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ORIGINAL RESEARCH

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Could there be a relationship between blood groups and varicocele? A multicenter case-control study with a Turkish population

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Abstract

Background: Although various factors contribute to the pathophysiology of varicocele, the underlying etiological causes have not yet been fully elucidated. Due to the existence of studies showing that there is a relationship between ABO blood group antigens and vascular diseases and that the risk of varicocele increases in men with various vascular diseases, this study aimed to investigate the association between ABO blood groups and varicocele. **Methods**: This multicenter study involved 6466 participants. The varicocele group included 2295 patients (1799 unilateral and 496 bilateral), while the control group consisted of 4171 individuals without varicocele. All participants visited urology outpatient clinics at 8 different hospitals in Turkey between 2018 and 2023. The groups were compared in terms of demographic data and blood groups. **Results**: The distribution of the blood groups in the control group and unilateral varicocele group was similar with the Turkish population. On the other hand, in bilateral varicocele group O blood group was found to be significantly lower than the control group ($p = 0.0001$), and non-O blood groups were found to be significantly higher than unilateral varicocele ($p = 0.022$) and control groups ($p = 0.008$). **Conclusions**: In conclusion, blood groups do not increase the risk of unilateral varicocele. However, patients without blood type O had a significantly higher likelihood of bilateral varicocele compared to those with blood type O. This study highlights a potential association between ABO blood groups and the etiology of varicocele, suggesting that genetically transmitted blood group antigens may contribute to its development within a multifactorial framework.

Keywords

ABO blood-group system; Etiology; Varicocele; Vascular diseases

¿Podría existir una relación entre los grupos sanguíneos y el varicocele? Un estudio multicéntrico de casos y controles en una población turca

Resumen

Antecedentes: Aunque diversos factores contribuyen a la fisiopatología del varicocele, las causas etiológicas subyacentes aún no se han elucidado completamente. Debido a la existencia de estudios que muestran una relación entre los antígenos del grupo sanguíneo ABO y las enfermedades vasculares, y que el riesgo de varicocele aumenta en hombres con diversas enfermedades vasculares, este estudio tuvo como objetivo investigar la asociación entre los grupos sanguíneos ABO y el varicocele. **Métodos**: El estudio multicéntrico incluyó a 6466 participantes. El grupo con varicocele incluyó a 2295 pacientes (1799 con varicocele unilateral y 496 con varicocele bilateral), mientras que el grupo de control estuvo compuesto por 4171 individuos sin varicocele. Todos los participantes asistieron a consultas externas de urología en 8 hospitales diferentes de Turquía entre 2018 y 2023. Se compararon los grupos en términos de datos demográficos y grupos sanguíneos. **Resultados**: La distribución de los grupos sanguíneos en el grupo de control y el grupo con varicocele unilateral fue similar a la de la población turca. Por otro lado, en el grupo con varicocele bilateral, se encontró que el grupo sanguíneo O era significativamente más bajo que en el grupo de control ($p = 0.0001$), y que los grupos sanguíneos no O eran significativamente más altos que en los grupos con varicocele unilateral ($p = 0.022$) y control ($p = 0.008$). **Conclusiones**: En conclusión, los grupos sanguíneos no aumentan el riesgo de varicocele unilateral. Sin embargo, los pacientes sin el grupo sanguíneo O presentaron una probabilidad significativamente mayor de tener varicocele bilateral en comparación con aquellos con el grupo sanguíneo O. Este estudio destaca una posible asociación entre los grupos sanguíneos ABO y la etiología del varicocele, sugiriendo que los antígenos de los grupos sanguíneos transmitidos genéticamente podrían contribuir a su desarrollo en un marco multifactorial.

Palabras Clave

Sistema de grupos sanguíneos ABO; Etiología; Varicocele; Enfermedades vasculares

1. Introduction

The term varicocele was coined by Curling in 1846 [1]. It is described as the enlarged, elongated, tortuous veins of the pampiniform plexus in the scrotum. Approximately 15% of the healthy male population, 35% to 44% of primary infertile men, and 45% to 81% of secondary infertile men have a varicocele [2–4]. It is known that varicocele negatively affects testicular volume, sperm function, fertilization, implantation and embryonic outcome [5–7]. However, despite its clinical importance, most of the studies in the literature address the clinical effects, treatment and the treatment outcomes of varicocele rather than investigating the etiology [8, 9]. Although many theories have been proposed, the etiology of varicocele has not been clearly elucidated.

