Blood grouping and Rh factor in Egyptian Patients with Non-infectious Uveitis

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Running Title: ABO and Rh factor in Non-infectious Uveitis.

Abstract:

Purpose: to determine the correlation between the ABO blood groups and Rh factor with non-infectious uveitis.

Methods: Cross-sectional study conducted on 175 Egyptian patients diagnosed with non-infectious uveitis. Venous blood sample (2ml) was taken from each patient to recognize the ABO and Rh blood group. Blood grouping results were collected and statistically analyzed.

Results: Most of our uveitic patients were found to have blood group O (34.9%), while other ABO blood groups were represented as following: blood group A in 33.1%, blood group B in 22.3% and blood group AB in 9.7%. Rh factor was positive in 92.6% of the study participants. Most common etiologies of uveitis were Behçet's disease, idiopathic, Vogt-Koyanagi-Harada (VKH), juvenile idiopathic arthritis (JIA) and Ankylosing spondylitis (AS) in the following percentages: 28%, 21.1%, 21.1%, 13.7%, and 11.4%, respectively. Most Behçet's patients had blood type A+ or O+ (33/49, 67.3%), similar to those with idiopathic uveitis with higher preponderance of blood type A and O (26/37, 70.3%). Also, more than half of JIA cases have associated with blood type A+ and O+ (16/24, 66.7%). On the other hand, VKH patients had a higher prevalence of blood type O and B (27/37, 72.9%). AS cases had nearly equal distribution of different blood type A+, B+, AB+ and O+ (30%, 25%, 20% and 25%, respectively).

Conclusion: Blood group O and A were most commonly associated with non-infectious uveitis. In addition, positive Rhesus factor was strongly associated with such cases.

Keywords: Blood groups, Rh factor, Non-infectious Uveitis

INTRODUCTION:

Uveitis is defined as inflammation of any part of the uveal tract: the iris, the ciliary body, and the choroid. Generally, most etiologies of uveitis can be classified as either non-infectious (autoimmune) or infectious[1].

Anatomically, there are several subtypes of uveitis, such as anterior uveitis, intermediate uveitis, posterior uveitis and pan-uveitis, with anterior uveitis accounting for approximately 50 to 80% of patients[2].

Uveitis is often seen in patients who have an autoimmune disease. In these conditions, the immune system falsely attacks the healthy tissue. In seronegative arthritis, uveitis is the most common extra-articular manifestation and is considered as a part of the classification criteria for seronegative spondyloarthropathies, including psoriatic arthropathy, AS, reactive arthritis (i.e. Reiter's syndrome) and arthritis associated with inflammatory bowel disease (i.e. enteropathic arthritis). In fact, acute anterior uveitis is described to occur in

about one third of patients with spondyloarthropathies. Other autoimmune conditions known to cause uveitis include: Behçet's disease, Rheumatoid arthritis (RA), Multiple sclerosis (MS), JIA, and Sarcoidosis[3].

The most important blood grouping system is the ABO system, and the antigens are disseminated in a broad range in this system. These antigens are found both in red cells and platelets and in tissues such as endothelial cells. Therefore, they are referred to as histo-blood group antigens[4].

In addition to the ABO system, the D antigen of Rh blood grouping system is considered one of the most important antigens. Individuals with D antigen are Rh+ and those with absent antigens are Rh− [5].

Over the years, the relationship between certain ABO blood groups and some diseases has been studied and found to increase vulnerability to various diseases. For example, humans with blood group O are more prone to peptic ulcer, while those with blood group A are more likely to have stomach cancer. Also, ABO blood groups have been described in relation to some infectious and non-infectious diseases[5]. Moreover, blood grouping is known as one of the major prognostic factors for different disorders such as cancers and vascular diseases[6,7].

Some studies have shown an association between some eye diseases such as myopia, nuclear cataract, and convergent squint with the blood group O. In contrast, other researchers have reported no significant association of myopia and cataracts with ABO blood groups[8].

