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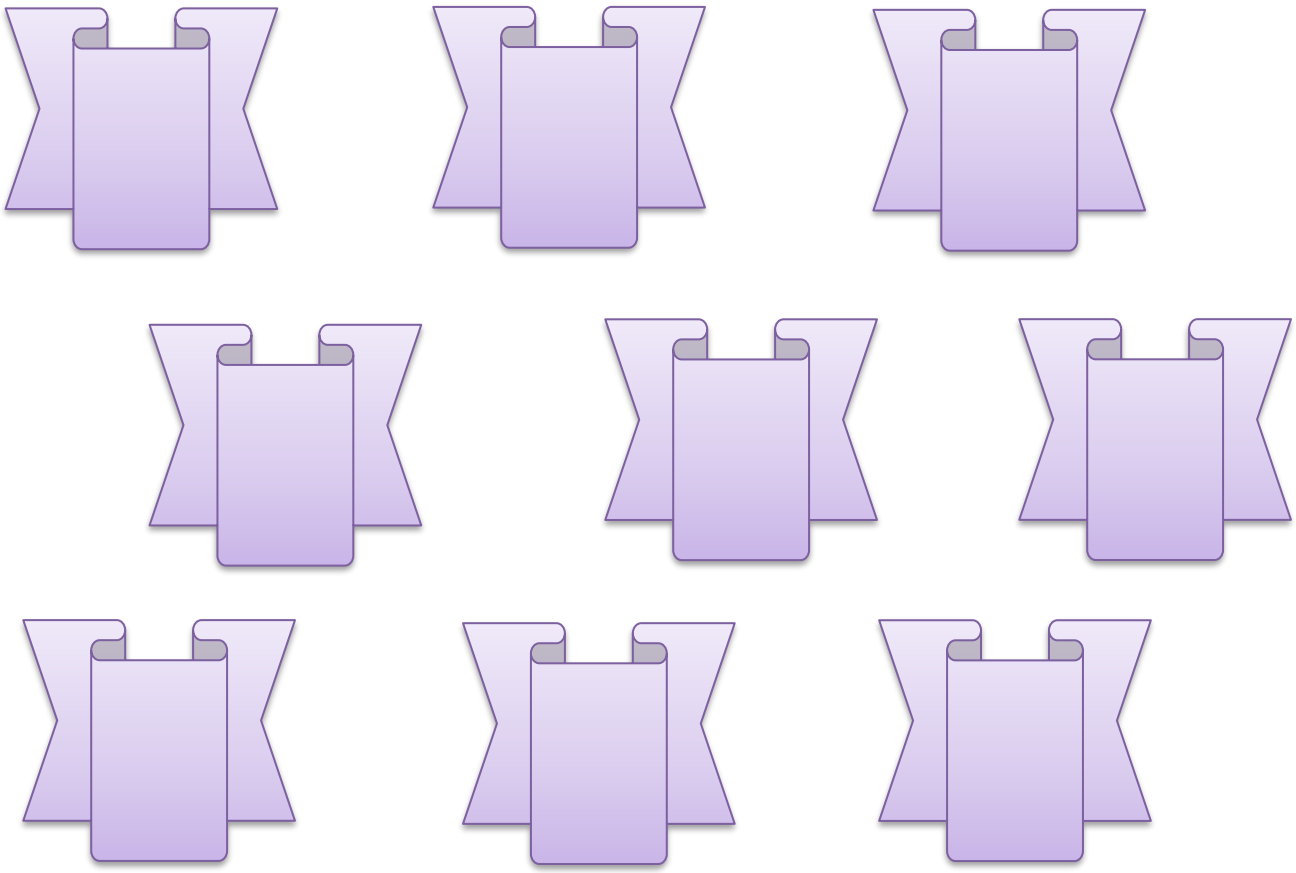

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Original Article

Antistreptolysin O Levels in Patients with Non-Infectious Uveitis

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ABSTRACT

Background: A proof of past streptococcal infection is usually required for the diagnosis of Post streptococcal uveitis, which is achieved by measuring the serum level of anti-streptococcal lysin O titer.

