

Etiologies and Demographic Distribution of Uveitis in a Referral Center in Iraq

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ABSTRACT

Purpose: To determine the etiologies and demographic distribution of uveitis in a referral center in Baghdad, Iraq and to compare the results with a similar study done in the same center in 2014.

Study Design: Descriptive observational study.

Place and Duration of Study: Ibn Al-Haitham Teaching Eye Hospital, Iraq, from January 2019 to June 2022.

Patients and Methods: Two hundred and fourteen patients with uveitis were included. They underwent complete ocular and relevant systemic examination. Data was collected and analyzed using descriptive statistics. Comparison was done with the data retrieved from 2014.

Results: Out of 264 patients, only 214(81%) completed follow up. Others did not show up again due to Corona virus Pandemic. There were 122(57%) females, 95(44.3%) were unilateral, 62(28.9%) were granulomatous, 62(28.9%) were anterior, 42(19.6%) were intermediate, 4(1.8%) were posterior and 106(49.7%) were pan uveitis cases. Cause was identified in 161(75.3%) patients while 53(24.7%) were considered idiopathic. Out of 214 patients, 84(39.2%) were due to infectious causes like tuberculosis, herpes (herpes zoster or simplex viruses) and toxoplasmosis. On the other hand, 130(60.7%) cases were non-infectious for example, Vogt-Koyanagi-Harada disease, Behçet disease, and connective tissue diseases such as Ankylosing Spondylitis or idiopathic.

Conclusion: A minor change was found from the 2014 study to 2023. Tuberculosis is now the most common cause of infectious uveitis instead of Toxoplasmosis. Furthermore, Idiopathic, Vogt-Koyanagi-Harada, and Behçet disease are the commonest causes of non-infectious uveitis.

Key Words: Granulomatous, Herpetic uveitis, Toxoplasmosis, Vogt-Koyanagi-Harada, Behçet Disease, Ankylosing Spondylitis.

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INTRODUCTION

Uveitis a Latin word for *grape* is defined as an inflammatory state of the uveal tract comprised of the Iris, Ciliary body and Choroid.¹ Practically, this term has been applied to any inflammation involving inside

of the eye including iritis, pars planitis, vitritis, retinal vasculitis (phlebitis and arteritis), choroiditis, retinitis and papillitis.²

Uveitis can be caused by infections, connective tissue diseases, autoimmune disorders, trauma to the eye, certain medications that can illicit ocular inflammation and rarely due to malignancies. Sometimes it can be only limited to the eye without any systemic manifestation as in pars planitis and serpiginous choroiditis.²

The Standardization of Uveitis Nomenclature (SUN) working group guidance on uveitis

terminology, endorsed by the International Uveitis Study Group (IUSG), classified uveitis anatomically according to the primary site of inflammation into; anterior (the anterior segment is the main site), intermediate (the vitreous), posterior (choroid and/or retina), and panuveitis (involving the whole uvea). Etiologically it is divided into infective (bacterial, viral, fungal), non-infective (without or with systemic involvement) and Masquerade (neoplastic and non-neoplastic).³

The SUN Working Group guidance included the following descriptions according to the timing of inflammation:

Onset: Sudden or gradual.

Duration: limited (for 3 months or less) or persistent.

Clinical Course: Acute (sudden and limited), recurrent (repeated episodes separated by inactive periods) or chronic (persistent with relapse less than 3 months after discontinuation of treatment). Remission is defined as no visible cells for 3 months or longer.³ Although etiologies of uveitis can be influenced by genetic and geographical factors, many cases are idiopathic.^{4,5}

This study was performed to identify etiologies of uveitis and compare with another older study done at the same center back in 2014.

METHODS

This is a descriptive, cross-sectional study which included 214 patients who attended uveitis clinic in Baghdad, Iraq from January 2019 to June 2022. Ethical approval was given by the scientific committee of Ibn Al-Haitham Teaching Eye Hospital. Uveitis clinic in Baghdad, Iraq is a government hospital which receives patients from all over the country as it is the only uveitis referral center. The patients were either: new, acute or chronic whether diagnosed or not, with no response to treatment, with recurrence or patients who developed complications. Cases not referred to this center were those with either first attack of uveitis or very straightforward cases.

The variables taken into consideration were sex, infectious or not, unilateral or bilateral anatomical location whether anterior, intermediate, posterior or pan uveitis, granulomatous or not, and clinical course; acute, chronic, and recurrent as illustrated in Table 1.