To the best of our knowledge, there is no study evaluating the association between non-infectious uveitis and ABO blood groups and Rh factors systems. Therefore, in this study we aim to recognize the correlation between the ABO blood groups and Rh factor with non-infectious uveitis.

MATERIAL AND METHODS:

This cross-sectional study was conducted between June 2021 and October 2021 in Mansoura Ophthalmic center, and rheumatology and rehabilitation clinic, Faculty of Medicine, Mansoura University, Egypt. After the approval from the

Institutional Research Board (R.21.05.1334) was taken, the study was carried out following the tenets of the Declaration of Helsinki. Before each procedure in the study, written informed consent was obtained from each participant.

Egyptian patients with non-infectious uveitis were collected from Rheumatology and rehabilitation clinic, Mansoura University Hospital and Uveitis clinic in Mansoura Ophthalmic center. The diagnosis of different systemic association was based on standard criteria for diagnosis of Behçet's Disease[9], VKH disease[10], RA[11], Seronegative spondyloarthropathies[12], JIA[13], sarcoidosis[14] and Systemic Lupus Erythematous (SLE)[15]. The Standardization of Uveitis Nomenclature Working Group criteria was used to make the diagnosis of uveitis[16]. Patient with any type of infectious uveitis was excluded from the study.

A complete ophthalmologic examination was performed to participants, including assessment of uncorrected and best corrected visual acuity (UCVA and BCVA), slit-lamp biomicroscopy for assessment of AC activity, IOP measurement using Goldmann applanation tonometry, and dilated fundus examination.

After obtaining the written informed consent, a 2 ml venous blood sample was taken from each patient to determine the ABO and Rh blood group. EDTA samples were rotated at a high speed to separate the plasma from the red blood cells. The process was carried using Ortho cassette method. A suspension solution of 5% red blood cells is made for the sample using a 0.9% salt solution. The sample drawing or the patient's name is recorded on the cassette. Ten microns of the suspension solution were added to the first 4 columns of the cassette (ABO & control).

Reverse process was carried to confirm results. Ten microns of suspension solution of A and B cells were added to columns 5 and 6 of the cassette. Forty microns of sample plasma were added to the same columns. The cassette was rotated for 5 minutes using Ortho Centrifuge. Finally, collection of the results was done according to Table 1.

Table 1: Interpretation of results of collected samples

Reaction of the cells with		Reaction of serum tested against			Interpretation
Anti-A	**Anti-B**	**A Cells**	**B Cells**	**O Cells**	**ABO Group**
-	-	+	+	-	O
+	-	-	+	-	A
-	+	+	-	-	B
+	+	-	-	-	AB

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using number and percent. Quantitative data were described using mean and standard deviation for parametric data after testing normality using Shapiro–Wilk test. Significance of the obtained results was judged at the (0.05) level.

RESULTS

The present study was carried out on 175 Egyptian uveitic patients. Data were analyzed to study the association of the ABO blood group and Rh factor with patients suffering from non-infectious uveitis. The mean age of patients was 27.49 ± 10.89 years with no appreciable difference between men and women (53.7% female and 46.3% male). Most of our uveitic patients were found to have blood group O (n=61, 34.9%). Other ABO blood groups were represented in our study as following: A blood group in 58 cases (33.1%), B blood group in 39 cases (22.3) and AB blood group in 17 cases (9.7%). Rh factor was positive in 162 (92.6%) of the study participants and negative in 13 (7.4%). Demographic data, ABO group and Rh factor distribution among studied population are presented in Table 2.
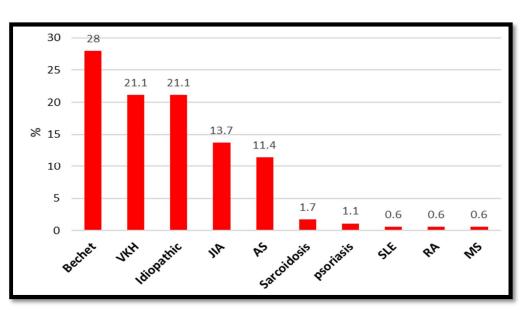
Various etiologies of uveitis were documented in our study with Behçet's disease being the most prevalent in 49 patients (28%), idiopathic and VKH each in 37 (21.1%), JIA in 24 (13.7%), AS in 20 (11.4%), Sarcoidosis in 3 (1.7%), Psoriasis in 2 (1.1%), RA, SLE and MS each in one patient (0.6%) Shown in Figure 1.
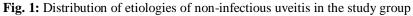
Table 2. Demographic and clinical characteristics