Aim of the work: This study aims to investigate the association between positivity of antistreptolysin O and non-infectious uveitis.

Patients and Methods: This cross-sectional study included 100 patients diagnosed with noninfectious uveitis at the ophthalmology outpatient clinic of Al-Azhar university hospital, Damietta, Egypt, in cooperation with Mansoura ophthalmic center from November 2022 to April 2023. ASO titer was measured for every patient, and it was considered positive if > 200 IU/ml.

Results: The median [IQR] ASO level was 130.5 [55 – 289.2] IU/ml with a range of [19.9 – 512.2] IU/ml. Its level was higher in the idiopathic, AS, and Arthritis patients than in other study patients, 205 [54.5 – 334.2], 223 [153 – 412], and 225 [40 – 225] respectively. However, this difference between the study groups was not significant statistically [P value > 0.05]. Our study revealed that no significant correlation between the ASO positivity and the degree of visual loss [P value = 0.48]. Correlation analysis between the ASO titer and the type of uveitis, anatomical site of uveitis, and AC score revealed no statistically significant correlation between them and the ASO titer [P = 0.9, 0.1, 0.3 respectively]. Also, we found no significant correlation between the ASO titer and IOP and BCVA.

Conclusion: ASO titer is significantly elevated in noninfectious uveitis, however, our results showed no significant correlation between the ASO and the type of uveitis.

Keywords: Noninfectious uveitis; ASO; Ocular inflammation; Iridocyclitis.

INTRODUCTION

Uveitis can affect any age group with an incidence of 24.9 cases per 100,000 persons [1]. It is usually considered a vision-threatening intraocular inflammatory disease. In developing countries, 25% of permanent vision loss is caused by uveitis and its consequences [2]. It can be categorized into anterior, intermediate, and posterior categories depending on the predominant anatomical site of inflammation. About 50% of cases of uveitis are anterior, making it the most common type. Based on the etiologic origin, it can be classified into infectious, non-infectious, or masquerade [neoplastic or non-neoplastic causes] [3].

Non-infectious uveitis [NIU] is an immune-mediated disease associated with Behcet, Vogt-Koyanagi-Harada [VKH], Juvenile idiopathic arthritis [JIA], Fuchs heterochromic iridocyclitis, HLA-B27-associated uveitis, and white dot syndrome [4-6].

Post-streptococcal uveitis is considered a clinical sign of an autoimmune disease known as a post-streptococcal syndrome which is a systemic disease that affects multi organs such as the heart, kidney, and skin [6].

Post-streptococcal uveitis is characterized by the presence of time interval between the infection and the onset of uveitis, recurrence of inflammation, and presence of other post-streptococcal syndrome features such as rheumatic fever, glomerulonephritis, and sometimes retinal vasculitis [7-9]. However, proof of past streptococcal infection is usually required for the diagnosis of Post streptococcal uveitis, which is achieved by measuring the serum level of anti-streptococcal lysin O titer [10].

So, in this study, we aimed to investigate the association between positivity of anti-streptolysin O and non-infectious uveitis

PATIENTS AND METHODS

This cross-sectional study included 100 patients diagnosed with noninfectious uveitis at the ophthalmology outpatient clinic of Al-Azhar university hospital, Damietta, Egypt, in cooperation with Mansoura ophthalmic center from November 2022 to March 2023.

The principles outlined in the Helsinki Declarations guided our research. Al-Azhar University's Ethical committee approved our study [IRB 0006]. Before recruiting anyone, each person gave their written consent.

We included the patients according to the following, all patients diagnosed with active non-infectious uveitis in the 30 days preceding the ASO blood test, while we excluded any patient diagnosed with infectious uveitis.

Data collection

Complete medical history and general examination were done for every patient upon enrollment. Full ophthalmic examination was done for each patient, including anterior and posterior segment examinations with special refinement to the following:

- Visual acuity assessment: best corrected visual acuity [BCVA] using Landolt's broken ring chart. In our study, sever visual loss was defined as BCVA ≤ 6/60 or LogMar = 1, Moderate visual loss was defined as BCVA= 6/60 – 6/12 or LogMar 0.9 – 0.3. However, no visual loss was determined if BCVA was > 6/12, or < 0.3 LogMar.