First identified by Landsteiner in 1900, ABO blood group antigens are found on the surface of erythrocytes and platelets and also seen in vascular epithelial cells [10]. It is also found as a membrane antigen in cervical, intestinal and mammary epithelial cells; in dissolved form in plasma, urine, faeces, saliva and breast milk [11]. ABO blood groups are divided into 4 different groups based on the presence of A and B antigens in the blood: A, B, AB and O [12]. ABO blood group has been suggested to be an important genetic factor associated with various types of diseases, including vascular pathologies, cardiovascular disease, many types of cancer, diabetes, and infections [13–19]. It is thought that differences in the antigenic structures of the blood groups, differences in aggregation and thrombosis via von Willebrand factor (VWF), or differences in serum cytokine levels that play a role in systemic inflammation may be related to the development of these diseases [17, 19–21].

Furthermore, evidence suggests a connection between varicocele and systemic vascular conditions. Studies have reported an increased prevalence of varicocele in individuals with coronary artery ectasia, coronary and leg varicose vein pathologies, indicating shared pathological mechanisms [22–24]. Considering the established role of ABO blood groups in vascular diseases, investigating a potential link between varicocele and blood groups is a logical next step.

This study is the first to explore the relationship between ABO blood groups and varicocele, providing a genetic perspective on its etiology. By examining this novel association, our findings are expected to contribute to the understanding of the multifactorial nature of varicocele and its underlying mechanisms.

2. Materials and methods

This retrospective study was conducted on 2313 patients with varicocele who were evaluated in the urology outpatient clinic for various reasons including infertility, scrotal-testicular pain, scrotal swelling and trauma between May 2018 and July 2023 in 8 different hospitals in 6 Turkish cities. Although varicocele was mainly diagnosed by physical examination, patients with scrotal Doppler ultrasound confirmation were included in this study to confirm the diagnosis and improve the quality of the study due to the retrospective nature of the study. Varicocele was required to be clinically significant, which means that the maximum diameter of the spermatic veins was >3 mm and venous reflux lasting >2 seconds in the standing position and/or during the Valsalva maneuver. Blood group data of these patients were also recorded. 18 patients with missing blood group information were excluded from the study, thus 2295 patients were included at the end of our study. In the patient group, 1799 patients had unilateral varicocele, and 496

patients had bilateral varicocele. The control group consisted of 4171 male patients without varicocele who applied during the same period and underwent scrotal examination and scrotal Doppler ultrasound due to similar complaints.

The patient groups consisted of patients with unilateral and bilateral varicocele, and these patients did not present with any additional scrotal anomalies, while the distribution of the control group was shown in Table 1.

TABLE 1. Diagnoses and frequency of participants in the control group.

Diagnosis	Frequency	Percent
Hydrocele	2629	63.0
Epididymal cyst	667	16.0
Nonspecific testicular pain	552	13.2
Inguinal hernia	119	2.9
Testicular microlithiasis	68	1.6
Spermatic cord cyst	33	0.8
Multiple ultrasound findings	25	0.6
Scrotal edema	23	0.6
Retractile testicle	19	0.5
Testicular trauma	12	0.3
Testicular hypoplasia	10	0.2
Vasectomy	8	0.2
Spermatocele	6	0.1
Total	4171	100.0

Patients with a history of malignancy, diabetes, and cardiovascular disease were not assessed in the patient or control groups and were excluded from the study due to their relevance to blood groups in the existing literature [15–17].

Shapiro-Wilk test was used to determine the distribution of variables. Differences in patient characteristics were evaluated using Kruskal Wallis test. The distribution of blood groups of the patient groups and the control group was presented as a pie chart. Differences in the distribution of blood groups of bilateral varicocele, unilateral varicocele patients and control groups were analysed by proportion test for difference in proportions. The odds ratio (OR) for the risk of bilateral varicocele according to ABO blood group among all participants was estimated with a 95% confidence interval (CI). All analyses were performed using SPSS (Statistical Package Programme for Social Sciences, v.24, IBM Corp., Armonk, NY, USA). p values less than 0.05 were considered statistically significant.