Number of patients	**175**
Age, mean in years ±SD (range)	**27.49 ± 10.89 (3-58)**
Gender, female patients (%)	**94 (53.7%)**
ABO groups (%)	
A	**58 (33.1%)**
B	**39 (22.3%)**
AB	**17 (9.7%)**
O	**61 (34.9%)**
Rh antigen (%)	
Rh positive	**162 (92.6%)**
Rh negative	**13 (7.4%)**
ABO groups and Rh in studied patients (%)	
• **A +**	**54 (30.9 %)**
• **B +**	**37 (21.1 %)**
• **AB +**	**14 (8.0 %)**
• **O +**	**57 (32.6 %)**
• **A -**	**4 (2.3 %)**
• **B -**	**2 (1.1 %)**
• **AB -**	**3 (1.7%)**
• **O -**	**4 (2.3 %)**

Fig. 1: Distribution of etiologies of non-infectious uveitis in the study group

Most Behçet's patients presented with uveitis had blood type A or O (33/49) and all of these patients had positive Rh factor. Only 2 patients with Behçet's uveitis had negative Rh factor and associated with blood type AB. This was nearly the same in patients with idiopathic uveitis with higher preponderance of blood type A and O (26/37); 23 were Rh positive and the remaining 3 had negative Rh. Also, more than half of JIA cases was associated with blood type A+ and O+ (16/24). On the other hand, VKH patients had a higher prevalence of blood type O and B (27/37); regarding Rh factor 2 out of 27 cases with type O and B had negative Rh factor in addition there was 2 VKH patients had negative Rh factor and fall in blood type A. AS cases had nearly equal distribution of different blood type A+ (6/20), B+ (5/20), AB+ (4/20) and O+ (5/20) with none of them experienced negative Rh factor. Distribution of ABO group and Rh factor in the study group is presented in Table 3.

Table 3. Distribution of ABO group and Rh factor in non-infectious according to their etiologies

Diagnosis (Number of cases)	A+ n=54	B+ n=37	AB+ n=14	O+ n=57	A- n=4	B- n=2	AB- n=3	O- n=4
Behçet's disease (49)	19	11	3	14	0	0	2	0
Idiopathic (37)	12	8	1	11	2	1	1	1
VKH (37)	5	8	3	17	2	1	0	1
JIA (24)	10	4	3	6	0	0	0	1
AS (20)	6	5	4	5	0	0	0	0
Sarcoidosis (3)	2	0	0	1	0	0	0	0
Psoriasis (2)	0	0	0	1	0	0	0	1
RA (1)	0	1	0	0	0	0	0	0
SLE (1)	0	0	0	1	0	0	0	0
MS (1)	0	0	0	1	0	0	0	0

VKH: Vogt-Koyanagi-Harada, JIA: juvenile idiopathic arthritis, AS: ankylosing spondylitis, RA: Rheumatoid arthritis, SLE: Systemic Lupus Erythematous, and MS: multiple sclerosis.

DISCUSSION

The blood grouping system plays a vital role in organ transplantation and blood diseases, but its association with the occurrence of some diseases, especially those with the autoimmune origin is not entirely understood[17]. The hypothesis in this study was that ABO blood grouping and Rh factor may be a factor associated with liability to autoimmune ocular condition especially non-infectious uveitis. The current study included 175 subjects selected from uveitis clinic. The patients' age ranged from 3 years to 58 years. Females to males' ratio was 1.1: 1.

