



Research Paper

Association between ABO and Rh blood groups and choroidal structural parameters in adult population

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ABSTRACT

Background: The ABO and Rh blood group systems have been associated with various systemic and ocular diseases. The choroid, as the most vascularized ocular structure, plays a critical role in retinal health. The choroidal vascularity index (CVI) has emerged as a robust metric for evaluating choroidal structure. This study aimed to investigate the association between ABO and Rh blood groups and choroidal structural parameters, including CVI, in a healthy adult population.

Methods: This prospective study included 164 healthy participants who underwent comprehensive ophthalmologic examination, including enhanced depth imaging optical coherence tomography (EDI-OCT). Subfoveal choroidal parameters—stromal area (SA), luminal area (LA), total choroidal area (TCA), and CVI—were measured using Image-J software. Participants were grouped according to ABO and Rh blood types. Statistical comparisons were conducted using Kruskal-Wallis, Mann-Whitney U, Chi-Square, and Spearman correlation tests.

Results: Among the 164 participants (55.5% female), blood type distributions were: A (36.6%), B (20.1%), AB (15.9%), and O (27.4%). Statistically significant differences were found between ABO blood groups for SA, LA, and TCA ($p < 0.05$). Blood group B exhibited significantly higher SA, LA, and TCA compared to other groups. However, CVI did not differ significantly among ABO or Rh groups ($p > 0.05$). No correlations were observed between age or axial length and choroidal parameters.

Conclusion: While SA, LA, and TCA values vary across ABO blood groups—particularly elevated in blood group B—CVI remains stable, suggesting a proportional expansion of stromal and vascular components. These findings imply a potential genetic influence of blood group antigens on choroidal morphology without affecting vascular density. Further large-scale, multiethnic studies are warranted to validate these associations.

1. Introduction

The ABO blood group system, consisting of four antigens (A, B, AB, and O), was discovered in 1900 by Karl Landsteiner and remains the most important blood group system. In this system, oligosaccharide antigens are present not only on red blood cells but also in many tissues and are referred to as histo-blood group antigens [1]. Following the ABO antigens, comes the D antigens of the Rh blood group system [2].

Over the years, the relationship between ABO blood groups and various diseases has been extensively studied. It has been shown that specific blood types are associated with susceptibility to certain diseases, including both infectious and non-infectious conditions [3]. ABO blood groups have been implicated as prognostic factors in cancers, vascular diseases, and other systemic conditions [3–5].

Studies have shown that peripapillary retinal nerve fiber layer (RNFL) and macular thickness are significantly determined by genetic factors [6]. There is a theoretical relationship between blood groups and the structural characteristics or disorders of the retina [7]. Recent advancements in imaging technologies, particularly the use of the choroidal vascularity index (CVI), have enabled detailed assessment of choroidal vascular structures. CVI, which represents the ratio of the vascular luminal area to the total choroidal area, provides a quantifiable metric for evaluating the vascular and stromal components of the choroid.

To the best of our knowledge, there is no research comparing the choroidal structural parameters among the groups with different blood types in an adult population. Therefore, we aimed to identify the association between choroidal structural parameters and ABO and Rh blood

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groups in an adult population.

2. Methods

This prospective study was conducted at the Kırşehir Ahi Evran University Training and Research Hospital between July 2023 and December 2023, including a total of 164 participants. Ethical approval was obtained from the Institutional Ethics Committee (Clinical Research Protocol No: 2023-11/76), and the study adhered to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before the research procedures.

The demographic characteristics, ABO blood groups, and Rh factors of the participants were recorded. Patients were selected from the individuals attending routine ophthalmologic examinations. Individuals with a best corrected visual acuity of 20/20 or more, no smokers, no drug use or alcohol consumption, no history of drug use in the last few months, and spherical equivalent between +2 D and -2 D were included in the study.

Any participant with a vitreoretinal disorder, IOP >21 mmHg, glaucomatous findings, previous ocular intervention, contact lens use, strabismus, amblyopia, ocular inflammatory disease, any systemic disease (diabetes mellitus, hypertension) and individuals with morbid obesity (BMI > 35) were excluded.

All participants underwent an ophthalmologic evaluation, including BCVA, intraocular pressure (IOP), axial length (AL) measurement with Lenstar LS 900 (Hagg-Streit AG, Koeniz, Switzerland), and dilated funduscopy.