3. Results

Demographic and blood group data of patients with unilateral and bilateral varicocele and control groups were summarized in Table 2 and Fig. 1. Fig. 1A also shows the blood group distribution of Istanbul, which demographically reflects the Turkish population as a whole [25]. In the Turkish population, A is the most common blood group with a percent of 43.82%, followed by O, B and AB with 33.8%, 15.22% and 7.16%, respectively [25]. In the control group of our study, blood group A was also the most common group with 43.42%, followed by blood groups O, B and AB with 33.9%, 15.3% and 7.38% respectively. The distribution of blood groups in the control group was similar to that of the Turkish population and no significant difference was observed with Turkish population. In the unilateral varicocele group, blood groups A, O, B and AB were observed at a rate of 43.86%, 33.35%, 14.45% and 8.34%, respectively, and the distribution of blood groups was similar to the control group and there was no significant difference between these groups. In the bilateral varicocele group, although there was a similar ranking with the control group, the percentage of blood group O was lower than the other groups. Blood group A was the most common blood group in bilateral varicocele group and no significant difference was found compared to the control group. O blood group was seen in 27.02% and was statistically significantly lower than the control blood group ($p < 0.001$). Blood groups B and AB showed no difference from the control group. In Turkey non-O blood group was found to be 66.2%, which is similar with the control group (66.1%), and unilateral varicocele group (66.65%), and no statistical difference was found between these groups. Non-O blood group was observed at a rate of 72.98% in the bilateral varicocele group and was statistically higher than the control group ($p = 0.008$), and unilateral varicocele group ($p = 0.022$).

Regarding blood group distribution, there is no difference between unilateral varicocele group and control patients, however, there is a significant difference between bilateral varicocele frequency and control patients in terms of O and non-O blood group distribution. The risk of bilateral varicocele frequency was investigated in blood group O and non-O blood groups. Compared to those with blood group O, those with non-O blood group had a higher risk of bilateral varicocele with an OR of 1.38 (95% CI, 1.125–1.7064; $p = 0.002$).

4. Discussion

Varicocele, characterized by the abnormal dilation and tortuosity of the internal spermatic veins in the pampiniform plexus, is a vascular pathology with an etiology that remains poorly understood and likely multifactorial [9]. Our study is significant as the first to explore the association between ABO blood groups and varicocele, potentially identifying a genetic factor in its development. This study represents that non-O blood types were associated with a higher risk of bilateral varicoceles compared to O blood types, highlighting a new potential pathway in varicocele pathogenesis.

Anatomical differences in the venous drainage of the left and right internal spermatic veins (a possible aetiological cause of the predominance of left-sided varicocele), insufficiency of the venous valves causing a venous reflux and increased hydrostatic pressure are the most popular theories attributed to the development of varicocele [26, 27]. While varicoceles are typically larger and more common on the left, bilateral involvement occurs in up to 50% of cases, with our study reporting a 21.61% bilateral varicocele rate [28]. The fact that varicocele can develop bilaterally at such a high rate is suggestive that the disease may be caused by a condition that can also affect the bilateral spermatic veins.

TABLE 2. Demographic and blood group data of the unilateral varicocele, bilateral varicocele and control groups.

	Control group (C)	Unilateral varicocele group (U)	Bilateral varicocele group (B)	*p*-value
Number of patients	4171	1799	496	
Median age (min–max)	42 (18–67)	28 (18–58)	30 (18–58)	
Blood group O (%/n)	33.9/1414	33.4/600	27.0/134	$p^{C,U} = 0.828$ $p^{C,B} \leq 0.001$ $p^{U,B} = 0.152$
Non-O blood groups (%/n)	66.1/2757	66.6/1199	73.0/362	$p^{C,U} = 0.759$ $p^{C,B} = 0.008$ $p^{U,B} = 0.022$
Blood group A (%/n)	43.4/1811	43.9/789	47.6/236	$p^{C,U} = 0.813$ $p^{C,B} = 0.221$ $p^{U,B} = 0.316$
Blood group B (%/n)	15.3/638	14.5/260	16.9/84	$p^{C,U} = 0.761$ $p^{C,B} = 0.704$ $p^{U,B} = 0.593$
Blood group AB (%/n)	7.4/308	8.3/150	8.5/42	$p^{C,U} = 0.734$ $p^{C,B} = 0.800$ $p^{U,B} = 0.967$

**p values were calculated with the proportion test. min: minimum; max: maximum.*

An overview of relevant studies on the etiology of varicocele suggests that there are publications in which the cause could not be determined, however, a hereditary transmission pattern was reported. Raman *et al.* [29] reported that 56.5% of first-degree relatives of patients with varicocele had clinical varicocele, and the prevalence of varicocele was found to be more than eight times higher in first-degree relatives compared to control. Gökçe *et al.* [30] reported a varicocele prevalence of 33.9% among first-degree relatives of men with varicocele. It was reported to be about 3 times higher than the control group. In a similar study by Mokhtari *et al.* [31], the prevalence of varicocele in first-degree relatives was 45.4%, compared with 11% in the control group. These studies strongly suggest that the prevalence of varicocele may be related to hereditary factors. Blood group antigens are also genetically transmitted. Unfortunately, blood groups were not evaluated in these studies. It is possible that the reason for the high incidence of varicocele in first-degree relatives in the previously mentioned studies is associated with blood group antigens. Blood group assessment and detailed genetic analysis with respect to the increased prevalence of varicocele in first-degree relatives will contribute to the identification of the etiology of varicocele.