All the patients underwent a complete ocular examination which included uncorrected and corrected

visual acuity, intraocular pressure, slit-lamp examination of the anterior chamber and fundus examination by the indirect slit-lamp biomicroscopy.⁶ Ocular tests were sent when needed like B-scan, optical coherence tomography (OCT) of the anterior segment, macula and optic disc, macular optical coherence tomography angiography, fundus autofluorescence and fundus fluorescein angiography.⁷

Systemic investigations which were done for all patients included complete blood picture, blood film, erythrocyte sedimentation rate (ESR), venereal disease research laboratory/Rapid Plasma Reagin tests done for Syphilis diagnosis, chest x-ray mostly for Tuberculosis and Sarcoidosis, Tuberculin skin test (TST) and Interferon Gamma Release Assays were used for the diagnosis of active or latent tuberculosis (TB).⁸⁻¹⁰ Quantiferon Gold is the one most accurate test for diagnosis of TB uveitis and T-SPOT test which is inferior to QFT. In some cases, they could be associated with false negative results in active TB so they were not used alone to diagnose ocular TB but where available a combination of both IGRAs and TST did offer the best sensitivity.¹⁰ Bronchial lavage was done when needed. In cases of strong clinical suspicion but with negative tests, the response to anti-TB therapy was taken into consideration. Other investigations were sent as required in collaboration with rheumatologists, internists, neurologists, dermatologists, obstetricians, and pediatricians to reach an accurate diagnosis and start a proper therapy. In some cases, the diagnosis was clear according to the clinical picture which indicated a particular etiology, others needed to be sent for investigations related to the suspected cause compatible with the clinical findings other than the routine ones like C-reactive protein (CRP), rheumatoid factor (RF), antinuclear antibody (ANA), especially for Juvenile idiopathic arthritis, Pathergy test for Behçet disease (BD), anti-neutrophil cytoplasmic antibody (ANCA) for granulomatosis with polyangiitis (GPA) previously known as Wegener's granulomatosis,¹¹ serum angiotensin-converting enzyme (ACE) and lysozyme for sarcoidosis,¹² serology for toxoplasmosis,¹³ human immunodeficiency virus (HIV), cytomegalovirus (CMV), herpes zoster virus (HZV), and herpes simplex virus (HSV),¹⁴ although not very helpful unless negative, culture for bacterial or fungal infections, antiphospholipid antibody, cancer screen tests, computed tomography (CT) or magnetic

resonance imaging (MRI) with and without contrast, lastly HLA-typing if needed. The modified diagnostic criteria were used for VKH diagnosis. HZV, HSV, CMV uveitis were diagnosed clinically, while BD was diagnosed according to the International Study Group reported in 1990. Most of the patients were managed in collaboration with physicians. When the case was not associated with an infectious cause or a systemic disease, it was labeled as idiopathic.

All the new or referred cases to Ibn Al-Haitham Teaching Eye Hospital from January 2019 to June 2022 were included in this study except post-traumatic, post-surgical and lens-induced.

RESULTS

According to the sex; female patients were more affected in this series; 122 (57%) while males were 92 (43%) patients. Details are shown in Table 1. According to the cause; there were 84 (39.2%) infectious cases and 130 (60.7%) were non-infectious. During data collection, it was noted that there was an age-related predilection toward infectious or non-infectious diseases. Below 40 years (which is defined as the beginning of middle age in adults), uveitis was non-infectious in 75 patients (79.79%), and infectious in 19 (20.21%), while above 40 years infectious uveitis was seen in 65(54.16%) and non-infectious in 55 (45.84%) patients.

Table 1: Characteristics of patients and uveitis.

Classification	Patients No.	%
Sex		
Male	92	43
Female	122	57
Cause		
Infectious	84	39.2
Non-Infectious	130	60.7
Laterality		
Unilateral	95	44.3
Bilateral	119	55.6
Anatomical Location		
Anterior Uveitis	62	28.9
Intermediat Uveitis	42	19.6
Posterior Uveitis	4	1.8
Panuveitis	106	49.7
Type of inflammation		
Granulomatous	62	28.9
Non-Granulomatous	152	71.0
Clinical course		
Acute	27	12.6
Chronic	161	75.2
Recurrent	26	12.1

VKH was the most common non-infectious cause of uveitis below 40 years in 22 (23.4%) patients. It most commonly affected middle and south of the Iraqi population (being darker than the northern), followed by BD. The commonest infectious etiology in this age group (< 40 years) was herpetic either HZV or HSV anterior uveitis in 8 (8.5%) patients as shown in Table 2. Ages 40 years and above showed that TB was the commonest cause of infections in 44 (36.66%) patients followed by herpetic uveitis, 19 (15.83%) patients as shown in Table 3. The first age group had 20 (21.2%), while the second had 33 (27.4%) idiopathic cases. Table 4 depicts further classification of idiopathic uveitis.

The remaining etiologies were arranged in declining order from the highest to lowest in frequency.

Table2: Etiologies of uveitis in patients with ages < 40 years.