Choroidal imaging was conducted using the enhanced depth imaging (EDI) mode of spectral-domain optical coherence tomography (Spectral OCT; software version 6.3.3.0, Heidelberg Engineering, Heidelberg, Germany). For each scan, the average of 100 images was calculated. To optimize image quality, automatic real-time averaging mode was employed to enhance the signal-to-noise ratio. Furthermore, eye tracking, EDI, and follow-up modes were enabled to reduce motion artifacts, improve choroidal visibility, and ensure consistency across all scans.

All EDI-OCT scans were performed by the same experienced technician between 10 AM and 12 PM to avoid diurnal variation. CVI measurements were carried out using Image-J software (Version 1.50a; National Institutes of Health, Bethesda, MD, USA). An area of 3000 µm in width was selected, 1500 µm nasally and 1500 µm temporally from the fovea. A line was drawn from the subfoveal retinal pigment epithelium (RPE) to the choroidal-scleral boundary, and measurements were manually taken. The region of interest (ROI) was defined using the Image-J ROI Manager. The image was adjusted with the Niblack automatic local thresholding method. The total area of the selected choroidal block, as well as the luminal area (LA) and stromal area (SA), were calculated. Finally, CVI was computed as the ratio of LA to total choroidal area (TCA). The total subfoveal choroidal area (TCA) was segmented into luminal (LA) and stromal (SA) components, and CVI was calculated as the ratio of LA to TCA. For the peripapillary area; by clicking on the nasal rim of the RNLF circular grid, a vertical line is placed at the center of the optic nerve with manual adjustment.

Mean, standard deviation, median, minimum, maximum value frequency and percentage were used for descriptive statistics. The distribution of variables was checked with kolmogorov-simironov test. Independent Kruskal-wallis and mann-whitney U test were used for the comparison of quantitative data. Chi-Square test was used for the comparison of the comparison of qualitative data. Spearman was used in the correlation analysis. SPSS 28.0 was used for statistical analyses. Statistical significance was set at a value of $p < 0.05$.

3. Results

A total of 164 participants, consisting of 73 (44.5 %) male and 91 (55.5 %) female, were enrolled in this study. Among these, 60 (36.6 %)

had blood type A, 33 (20.1 %) had blood type B, 26 (15.9 %) had blood type AB, and 45 (27.4 %) had blood type O. The mean age of the participants was 41.8 ± 12.2 years, with a range from 18 to 69 years (Table 1). In terms of demographic variables, no statistically significant differences were found between ABO blood groups regarding age ($p > 0.05$) and gender ($p > 0.05$).

Kruskal-Wallis tests revealed statistically significant differences in the SA, LA, and TCA between ABO blood groups (all $p < 0.05$). The SA values were significantly higher in participants with blood type B compared to those with other ABO blood groups (all $p < 0.05$), whereas no significant differences in SA values were observed between blood types A, AB, and O (all $p > 0.05$) (Table 2).

Both LA and TCA values were significantly higher in participants with blood types B and O compared to those with blood type A ($p < 0.05$), while no significant differences were found between blood types A and AB ($p > 0.05$).

No statistically significant differences were observed in axial length (AL), choroidal vascularity index (CVI), posterior stromal area (P-SA), posterior luminal area (P-LA), posterior total choroidal area (P-TCA), or posterior CVI among ABO blood groups (all $p > 0.05$) (Table 2)

No significant correlations were found between the SA, LA, TCA, CVI, P-SA, P-LA, P-TCA, and P-CVI parameters and age or AL (all $p > 0.05$) (Table 3).

4. Discussion

Blood groups are classified based on the presence or absence of hereditary antigenic substances on the surface of red blood cells. Previous studies have demonstrated that variations in blood groups can be associated with a wide range of diseases [3,4].

The choroid is the most vascularized tissue in the body, with its vascular network originating from the short and long posterior ciliary arteries. It is composed of blood vessels embedded in stromal tissue, which includes connective tissue, melanocytes, nerves, and extracellular fluid [2]. The vascular layer of the choroid can be divided into three distinct layers: the innermost choriocapillaris, the intermediate Sattler's layer, characterized by small-caliber vessels, and the outermost Haller's layer, which contains large-caliber vessels [8].