The functions of the ABO blood group antigens, other than blood group identification, are not fully understood. These antigens have also been detected in seminal fluid, on the surface of spermatozoa and cervix uteri [11, 32]. Consequently, their potential association with male infertility has long been a research focus. Although various studies exist, findings are often contradictory or inconclusive. It has been hypothesized that ABO blood group incompatibility between couples could contribute to unexplained infertility. For instance, cervical mucus antibodies against incompatible blood group antigens might immobilize or block sperm [33]. However, no large-scale randomized controlled trials have validated these hypotheses, and many studies report no significant difference in ABO blood group distributions between fertile and infertile men [34]. These antigens are expressed in platelets and vascular endothelial cells as well as in red blood cells [35]. There are many studies in the literature suggesting that the amount of von Willebrand factor (VWF) and platelet function differ in different blood groups, and therefore there may be differences in blood viscosity and venous stasis [36, 37]. It was observed that people with blood type O had about 25% lower VWF levels than those with non-O blood group [38, 39]. Blood group antigens may have an indirect effect on blood viscosity through these factors. It is possible that variations in clotting factors associated with different blood groups may contribute to the occurrence of varicocele by affecting blood flow in the spermatic vessels and resulting in stasis. In our study, the fact that non-O blood groups constitute a risk factor for the incidence of bilateral varicocele may be related to the increased viscosity in these blood groups compared to group O. Likewise, an increase in blood viscosity due to an increase in the mean platelet volume (MPV) is also a risk factor for cardiovascular and cerebrovascular diseases [40]. Although limited in number, studies have demonstrated that the varicocele incidence is correlated with increased mean platelet volume [41, 42]. Platelet volume has been reported to be linked to platelet function and activation [43]. It is consequently possible that there is a link between varicocele and platelet function. It is also probable that blood group