Etiology	No.	%
Vogt-Koyanagi-Harada disease	22	23.4
Idiopathic	20	21.2
Behcet Disease	11	11.7
Herpetic	8	8.5
Tuberculosis	6	6.4
Pars planitis	6	6.4
Fuchs' heterochromiciridocyclitis	6	6.4
Juvenile Idiopathic Arthritis	5	5.3
Toxoplasmosis	4	4.3
Rheumatoid Arthritis*	2	2.2
Serpiginous Choroiditis	1	1.06
Diabetes Mellitus**	1	1.06
Multiple Sclerosis	1	1.06
Cytomegalovirus retinitis	1	1.06
Total No.	94	100

*Reference¹⁵**Reference¹⁶

Table 3: Etiologies of uveitis in patients 40 years and above.

Etiology	No.	%
Tuberculosis	44	36.66
Idiopathic	33	27.5
Herpetic anterior uveitis	19	15.83
Vogt-Koyanagi-Harada disease	7	5.83
Behcet disease	5	4.16
Fuchs' heterochromiciridocyclitis	4	3.33
Toxoplasmosis	2	1.66
Diabetes Mellitus	2	1.66
Ankylosing spondylitis	2	1.66
Inflammatory bowel disease	1	0.83
Multifocal Choroiditis with Panuveitis	1	0.83
Total No.	120	100

Table 4: Classification of Idiopathic Uveitis.

Anatomical Location	Less than 40 Years	%	More Than 40 Years	%
Intermediate uveitis (IU)	9	45	17	51.5
Acute anterior uveitis (AAU)	6	30	6	18.2
Panuveitis	4	20	6	18.2
Chronic anterior uveitis (CAU)	1	5	4	12.1
Total	20	100	33	100

DISCUSSION

Ibn Al-Haitham Teaching Eye Hospital is the only tertiary referral center in Iraq that receives patients of all age groups (infants aged 0-1 year to senior adults aged 60 years and above) whether new or cases who have not been diagnosed or responded to therapy. This study showed that among the most common causes of uveitis in patients less than 40 years was VKH, followed by idiopathic then BD. From 40 years and above; tuberculosis, idiopathic and herpetic anterior uveitis were the most common.

In comparison to a study done in the same center in 2014, the results showed that toxoplasmosis and tuberculosis were the most common infectious causes, while VKH, BD and pars planitis, were the most common non-infectious causes.¹⁷ It shows that toxoplasmosis has decreased greatly while TB showed an apparent rise. This reflects either, a decline in the community's socioeconomic status leading to increased poverty, ignorance, crowdedness and diseases or an improvement in the investigational tools resulting in a more accurate diagnosis, in either way, this requires further studies.

In Jordan (the country to the west of Iraq), autoimmune-mediated uveitis associated with BD and seronegative Spondyloarthropathy represented a high percentage.¹⁸ While in Iran (east of Iraq), the most common etiologies were Idiopathic, toxoplasmosis, BD and Fuch's heterochromia iridocyclitis.¹⁹ In Turkey (north of Iraq), BD was the most common cause of non-infectious uveitis while toxoplasmosis was the most common infectious etiology followed by herpetic uveitis.²⁰

In Saudia Arabia (south of Iraq), TB was the most common infectious cause followed by herpetic anterior uveitis and toxoplasmosis. The non-infectious causes were VKH followed by BD. The results of this study were most similar to ours which could be due to geographical or genetic reasons or both.²¹ In India, TB was the commonest infectious etiology, whereas the

most common non-infectious causes were spondyloarthropathies and trauma.²²

Herpetic uveitis followed by toxoplasmosis and TB were the infectious causes in a large study done in Greece, while the non-infectious were sarcoidosis, white dot syndromes, and ankylosing spondylitis.²³ In all these studies, we noticed that TB was still present in different countries across the world and needs active efforts for its eradication.

Early diagnosis and treatment of uveitis can assist in controlling the high rate of visual morbidity, such as cataract, glaucoma, optic disc atrophy and blindness. The serious systemic associations sometimes can even lead to death. Thus, it is a significant health problem causing dysfunction to the patients and their families since most of them are young in the working age group. This results in increase in the burden on society to provide resources and caregivers to deal with uveitis complications.

CONCLUSION

TB is endemic in our country and it has been increasing, while toxoplasmosis is under control. TB is also still present in a lot of countries in the world, this should be kept in mind when trying to diagnose a case of uveitis either from Iraqi citizens or immigrants to or from Iraq. On the other hand, VKH is the number one non-infectious etiology affecting the middle and south of the Iraqi population and BD in north. These results should raise suspicion about reaching an early diagnosis and starting the proper treatment to avoid significant visual morbidity associated with uveitis that could end with blindness or even death.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board (AEWEH/MS/17).

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