The primary function of the choroidal vascular network is to supply nutrients and oxygen to the outer retina. The retina is one of the tissues with the highest metabolic rate relative to its weight. Even within the veins of the choroid, oxygen levels remain elevated. The retinal pigment epithelium (RPE) located over the choriocapillaris is exposed to higher

Table 1

The distribution of demographic variables, blood groups and choroidal parameters.

	Min-Max	Median	Mean±SD
Age (years)	18–69	45	41.8 ± 12.2
Gender (n)	Female	91(55.5 %)	
	Male	73(44.5 %)	
AL (mm)	21.2–25.6	23.5	23.5 ± 0.8
SA (x10 ⁴)	14.1–109.2	49.9	51±14.3
LA (x10 ⁴)	41.9–139.2	93.7	94.8 ± 17.7
TCA (x10 ⁴)	56.1–243	143.1	145.7 ± 31.2
CVI	0.55–0.75	0.66	0.65±0.03
P-SA (x10 ⁴)	17.3–103.3	59.2	59.6 ± 17.2
P-LA (x10 ⁴)	47.5–217.4	125.9	128.3 ± 34.5
P-TCA (x10 ⁴)	64.8–307	185.8	187.9 ± 50
P-CVI	0.56–0.75	0.68	0.68±0.03
Blood Type n(%)	A	60(36.6 %)	
	B	33(20.1 %)	
	AB	26(15.9 %)	
	O	45(27.4 %)	

AL, axial length; SA, stromal area; LA, luminal area; TCA, total choroidal area; CVI, choroidal vascularity index; P-SA, posterior stromal area; P-LA, posterior luminal area; P-TCA, posterior total choroidal area; P-CVI, posterior choroidal vascularity index.

Table 2
Comparative analysis of demographic values and choroidal parameters in different blood types.

			Blood Type A	Blood Type B ¹	Blood Type AB	Blood Type O ²	p	
Age	Mean±SD		42.2 ± 11.2	42.1 ± 11.5	42.4 ± 15.1	40.7 ± 12.6	0.978	K
	Median		44.5	46	40.5	47		
Gender	Female	n(%)	35(58.3)	19(57.6)	13(50)	24(53.3)	0.883	X ²
	Male	n(%)	25(41.7)	14(42.4)	13(50)	21(46.7)		
AL (mm)	Mean±sd		23.6 ± 0.7	23.5 ± 0.9	23.4 ± 0.8	23.6 ± 0.9	0.301	K
	Median		23.6	23.4	23.2	23.6		
SA (x10 ⁴)	Mean±sd		47±11	57±11.1	49.2 ± 15.6	52.9 ± 17.5	0.003	K
	Median		45.9 ¹	57.8	49.5 ¹	50.2 ¹		
LA (x10 ⁴)	Mean±sd		88.9 ± 13.9	101.7 ± 15.8	93.8 ± 20.8	98.1 ± 19.5	0.001	K
	Median		87.3 ^{1,2}	98.8	96.2	97.3		
TCA (x10 ⁴)	Mean±sd		135.8 ± 24.2	158.7 ± 26	143±35.4	151±36.3	0.001	K
	Median		135.1 ^{1,2}	156.9	144.3	147.4		
CVI	Mean±sd		0.66±0.03	0.64±0.02	0.66±0.04	0.66±0.03	0.058	K
	Median		0.65	0.65	0.65	0.65		
P-SA (x10 ⁴)	Mean±sd		57.2 ± 17.1	62.2 ± 18.7	60.5 ± 15.2	60.5 ± 17.3	0.536	K
	Median		54.4	63.1	59.3	64.1		
P-LA (x10 ⁴)	Mean±sd		125.5 ± 32.9	129.9 ± 39.9	129±34.9	130.5 ± 3.1	0.864	K
	Median		125.5	122.1	124.3	132.3		
P-TCA (x10 ⁴)	Mean±sd		182.7 ± 48.5	192.1 ± 56.7	189.5 ± 47.7	190.9 ± 49.2	0.792	K
	Median		178.5	191.5	185.8	195.1		
P-CVI	Mean±sd		0.69±0.03	0.68±0.03	0.68±0.04	0.69±0.03	0.538	K
	Median		0.69	0.68	0.68	0.68		

AL, axial length; SA, stromal area; LA, luminal area; TCA, total choroidal area; CVI, choroidal vascularity index; P-SA, posterior stromal area; P-LA, posterior luminal area; P-TCA, posterior total choroidal area; P-CVI, posterior choroidal vascularity index.