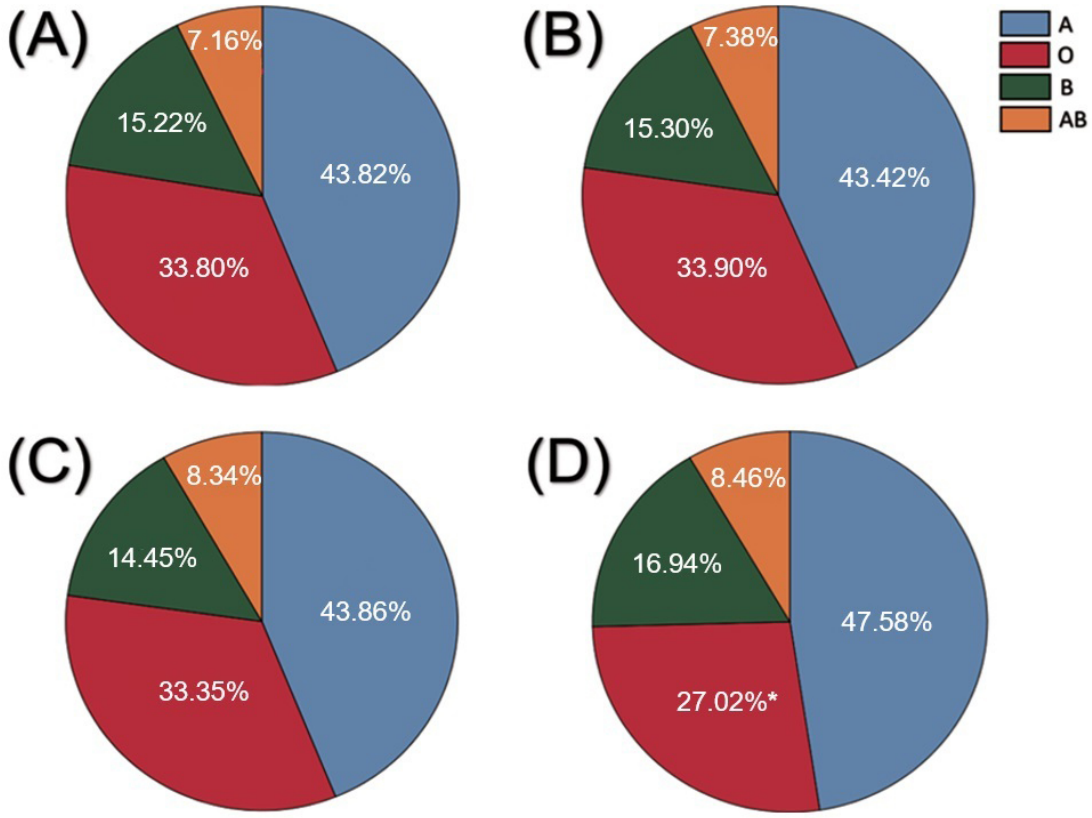

FIGURE 1. Blood group distribution in different groups. (A) General population in Turkey. In Turkey, blood groups A, O, B and AB represent 43.82%, 33.80%, 15.22% and 7.16%, respectively. (B) Control group. In the control group, blood groups A, O, B and AB were 43.42%, 33.90%, 15.30% and 7.38%, respectively. (C) Unilateral varicocele group. In the unilateral varicocele group, blood group A is the most common with 43.86%, followed by blood group O with 33.35%, blood group B with 14.45% and blood group AB with 8.34%. (D) Bilateral varicocele group. In the bilateral varicocele group, as in the control and unilateral varicocele groups, blood group A is the most common and the incidence rate is 47.58%. Blood group O is reported in 27.02% of the patients and is significantly lower than in the control group (*$p \leq 0.001$), blood group B is identified in 16.94% and AB in 8.46%.

antigens, which cause alterations in platelet function, may play a role in the etiology of varicocele.

In previous studies investigating the etiology of varicocele, there is substantial evidence that varicocele may be associated with general systemic vascular disorders [23]. The publications showing that the presence of peripheral varicose veins is positively associated with varicocele which suggest that there is a possible common pathological step between the two diseases [23, 24]. Another study reported an increased incidence of varicocele in patients with coronary artery ectasia [22]. Sakamoto *et al*. [44] found that patients with bilateral varicocele might have a higher chance of being associated with venous abnormalities than those with unilateral varicocele. It is well-known that vascular diseases are more common in non-O blood groups [45]. The results of our study suggest that non-O blood groups are at risk of developing bilateral varicocele. This may suggest that individuals with specific blood groups might have variations in their vascular structure or function that predispose them to have bilateral varicocele, which involves both sides of the venous system, unlike unilateral varicocele. Blood groups could be linked to genes that influence the development and competence of venous valves. In cases of bilateral varicocele, a systemic weakness in venous valves might be involved, while unilateral varicocele could be more related to local anatomical factors (*e.g.*, compression of the left renal vein). It is also likely that blood group antigens are involved in the development of varicocele through their expression in the vascular epithelium and functional effects via coagulation factors.

The observed differences in the prevalence of bilateral varicocele between non-O and O blood group patients (33.9% *vs.* 27% and 66.1% *vs.* 73%) represent a nuanced finding in our study. Although these absolute differences appear modest, the statistical significance in this large cohort suggests that these patterns are unlikely to result from random variation. This points to the potential involvement of ABO blood groups in bilateral varicocele, potentially mediated by genetic, immune, or vascular mechanisms, which merit further exploration.

Varicocele is a multifactorial condition, and ABO blood group, while not the primary determinant, may play a contributory role in certain patient populations. Even small differences in predisposition can, when aggregated in large cohorts, refine risk stratification tools and enhance patient-specific management strategies. For example, this association may help identify non-O blood group patients who are at a relatively higher risk for bilateral varicocele and guide discussions on fertility

management.

These findings also underscore the importance of continued investigation into the biological mechanisms linking ABO blood groups and varicocele. While our study does not establish causality, it raises critical questions about the role of genetic and immunological factors in testicular vein pathophysiology. Future research should focus on whether ABO blood group impacts endothelial function, immune responses, or vascular tone, contributing to varicocele formation.

Additionally, these insights have potential implications for clinical practice. Understanding the relationship between ABO blood groups and varicocele could aid clinicians in risk assessment and personalized counseling for affected individuals. Investigating these mechanisms further may also advance our understanding of varicocele pathophysiology, paving the way for more targeted diagnostic and therapeutic approaches. Longitudinal studies examining the impact of ABO blood groups on fertility outcomes in varicocele patients would provide valuable insights and help validate these findings.