- Intraocular pressure measurement using Applanation tonometry.

- Fundus examination using slit lamp biomicroscope with a 90 D lens.

- Gonioscopy by applying the 3-mirror gonioscopy lens.

- Intraocular inflammation in uveitis was graded using the SUN grading system, in which grading of aqueous cells [AC] cells and flare was based on the Standardized Uveitis Nomenclature working group grading scheme.

AC cells grading was determined using a high-intensity 1 x 1 mm slit beam based on the Standardization of Uveitis Nomenclature [SUN] grading scheme [Table 1] [11].

Laboratory investigations for exclusion of any infectious etiology of uveitis according to the clinical presentation of each case were done.

Venous samples from peripheral blood of uveitic patients was obtained. The samples were left for clotting at room temperature for 30

minutes, then serum was separated for assay of ASOT by nephelometry at the central laboratory of clinical pathology department.

Statistical analysis

Analysis of our data was done using the SPSS statistical software [version 26] [IBM, Chicago, Illinois, USA]. Dichotomous variables were described as numbers and percentages [N [%]], and were analyzed using the Chi-Square Test. The normality of continuous variables was tested by the Kolmogorov-Smirnov test. The parametric data were compared within groups using the One-way ANOVA test. A p-value of < 0.05 was considered significant.

RESULTS

Our study included 100 patients diagnosed with non-infectious uveitis. The mean age was 33.5 ± 13.4 years with a range of 7 – 67 years. Female patients were more prevalent than a male with a female-to-male ratio of 1.4**.** In terms of the types of uveitis, 39% of our patients were Behcet, 30% were idiopathic, 11% were AS, 9% were VKH, 5% were JIA, 3% were arthritis, and the other 3% were ulcerative colitis [1%], SLE [1%], and enthesis related uveitis [1%]. As regards the site of uveitis, the Anterior segment was the most common site in our study, which represent 72% followed by the posterior uveitis which represent 19% [table 2].

According to the AC cell score, most of the patients had moderate scores [47% in right side and 43 % in left side]. In terms of the association between the type of uveitis and study variables, we found a significant association between gender and the type of uveitis [P value = 0.01], in which the male gender was higher in Behcet uveitis than females, however, the female gender was higher in the idiopathic type than males. However, we found no significant association between the type of uveitis and its anatomical site [P = 0.2].

As regards the ASO titer, the median [IQR] ASO level was 130.5 [55 – 289.2] IU/ml with a range of [19.9 – 512.2] IU/ml. Its level was higher in the idiopathic, AS, and Arthritis patients than in Behcet, VKH, and JIA, 205 [54.5 – 334.2], 223 [153 – 412], and 225 [40 – 225] versus 106 [45 – 247], 73 [26 – 253], and 9 [7 – 11.5] respectively. However, this difference between the study groups was not significant statistically [P value = 0.43]. Also, ASO titer was higher in posterior uveitis, and anterior uveitis than in the intermediate and pan uveitis 173 [59.5 – 261], 158 [50 – 297] versus 106 [83 – 128.2], and 173 [59.5 – 261] respectively [P value = 0.34].

In our study the ASO titer was considered positive if > 200 IU/ml, based on this we found that, most of the positive cases were idiopathic [33.3%], Behcet [31%], AS [16.7%], VKH [7.1%], JIA [7.1%], Arthritis [4.8%] respectively with no significant association between the type of uveitis and ASO positivity. Also, our study revealed that no significant correlation between the ASO positivity and the degree of visual loss [P value = 0.48] [table 3].

In terms of the BCVA, the median [IQR] BCVA was 0.47 [0.17 – 0.77]. Within group comparison between the different types of uveitis regarding the BCVA revealed, no significant difference between them [P value = 0.3]. Also, the difference between every 2 types was not significant [P value > 0.05 for all] except for the difference between the Behcet and idiopathic uveitis which was statistically significant [P = 0.04]. In our study 63% of the included patients had visual loss [< 6/12], 19% had moderate visual loss [6/60 – 6/12], and 17% had high visual loss [≤ 6/60].