^K, Kruskal-Wallis (Mann-Whitney u test) ^{X²}, Chi-Square test.

¹, Difference with group blood type B, *p* < 0.05.

², Difference with group blood type O, *p* < 0.05.

Bolded values represent significant, *p* < 0.05.

Table 3
Spearman correlation of choroidal parameters with age and axial length.

		SA	LA	TCA	CVI	P-SA	P-LA	P-TCA	P-CVI
Age	r	-0.048	-0.034	-0.038	0.038	-0.034	-0.097	-0.073	-0.097
	p	0.540	0.668	0.631	0.628	0.670	0.217	0.354	0.217
AL	r	-0.048	-0.081	-0.061	0.018	-0.087	-0.124	-0.113	-0.008
	p	0.543	0.300	0.437	0.820	0.269	0.114	0.149	0.922

AL, axial length; SA, stromal area; LA, luminal area; TCA, total choroidal area; CVI, choroidal vascularity index; P-SA, posterior stromal area; P-LA, posterior luminal area; P-TCA, posterior total choroidal area; P-CVI, posterior choroidal vascularity index.

r, Spearman Correlation.

oxygen levels than any other tissue in the body, making it particularly susceptible to oxidative damage [9].

Normal choroidal vascularization, in terms of both structure and function, is critical for retinal health. Alterations in choroidal blood volume and/or impaired blood circulation can lead to photoreceptor dysfunction, contributing to the development of diseases such as central serous retinopathy, age-related macular degeneration, polypoidal choroidal vasculopathy, pathological myopia, and Vogt-Koyanagi-Harada disease. Therefore, choroidal thickness has been identified as a significant biomarker for various ocular and systemic diseases [10–13].

Currently, with advancements in OCT software and technological modifications, Enhanced EDI mode enables the *in vivo* cross-sectional imaging of the choroid. Numerous studies have compared choroidal thickness across various ocular diseases and other systemic conditions. However, some of these studies present inconsistent and conflicting results due to the choroidal thickness being either exceptionally thin or thick, which complicates the interpretation of the data. To address these challenges, Sonoda et al. [14] introduced the choroidal vascularity ratio, a quantitative parameter calculated by measuring the luminal and interstitial areas in the choroid. Subsequently, Agrawal et al. [15] refined this approach by binarizing EDI SD-OCT images, developing a new quantitative parameter known as the CVI. The CVI is derived by dividing the luminal area by the total choroidal thickness. This quantitative parameter has emerged as a more reliable marker for assessing choroidal morphology and physiology.

The association between blood groups and ocular diseases has been a subject of investigation in the literature, with some conflicting findings, particularly regarding glaucoma. Khan et al. [16] revealed that blood group B was associated with all forms of glaucoma, while the Rh-negative allele was specifically linked to primary open-angle glaucoma (POAG). Leske et al. [17] found no significant association between ABO blood groups and POAG. In contrast, Garg and Pahwa [18] reported that blood groups A and B were more prevalent in patients with POAG and narrow-angle glaucoma, whereas blood groups AB and O were significantly less common. Similarly, another study found a higher prevalence of blood group B among patients with congenital glaucoma compared to controls [19]. These conflicting results indicate that the genetic basis of glaucoma is complex, likely involving autosomal dominant, recessive, or multifactorial inheritance patterns.

In our study, no significant differences were found in CVI between the ABO and Rh blood groups. However, the SA values were significantly higher in the B and O blood groups compared to the A, AB, and O groups. Additionally, the LA and TCA values were significantly higher in the B and O groups compared to the A group. Despite these structural differences, the CVI remained unchanged. This suggests that while the stromal and luminal areas expand in certain blood groups, they do so proportionally, preserving the vascular-to-stroma ratio in the choroid. These findings imply that ABO blood groups may have a significant effect on choroidal morphology, but rather than directly altering vascular density, these changes likely result from a balanced expansion of both

stromal and vascular components. In other words, while certain blood groups exhibit an increase in stromal and luminal areas, the overall vascular-stroma ratio remains relatively stable.