These findings indicate that non-O blood groups may contribute to the occurrence of bilateral varicocele. The etiology of unilateral varicocele may involve factors other than blood group antigens such as anatomical factors. It is also quite logical that a blood type-related condition would affect varicocele bilaterally rather than unilaterally. However, there are several limitations in this study. First, some important information like as body mass index (BMI) may have been overlooked due to the retrospective nature of the study. There are also studies in the literature that address the relationship between varicocele and body mass index (BMI). Overall, varicocele has been found to be more prevalent in people with a low BMI [46]. On the other hand, some studies have reported no significant difference in BMI between individuals with and without varicocele [47]. The negative correlation between varicocele prevalence and BMI may be due to confirmation bias. It may be more challenging to detect a varicocele in obese patients as the spermatic cord and surrounding tissues are thicker, which may lead to incomplete detection [48]. As the BMI of all 6466 participants was not available, BMI could not be analysed in our study. Second, to fully identify the aetiopathogenesis of blood groups in the development of bilateral varicocele, all patients and the control group should be examined along with genetic, immunological and coagulation parameters. In this study these parameters were not analysed. Thirdly, larger prospective studies and genetic studies are needed to further investigate the relationship between blood groups and varicocele. Lastly, the findings are limited to the Turkish population which limiting the expansion of data. To further validate the findings, additional studies involving diverse ethnic populations are recommended. This is particularly important as the distribution and frequency of blood types may vary across different ethnic and national groups, and such studies could provide a broader perspective on the generalizability of the results.

5. Conclusions

This research shows that there is a significant association between the development of bilateral varicocele and non-O blood groups. Compared with blood group O, males with non-O blood groups are 1.38 more likely to have bilateral varicocele. These findings underscore that blood groups may be involved in the development of bilateral varicocele. Further studies involving various ethnic populations, along with fundamental research on genetic variations in varicocele, are required to validate this association and uncover the underlying mechanisms.

AVAILABILITY OF DATA AND MATERIALS

Not applicable. The data cannot be shared due to full compliance with the data protection law of the local administration.

AUTHOR CONTRIBUTIONS

GÇ—designed the research study; wrote the manuscript. GÇ, ST, HD, MHG, CD, AE, FO and MVK—performed the research. TT—provided help and advice on the research process. GÇ, ST, HD, MHG and TT—analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of Başakşehir Çam and Sakura City Hospital (approval number KAEK/2023.06.230) and was conducted in accordance with the Declaration of Helsinki. Informed written consent to participate in the study was provided by all participants.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Curling TB. Cases of varicocele treated by pressure, with observations. Medico-Chirurgical Transactions. 1846; 29: 259–268.

[2] Nistal M, González-Peramato P. Varicocele, the most common cause of treatable infertility. In Nistal M, González-Peramato P (eds.) Testicular vascular lesions (pp. 159–169.). 1st edn. Springer: Cham. 2024.

[3] Shah R, Agarwal A, Kavoussi P, Rambhatla A, Saleh R, Cannarella R, *et al*. Consensus and diversity in the management of varicocele for male infertility: results of a global practice survey and comparison with guidelines and recommendations. The World Journal of Men's Health. 2022; 41: 164–197.

[4] Neto FTL, Campos LR, Roque M, Esteves SC. From pathophysiology

to practice: addressing oxidative stress and sperm DNA fragmentation in varicocele-affected subfertile men. International Brazilian Journal of Urology. 2024; 50: 530–560.

[5] Kavoussi P, Birowo P, Saleh R, Shah R, Agarwal A. Varicocele and male infertility conundrum: making sense of a never-ending story for the busy clinician. Arab Journal of Urology. 2024; 22: 1–5.

[6] Krishan A, Vukina J, Pearce I, Modgil V. Male factor infertility: a contemporary overview of investigation, diagnosis and management. Journal of Clinical Urology. 2024; 17: 456–68.

[7] Babaei A, Moradi S, Hoseinkhani Z, Rezazadeh D, Dokaneheifard S, Asadpour R, *et al*. Expression of hypoxia-inducible factor1-α in varicocele disease: a comprehensive systematic review. Reproductive Sciences. 2022; 29: 2731–2743.

