies on factors that predispose to RVO, advanced age, diabetes mellitus (DM), hypertension (HT), thrombophilia (Protein C and S deficiencies, antithrombin factor V Leiden mutation, hyperhomocysteinemia and anticardiolipin antibodies) were identified. Glaucoma is the most common eye disease predisposing to RVO [6–11].

ABO blood group system was first described by Karl Landsteiner in 1901 [12]. These antigens are expressed on the surface of red blood cells and some other tissues like platelets, vascular endothelium. People may have 4 different blood group phenotypes on the ABO blood type scale. Moreover, another blood group system with great clinical importance is the rhesus blood group system. People are called Rh-positive or Rh-negative according to the synthesis of rhesus proteins [13].

Lots of researches proved blood groups differences have implications on diseases. Coagulopathy is one of the conditions which is associated with ABO groups [14, 15]. Especially the relation of cardiovascular diseases with blood groups has been discussed in many studies. It has been reported that patients with

blood groups A and B mostly have coronary artery disease, ischemic heart disease and myocardial infarction. The cause of this situation is attributed to the effect of ABO blood groups on the plasma levels of factor VIII (FVIII) and vonWillebrand factor (vWF) [16–18]. The mechanism of the blood groups antigens' effect on the levels of FVIII and vWF is unclear. Both FVIII and vWF glycoproteins are lower (approximately 25%) in plasma of O blood group. High levels of FVIII and vWF is associated with thromboembolic diseases [19, 20].

There are few studies in the literature on the relationship between retinal vein occlusion and blood groups. Therefore, we planned to examine retinal vein occlusions in terms of possible risk factors and blood groups.

## Methods

Patients with retinal vein occlusion who were followed up between February 2019 and May 2020 at Balikesir University Faculty of Medicine, Department of Ophthalmology were included in this retrospective study. Written permission was obtained from the local ethics committee and the study was adherent to the Declaration of Helsinki. Patients with deficient blood type, thrombophilia history and glaucoma were not included in the study. Patients' detailed ophthalmological examinations, systemic diseases, demographic characteristics and blood groups were recorded. We determined the blood group records based on the tests performed in the biochemistry laboratory of our hospital. Blood groups were divided into 2 groups as O and non-O. A, B and AB blood groups were defined as non-O. The control group was randomly selected from the patients who applied to the outpatient clinic due to refractive error and whose records were complete with the characteristics specified in the study.

All values were reported as mean  $\pm$  standard deviation (SD). The normality of the data distribution was evaluated using the Shapiro-Wilk test. Chi-square test was used for categorical variables and an independent t test was used for continuous variables. In addition, univariate and multivariate logistic regression models were applied to evaluate independent relationships between blood groups and other possible factors and RVO. Odds ratio (OR) and 95 % confidence intervals (CI) are reported. A  $p$  value  $< 0.05$  was considered statistically significant. Analyses were carried out using SPSS software package version 20.0 (IBM, Armonk, NY).

## Results

A total of 116 patients were included in this study. There were 38 patients (with RVO) in the first group and 78 patients in the second group (without RVO). The mean age of the first group was  $61.8 \pm 11.3$  years, and the mean age of the second group was  $62.6 \pm 11$  years ( $p = 0.696$ ). 14 (36.8%) of the RVO patients and 42 (53.8%) of the control group were female. There was no significant difference between the groups in terms of age and gender ( $p = 0.696$ ,  $p = 0.064$ ). The demographic and clinical characteristics of the study groups are given in Table 1.

In the RVO group, non-O blood type was 78.9% of the total number; the same ratio was 38.5% for the non-RVO group. Non-O type blood group was significantly higher in the group with RVO ( $p < 0.001$ ). Rh positivity was similar for the two groups ( $p = 0.319$ ). Considering whether hypertension and diabetes mellitus make a difference between the two groups; only hypertension has found to be effective enough to make a significant difference. The rate of hypertension in the RVO group was significantly higher than the control group ( $p = 0.037$ ). There was no difference between the groups for diabetes mellitus and anticoagulant drug use rates ( $p = 0.475$ ) ( $p = 0.566$ ) (Table 1).

According to the results of univariate logistic regression analysis, the non-O group and the presence of HT were found to be risk factors for RVO. (OR 2.47, 95% CI 1.00-6.09,  $p = 0.049$ ; OR 2.22, 95% CI 1.00-4.90,  $p = 0.048$  respectively). When the analysis is repeated in the multiple regression analysis; although non-O blood group and hypertension seemed effective, there was no statistical significance (Multiple Regression Analysis results: OR 2.47.95% CI 0.97–6.06,  $p = 0.057$ ; OR 2.18, 95% CI 0.97–4.88,  $p = 0.057$ ) (Table 2).

## Discussion

According to the univariate logistic regression analysis results of our study, patients with non-O blood group and HT patients show a predisposing effect in terms of retinal venous occlusion. This effect is not statistically significant in multivariate analysis.