According to the IOP, it was within the normal range, which was 13 [11 – 16] mmHg. By comparing the different types of uveitis regarding the IOP, we found that, it was significantly lower in the VKH which was 11 [11 - 14.5] mmHg, with a statistically significant difference between the other types [P value = 0.001].

Correlation analysis between the ASO titer and the type of uveitis [Fig. 1], Anatomical site of uveitis [Fig. 2], and AC score revealed no statistically significant correlation between them and the ASO titer [P = 0.9, 0.1, 0.3 respectively]. Also, we found no significant correlation between the ASO titer and IOP and BCVA.

Table [1]: Scheme for grading of anterior chamber and vitreous cells and flare [11]

Grade	Aqueous cell grading [Cells in field]	Description of aqueous flare grading	Vitreous cell grading [Cells in retro-lental space] High intensity 1 × 0.5 mm slit beam]	Description of vitreous haze/ flare
0	<1	Absence of flare	No cells	No Flare
0.5+	1-5	-	1-10	Trace
1+	6-15	Faint plasmoid aqueous	11-20	Clear optic disc and vessels, hazy nerve fiber layer
2+	16-25	Moderate [iris and lens details clear]	21-30	Hazy optic disc and vessels
3+	26-50	Marked [iris and lens details hazy]	31-100	Marked [Hazy optic disc details]
4+	>50	Intense flare [fibrinous exudates]	>100	Intense [minimal/no optic disc details]

Table [2]: Demographic and baseline clinical data of the patients

Variables		Mean ± SD or N [%] [n=100]
Age [Years]	Mean ± SD	33.5 ± 13.4
	Range	7 - 67
Gender. N [%]	Male	41 [41%]
	Female	59 [59%]
Anatomical sites of the uveitis	Anterior	72 [72%]
	Posterior	18 [18%]
	Intermediate	4 [4%]
	Anterior and intermediate	3 [3%]
	Pan uveitis	3 [3%]
Diagnosis of the Uveitis	Behcet	39 [39%]
	Idiopathic	30 [30%]
	Ankylosing spondylitis	11 [11%]
	Vogt-Koyanagi-Harada	9 [9%]
	Juvenile idiopathic arthritis	5 [5%]
	Arthritis	3 [3%]
	Ulcerative colitis	1 [1%]
	Systemic lupus erythematosus	1 [1%]
	Enesthitis	1 [1%]

Table [3]: Correlation analysis between the positivity of ASO titer and types of uveitis, and visual loss

		Positivity		P value [a]
		Positive [n=42]	**Negative [n=58]**	
Type of uveitis	Behcet	13 [31%]	26 [45.6%]	0.49
	Idiopathic	14 [33.3%]	15 [26.3%]	
	Arthritis	2 [4.8%]	1[1.8%]	
	Ankylosing spondylitis	7 [16.7%]	4[7%]	
	Vogt-Koyanagi-Harada	3 [7.1%]	6[10.5%]	
	Juvenile idiopathic arthritis	3 [7.1%]	2[3.5%]	
Visual loss	Sever visual loss	8 [19%]	9 [15.8%]	0.48
	Moderate visual loss	22 [52.4%]	25 [43.9%]	
	No visual loss	12 [28.6%]	24 [41.3%]	