[8] Cannarella R, Shah R, Hamoda TAA, Boitrelle F, Saleh R, Gul M, *et al*. Does varicocele repair improve conventional semen parameters? A meta-analytic study of before-after data. The World Journal of Men's Health. 2024; 42: 92–132.

[9] Agarwal A, Cannarella R, Saleh R, Boitrelle F, Gül M, Toprak T, *et al*. Impact of varicocele repair on semen parameters in infertile men: a systematic review and meta-analysis. The World Journal of Men's Health. 2023; 41: 289–310.

[10] Landsteiner K. On the knowledge of the antifermentative, lytic, and agglutinating effects of blood serum and lymph. Zentralbl Bakteriol. 1900; 27: 357–362. (In German)

[11] Ravn V, Dabelsteen E. Tissue distribution of histo-blood group antigens. Journal of Pathology, Microbiology and Immunology. 2000; 108: 1–28.

[12] Yamamoto F. A historical overview of advances in molecular genetic/genomic studies of the ABO blood group system. Glycoconjugate Journal. 2022; 39: 207–218.

[13] Beyazal OF. The relationship between the ABO blood group and chronic venous disease in deep vein thrombosis. Journal of Cardiology & Cardiovascular Surgery. 2024; 2: 1–5.

[14] Cornu-Thenard A, Dab W, de Vicenzi I, Valty J. Relationship between blood groups (ABO) and varicose veins of the lower limbs. A case-control study. Phlebology. 1989; 4: 37–40.

[15] Abegaz SB. Human ABO blood groups and their associations with different diseases. BioMed Research International. 2021; 2021: 6629060.

[16] Lilova Z, Hassan F, Riaz M, Ironside J, Ken-Dror G, Han T, *et al*. Blood group and ischemic stroke, myocardial infarction, and peripheral vascular disease: a meta-analysis of over 145,000 cases and 2,000,000 controls. Journal of Stroke and Cerebrovascular Diseases. 2023; 32: 107215.

[17] Cui H, Qu Y, Zhang L, Zhang W, Yan P, Yang C, *et al*. Epidemiological and genetic evidence for the relationship between ABO blood group and human cancer. International Journal of Cancer. 2023; 153: 320–330.

[18] Getawa S, Bayleyegn B, Aynalem M, Worku YB, Adane T. Relationships of ABO and Rhesus blood groups with type 2 diabetes mellitus: a systematic review and meta-analysis. Journal of International Medical Research. 2022; 50: 1–16.

[19] Noori M, Shokri P, Nejadghaderi SA, Golmohammadi S, Carson-Chahhoud K, Bragazzi NL, *et al*. ABO blood groups and risk of human immunodeficiency virus infection: a systematic review and meta-analysis. Reviews in Medical Virology. 2022; 32: e2298.

[20] Neshat S, Rezaei A, Farid A, Javanshir S, Dehghan Niri F, Daneii P, *et al*. Cardiovascular diseases risk predictors: ABO blood groups in a different role. Cardiology in Review. 2024; 32: 174–179.

[21] Hernaningsih Y. ABO blood group and thromboembolic diseases. In Fatima-Shad K (ed.) Blood groups-more than inheritance of antigenic substances (pp. 39–49). 1st edn. IntechOpen: London. 2022.

[22] Yetkin E, Kilic S, Acikgoz N, Ergin H, Aksoy Y, Sincer I, *et al*. Increased prevalence of varicocele in patients with coronary artery ectasia. Coronary Artery Disease. 2005; 16: 261–264.

[23] Lai YW, Hsueh TY, Hu HY, Chiu YC, Chen SSS, Chiu AW. Varicocele is associated with varicose veins: a population-based case-control study. International Journal of Urology. 2015; 22: 972–975.

[24] Chen D, Luo Q, Fan W, Chen C, Liu G. The association between varicocele and other vascular diseases: a systematic review and meta-analysis. Phlebology. 2022; 37: 233–240.

[25] Eren C. Analysis of distribution of ABO and Rh blood groups in İstanbul Province. Dicle Medical Journal. 2019; 46: 241–246. (In Turkish)

[26] Braedel H, Steffens J, Ziegler M, Polsky M, Platt M. A possible ontogenic etiology for idiopathic left varicocele. The Journal of Urology. 1994; 151: 62–66.

[27] Dieleman F, Hamming JF, Erben Y, van der Vorst JR. Nutcracker syndrome: challenges in diagnosis and surgical treatment. Annals of Vascular Surgery. 2023; 94: 178–185.