There are 2 studies on the subject in the literature. In the study of White in 1978, no relationship was found between ABO blood groups and retinal vein occlusions. Interestingly, individuals with blood type A have been reported to have worse visual prognosis than other blood groups [21]. Borella et al. stated that non-O blood group and thrombophilia were observed more in RVO patients [10]. The difference of our study from this study is that some demographic and systemic features that may affect the development of RVO are evaluated by regression analysis.

The relationship between ABO blood group differences and vascular occlusions has been researched for many years and studies have been carried out by many different disciplines. When the published reviews on this subject are examined, it is seen that vascular occlusions of both arterial and venous system can be affected by the patient's blood type [14, 22]. A large-scale study with more than 1.5 million blood donors also showed that there was a significant difference between O type and non-O type blood groups in terms of both arterial and venous thromboembolic events, and those with non-O group were at higher risk for thromboembolic events. When A, B and AB groups were evaluated among themselves in the same study, it was stated that the group that created the most susceptibility to vascular occlusions was the AB group and the tendencies of groups A and B to vascular occlusions were found to be similar [19]. Although this relationship has been demonstrated in many studies, it can be said that the events related to venous vascular structures are affected more with ABO blood groups when the venous and arterial originated events are examined [22].

There are few studies in the literature investigating the relationship between Rh blood group and vascular occlusions. In an article published in 1973, no relationship was found between myocardial infarction and

Rh blood group [23]. Similarly, in another previous study, no relationship was found between coronary artery disease and Rh positivity [24]. In our study, results consistent with the literature were obtained.

It is well known that advanced age, hypertension and diabetes mellitus are risk factors for vascular occlusions. This has also been shown for both retinal artery and vein occlusions. In the reviews published on retinal vascular occlusions, it was stated that advanced age and cardiovascular risk factors increase the risk of all retinal vascular occlusions [1, 25]. Similarly, in studies conducted specifically for retinal vein occlusions, advanced age, hypertension and diabetes mellitus were reported to be risk factors [8, 9]. In our study, too hypertension was identified as a predictive factor for retinal venous occlusions. However, diabetes mellitus was found to have no significant effect.

The most important limiting factor of our study is its retrospective design. Apart from this, the relatively low number of patients is another limiting factor. However, the incomplete records of the patients who were examined for thrombophilia caused many patients to be excluded from the study. Despite these limitations, our study is important, because it is the first study in which the effect of ABO blood groups on retinal venous occlusions was evaluated by regression analysis.

Consequently, non-O blood type may predispose to retinal venous occlusions. Randomized controlled trials will guide in this regard.

## **Declarations**

### **Conflict of interests:**

The authors have no conflict of interests to declare.

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### **Contributors:**

Design of the study [Mehmet Murat Uzel], [Ömer Can Kayıkçıoğlu] and [Cenap Güler]; conduct of the study [Pınar Kaya] and [Mehmet Murat Uzel]; analysis and interpretation [Pınar Kaya] and [Mehmet Murat Uzel]; and literature search [Pınar Kaya], [Mehmet Murat Uzel], [Ömer Can Kayıkçıoğlu] and [Cenap Güler]. All authors read and approved the final manuscript.

### **Availability of data and material:**

All data will be available upon request.

### **Consent to participate:**

All participants gave written informed consent for participation in the study.

### **Consent for publication:**

All participants gave written informed consent for their data to be published.

### **Ethics approval:**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board/Ethics Committee of Balikesir University (date: 25/02/2021, protocol no: 2021/06).

### **Language editing:**

The text was reviewed by a native English speaker.

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## Tables

Table 1

## Demographic and clinical characteristics of the study groups

	RVO group (n=38) (Mean ± SD)	Control group (n=78) (Mean ± SD)	p value
Age (year)	61.8±11.3	62.6±11	0.696
Gender (F/M)	14/24	42/36	0.064
Blood group			
O	8	48	
A	18	16	<b>&lt;0.001*</b>
B	8	14	
AB	4	0	
Rh positivity	22	40	0.319
Hypertension	20	26	<b>0.037*</b>
Diabetes Mellitus	19	37	0.475
Anticoagulant drug use	11	23	0.566

RVO: Retinal venous occlusion

\*Bold value indicates statistically significant result.

Table 2

## Results of logistic regression analysis of possible factors affecting retinal vein occlusion

	Univariate			Multivariate		
	OR	95% CI	p value	OR	95% CI	p value
Age	0.99	0.95-1.02	0.693			
Gender (Female)	0.50	0.22-1.10	0.085			
Non-O group	2.47	1.00-6.09	0.049	2.47	0.97-6.06	0.057
Rh positivity	1.30	0.59-2.85	0.503			
Hypertension	2.22	1.00-4.90	0.048	2.18	0.97-4.88	0.057
Diabetes Mellitus	1.10	0.51-2.40	0.795			
Anticoagulant drug use	0.97	0.41-2.28	0.952			