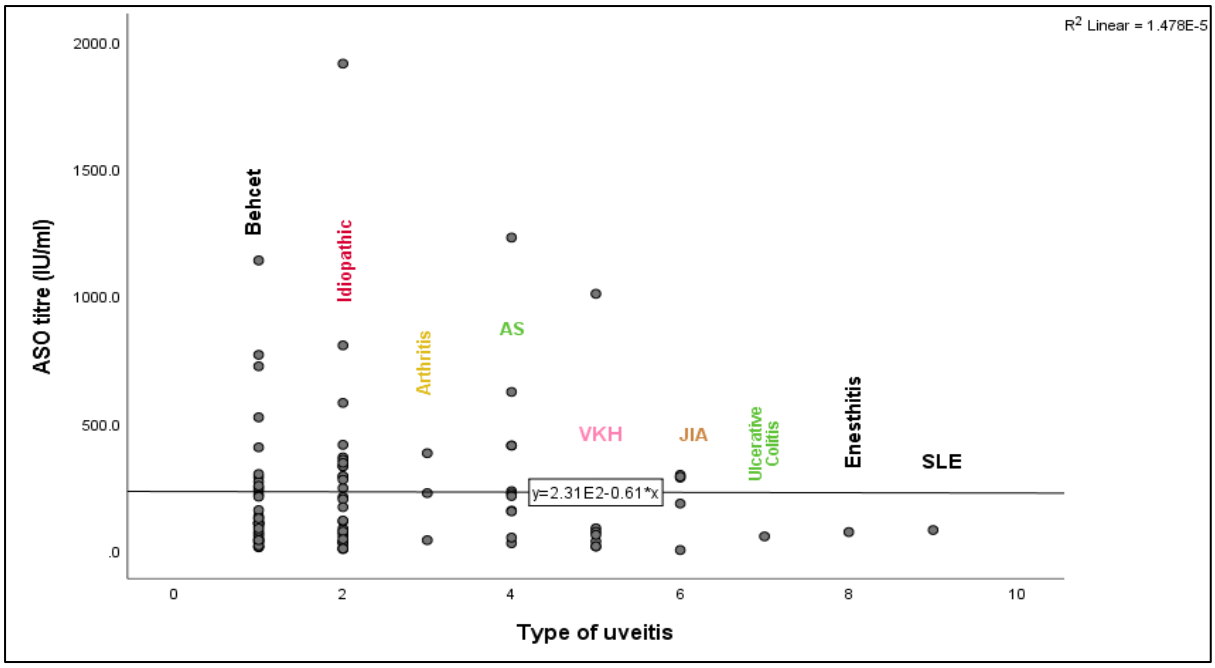

Figure [1]: Correlation between the ASO level and type of uveitis

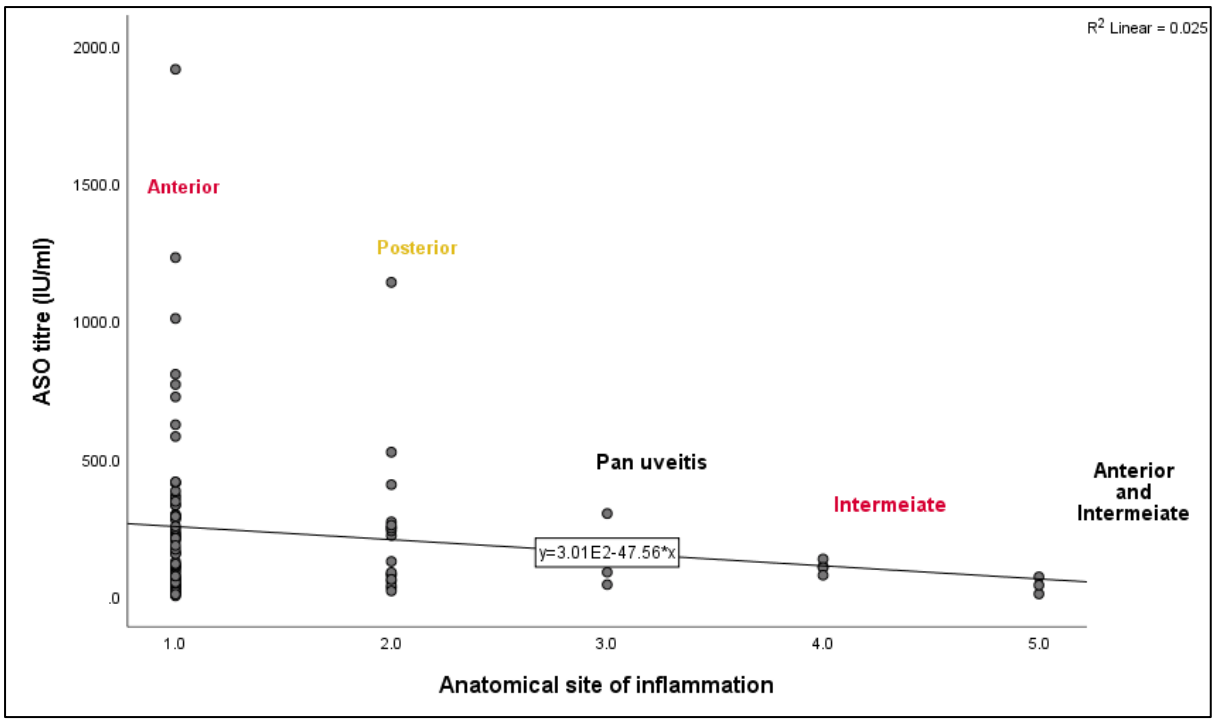

Figure [2]: Correlation between the ASO level and the anatomical site of uveitis

DISCUSSION

As noninfectious uveitis is a sign of multiple diseases, there are many risk factors for its onset and progression. Demographics such as age, gender, and race are considered important risk factors. However, there are multiple external factors for the disease development, such as smoking, pregnancy, low vitamin D level, Diabetes, thyroid disorders, some medications, and autoimmune reactions that may occur post streptococcal infections [12, 13]. Poststreptococcal uveitis is uncommon, so its diagnosis needs highly suspicious ophthalmologist [13]. Antibodies against streptolysin o antigen are usually elevated 3 weeks after streptococcal infections and remain elevated for three months. This ASO titer can be used for diagnosis of post-streptococcal diseases such as noninfectious uveitis [14].

Our study showed that the median ASO titer in our patients was 130.5 [19.9 – 512.2] IU/ml. The highest ASO titer was found in AS, and arthritic patients, which agreed with **Curragh *et al.*** [15].

ASO titer was considered positive if > 200 IU/ml, based on this we found that most of the positive cases were idiopathic [34.1%], Behcet [31%], AS [15.9%], VKH [6.8%], JIA [6.8%], and Arthritis [4.5%] respectively.

According to the majority of research, anterior uveitis is the most prevalent kind of intraocular inflammation. Posterior uveitis, and panuveitis comes after; whereas intermediate uveitis constitutes the least common form [16, 17].

Uveitis' underlying etiology is frequently unknown, leading to the term "idiopathic" being applied to the condition. In between 30 and 60 percent of patients, it is typically unknown. This comes in agreement with our observations, as 30% of our patients had an unknown origin; yet, most patients contributed to Bechet disease with 39%. On the other hand, Enesthitis, ULC, and SLE was the least common etiologies [16, 17].