[28] Abdulmaaboud MR, Shokeir AA, Farage Y, Abd El-Rahman A, El-Rakhawy MM, Mutabagani H. Treatment of varicocele: a comparative study of conventional open surgery, percutaneous retrograde sclerotherapy, and laparoscopy. Urology. 1998; 52: 294–300.

[29] Raman JD, Walmsley K, Goldstein M. Inheritance of varicoceles. Urology. 2005; 65: 1186–1189.

[30] Gökçe A, Davarci M, Yalçinkaya FR, Güven EO, Kaya YS, Helvaci MR, *et al*. Hereditary behavior of varicocele. Journal of Andrology. 2010; 31: 288–290.

[31] Mokhtari G, Pourreza F, Kamran AN, Jamali M. Comparison of the prevalence of varicocele in the first-degree relatives of patients with varicocele and with male kidney donors. Current Urology. 2008; 1: 81–83.

[32] Ewald DR, Sumner SCJ. Blood type biochemistry and human disease. Wiley Interdisciplinary Reviews: Systems Biology and Medicine. 2016; 8: 517–535.

[33] Isojima S, Tsuzuku O. Problem of ABO blood group incompatibility and sterility: the effect of blood group antibody on spermatozoa. American Journal of Obstetrics and Gynecology. 1968; 102: 304–306.

[34] Prasad B, Lalit A, Sharma NC. Distribution of ABO blood group among fertile and infertile males in central India: a pilot study. International Journal of Medical Science and Public Health. 2015; 4: 1708–1710.

[35] Greenwell P. Blood group antigens: molecules seeking a function? Glycoconjugate Journal. 1997; 14: 159–173.

[36] Miller C, Haff E, Platt S, Rawlins P, Drews C, Dilley A, *et al*. Measurement of von Willebrand factor activity: relative effects of ABO blood type and race. Journal of Thrombosis and Haemostasis. 2003; 1: 2191–2197.

[37] Kaur M, Singh A, Bassi R, Kaur D. Blood group distribution and its relationship with bleeding time and clotting time. National Journal of Physiology, Pharmacy and Pharmacology. 2015; 5: 253–257.

[38] Jenkins P, O'Donnell J. ABO blood group determines plasma von Willebrand factor levels: a biologic function after all? Transfusion. 2006; 46: 1836–1844.

[39] Gill J, Endres-Brooks J, Bauer P, Marks W, Montgomery R. The effect of ABO blood group on the diagnosis of von Willebrand disease. Blood. 1987; 69: 1691–1695.

[40] Khode V, Sindhur J, Kanbur D, Ruikar K, Nallulwar S. Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: a case control study. Journal of Cardiovascular Disease Research. 2012; 3: 272–275.

[41] Appiah SK, Nkansah C, Mensah K, Osei-Boakye F, Serwaa D, Bani SB, *et al*. Plasma von Willebrand factor antigen levels and its relation with ABO blood group, age and sex. SciMedicineJournal. 2022; 4: 63–72.

[42] Montgomery RR, Flood VH, Haberichter SL. Von Willebrand factor structure and function. In Federici AB, Berntorp EE, Lillicrap D, Montgomery RR (eds.) Textbook of von Willebrand disease: basic and clinical aspects (pp. 23–38). 2nd edn. John Wiley-Blackwell: Hoboken. 2024.

[43] Bodrova VV, Shustova ON, Khaspekova SG, Mazurov AV. Platelet reticulated forms, size indexes and functional activity. Interactions in healthy volunteers. Platelets. 2022; 33: 398–403.

[44] Sakamoto H, Ogawa Y. Is varicocele associated with underlying venous abnormalities? Varicocele and the prostatic venous plexus. The Journal of Urology. 2008; 180: 1427–1431.

[45] Wu O, Bayoumi N, Vickers MA, Clark P. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. Journal of Thrombosis and Haemostasis. 2008; 6: 62–69.

[46] Hu X, Yang X, Zhao J, Guan T, Dai Q, Yang J, *et al*. Association between body mass index and varicocele among 211 989 Chinese reproductive-age males. International Journal of Urology. 2022; 29: 853–859.

[47] Ghanizadeh A, Nasseh H, Kazemnezhad E. Comparison of somatometric indices in patients with grade III varicocele with non-varicocele patients. Translational Research in Urology. 2023; 5: 84–88.

[48] Alsaikhan B, Alrabeeah K, Delouya G, Zini A. Epidemiology of

varicocele. Asian Journal of Andrology. 2016; 18: 179–181.

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