Genetic factors play a fundamental role in the development, maintenance, and integrity of the choroidal structure. This is most clearly demonstrated in inherited chorioretinal disorders such as choroideremia and gyrate atrophy. Choroideremia results from mutations in the CHM gene, leading to dysfunction of Rab escort protein-1 (REP1) and subsequent progressive degeneration of the choroid and retina, ultimately resulting in blindness [20]. Likewise, gyrate atrophy is caused by mutations in the OAT gene, which lead to ornithine aminotransferase deficiency and progressive chorioretinal degeneration [21]. Although hereditary chorioretinal disorders were excluded from the present study, they nevertheless underscore the fundamental role of genetic mechanisms in shaping choroidal morphology.

Beyond monogenic disorders, choroidal thickness and choroidal volume have also been shown to be heritable traits. In a twin study conducted in the Amish population, a heritability estimate of approximately 0.40 was reported for choroidal thickness, indicating a moderate genetic contribution [22]. In contrast, a study performed in healthy Korean twins demonstrated a substantially higher heritability of 0.76 for choroidal volume, suggesting a strong genetic influence on this parameter [23]. Collectively, these findings indicate that interindividual variability in choroidal structure is largely genetically determined and provide important biological support for the interpretation of our results.

The fact that CVI did not change suggests that genetic variations in ABO blood groups might influence choroidal structure without necessarily affecting vascular density. Future, larger-scale studies are needed to explore how ABO blood groups may affect choroidal morphology and vascular indices in greater detail.

Teberik et al. [24] investigated the relationship between ABO blood groups, Rh factor, and retinal and choroidal thickness. They observed a statistically significant increase in temporal retinal thickness at a distance of 1000 μm from the fovea in individuals with blood group B. However, no significant differences were noted in other retinal regions or in choroidal thickness. Despite this observation, the authors concluded that neither the ABO blood group nor the Rh factor had a substantial impact on retinal or choroidal thickness. Several studies have suggested that the ABO blood group may have a significant role in the pathogenesis of peripheral vascular disease, cerebral ischemia, venous thromboembolism, and cardiovascular disorders. This association was primarily attributed to the lower levels of coagulation proteins, particularly factor VIII and von Willebrand factor (vWF), observed in individuals with blood group O [25].

Another study examined the relationship between ABO and Rh blood groups and peripapillary nerve fiber layer thickness as well as macular thickness. The results showed that participants with blood group AB exhibited significantly higher mean and central macular thickness compared to those with other ABO blood groups [26]. Furthermore, the average macular thickness was notably thinner in the Rh⁻ group compared to the Rh⁺ group. The authors concluded that retinal structural indices might be influenced by genetic factors associated with blood group antigens. The discrepancies observed across studies may be attributed to racial differences.

The ABO and Rh blood group antigens are located on chromosomes 9q34 and 1p36, respectively. In a large-scale genome-wide association study, conducted in the United States with 68,423 participants, 139 genetic loci associated with macular thickness were identified. The findings revealed that many of these genes are highly expressed in the retina. One of these loci is located on chromosome 9. Given that the ABO blood group gene is also located on chromosome 9, this is a potential link between genetic loci influencing blood groups and choroidal morphology [27].

To conclude, to the best of our knowledge, this is the first study to evaluate the relationship between ABO and Rh blood groups and the

CVI. There were no significant differences in CVI between the groups. However, the higher values of SA and LA in blood group B, compared to other groups, may be associated with genetic factors. Although definitive causal associations between ABO or Rh blood groups and specific ocular diseases have not yet been established, variations in choroidal structure may influence susceptibility to disorders in which the choroid plays a central pathophysiological role, including central serous chorioretinopathy, age-related macular degeneration, and pachychoroid spectrum diseases. Therefore, our findings may be considered as a basis for future risk assessment and for understanding the biological mechanisms of retinochoroidal pathologies.

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Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of Kırşehir Ahi Evran University Faculty of Medicine (Protocol No: 2023–11/76, Date: 06/06/2023) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all individual participants included in the study.

CRediT authorship contribution statement

Özkan Kocamış: Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Tülal Karacan Erşekerci:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Data curation. **Kemal Örneke:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that there is no conflict of interest. The authors received no financial support for the research, authorship, and/or publication of this article.

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