Other studies held in different countries are consistent with our findings, in Turkey, Behçet uveitis is the leading contributor to non-infectious uveitis. Moreover, Saudi Arabia, China, Iran, Iraq, and Japan [6.5-32.2%] all have high rates of it [18-22].

As regards the IOP, it was within normal range in all types of uveitis in our study, except for the VKH and JIA which was lower than other types, which disagree with **Daniel *et al.*** [23], who reported that the mean annual incidence rates for IOP ≥21mmHg and IOP ≥ 30 mmHg are 14.4% and 5.1% per year respectively. Hypotony that occurred in some cases in our study is explained by that in some types of HLA B-27 related uveitis is associated with reduced aqueous humor production and increased uveoscleral outflow [24].

Visual acuity in our patients was assessed using BCVA. [LogMar] and was found to be with a median of 0.47 [0.17 – 0.77] in the right eyes, and 0.38 [0.17 – 0.77] in the left eyes. Also, we found that Arthritis and VKH are the most common two types in which the vision is more affected than other types. Similar findings were also reported by **Pistilli *et al.*** [25]. In our study we found no significant correlation between the degree of visual loss and the positivity of ASO titer, so the severity of visual loss cannot be predicted by the ASO titer.

Our study has some limitations such as small sample size, and absence of control group, and although, we didn't find significant correlation between ASO titer and type of uveitis, its level was significantly elevated in noninfectious uveitis. So, further larger studies are needed to prove the correlation.

In conclusion, ASO titer is significantly elevated in noninfectious uveitis, however, our results showed no significant correlation between the ASO and the type of uveitis.

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