In this study, blood group O was predominant (34.9%), followed by A (33.1%), B (22.3%) and AB blood group which had the lowest percentage (9.7 %). The current study results agreed to some extent with a study conducted by Swelem et al[18] which reported that blood groups A and O had the highest percentage in a healthy Egyptian population while the least frequency was for blood group AB. They stated that the frequencies of blood groups A, O, B and AB were 39.4%, 25.9%, 24.1% and 10.6%, respectively.

In this study the incidence of Rh negative was 7.4% and that of Rh positive was 92.6%. Geographically, higher incidence of Rh positive was reported in Japanese (99.7%) while it was 94.3% in India, and lower in European population (83%)[19].

Similarly, the association of blood groups and Rh factor was studied in patients in the different types of uveitis. Interestingly, in Behçet's disease the frequency of blood type A + was the highest (n=19/49, 38.8%) followed by blood type O + (n=14/49, 28.6%). In contrary, VKH cases have a higher prevalence of blood type O + (n=17/37, 45.9%) followed by blood type B + (n=8/37, 21.6%). Idiopathic uveitis has nearly similar association with blood type A + (n=12, 32.4%) and blood type O + (n=11, 29.7%).

Although, no studies were found in literature to correlate between Uveitis and blood grouping, other studies have been conducted in different entities in ophthalmology. For example, in glaucoma, few research have contradictory findings that explore the association between the ABO blood groups and the different patterns of glaucoma. In a study conducted by Leske et al[20] they could not discover any correlation between primary open-angle glaucoma (POAG) and the ABO blood groups. In another research performed by Khan et al[8], they found a correlation between blood group B and Rh− in Pakistani POAG patients.

Also, some studies have shed some light on some aspects of the pathogenesis and association between ABO blood type and Rh factor with some autoimmune diseases like Behçet's disease. ABO blood group antigens have been found on most epithelial cells and in mucosa secretions. A/B antigens have been found in the oral epithelium of persons with blood groups A and B, respectively. The changes in expression of carbohydrate ABO antigens in the epithelia has been found to be related to epithelial differentiation and cell maturation patterns, for example, the wound healing process and oral mucosa malignant disorders. A strong association of periodontal diseases with Behçet's disease has also been demonstrated. Recurrent oral ulcers are the main finding associated with Behçet's disease. Thus, the relation of ABO antigens in oral ulcer patients with Behçet's disease may be critical[21].

The limitations in our study could be the relatively small sample size. Also, the absence of a control group is considered a weak point, but our aim was to study the prevalence of blood type ABO and Rh factor in non-infectious uveitis. Additionally, it was difficult to compare our results with other studies since there was no previous research has been done on the correlation between ABO blood groups and non-infectious uveitis. However, this may be considered a strong point as our research will contribute to the literature obtaining a basic knowledge of the blood grouping in non-infectious uveitis. Investigation of the blood group distribution rates of uveitic patients in a regional basis would obviously contribute to the knowledge of genetics in non-infectious uveitis.

CONCLUSIONS

From what was mentioned above it is clear that, the blood groups O and A were the most commonly associated with the non-infectious uveitis. In addition, positive Rhesus factor was strongly associated with such cases.

Further studies are required concerning the predisposing role of the ABO blood type and Rh factor for the non-infectious uveitis. Nonetheless, unraveling the possible relationship between the blood group and the pathogenesis of non-infectious uveitis would enhance the predictive power for the development of uveitis. Further Multi-center studies with larger sample size may be essential to define the correlation between ABO blood groups and Rhesus factor with activity of disease in non-infectious uveitis.

Author Contributions

All authors were involved in the literature search, drafting, revising, and final approval of the paper.

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