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RESEARCH ARTICLE

PATTERNS OF UVEITIS AT A TERTIARY REFERRAL CENTER IN YEMEN: ONE CENTRAL RETROSPECTIVE STUDY

Essam Yahiya Al-Shamahi[1,2], Najeeb Mothana Muhsin[3], Emad Hassan Al-Shamahi[1,2], Hassan Abdulwahab Al-Shamahy[1,3]

[1]*The Eye Consultation Center, Sana'a city, Yemen.*
[2]*Opthalmology Department, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.*
[3]*Medical Microbiology and Clinical Immunology Department, Faculty of Medicine and Health Sciences, Sana'a University.*
[4]*Medical Microbiology department, Faculty of Medicine, Genius University for Sciences & Technology, Dhamar city, Republic of Yemen.*

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***Address for Correspondence:**
Dr. Hassan A. Al-Shamahy, Faculty of Medicine and Heath Sciences, Sana'a University. Faculty of Medicine, Genius University for Sciences and Technology, Dhamar/Sana'a, Yemen. The Eye Consultation Center, Sana'a city, Yemen. Tel- +967-1-239551; E-mail: *shmahe@yemen.net.ye*

Abstract

Background: Uveitis is described as a disorder of the eye so as to leads to the iris, ciliary body, choroid, and adjacent parts of the eye inflammation. The disturbances may produce impermanent or continuing visual impairment or sightlessness.
Purpose: The main purpose of the study was to reveal the causes of uveitis in a referral center in Sana'a city, Yemen. Sequentially the study was conducted to assist in the development and design of preventive policies and diagnostic methods for uveitis in Yemen.
Methods: This cross-sectional, retrospective analysis integrated 65 uveitis patients who were referred to the Eye Consulting Center clinic, from January 2021 to the end of December 2021. Data concerning patient gender, age and anatomical location of disease, clinical and pathological manifestations were collected then evaluated.
Results: The mean patient age at onset of uveitis was 36.3 ± 13.4 (range: 9-75) years. The female to male ratio was 2.6: 1. Sixty-seven percent participated uveitis patients suffered from bilateral involvement. The predominant type was Pan-uveitis (46.2%), anterior acute uveitis (36.9%), intermediate acute uveitis (12.3%) while posterior acute uveitis was less common (4.6%). Considering medical conditions, 53.8% of patients had acute uveitis and 46.2% had chronic uveitis. Laterality, 38.5% had unilateral uveitis while most patients had bilateral uveitis. Also, 53.8% of patients developed complications. Given the possible causes, the most common diagnoses were 'idiopathic' (32.3%), HLA-B27-positive (21.5%), Behçet's syndrome (13.8%), and granulomatous uveitis (TB) (9.2%)., seronegative spondyloarthropathy (6.2%), Fuch's uveitis (6.2%), followed by less common Vogt Koyanagi Harada (4.6%), herpetic uveitis (3.1%), and toxoplasmosis (3.1%).
Conclusions: On the contrary to most uveitis epidemiologic studies the uveitis etiologic and clinical patterns were diverse in a tertiary referral center in Sana'a city, Yemen. Pan-uveitis and anterior acute uveitis were the most frequent clinical pattern in this study, and the most common related causes were HLA-B27 positive and Behçet's syndrome.
Keywords: Behçet's syndrome, complications, Epidemiology, HLA-B27, Panuveitis, retrospective study, Uveitis, Yemen.

INTRODUCTION

Uveitis is a disease that threatens to inflame the vision within the eye of the uvea tissue with or without injury to the following tissues such as the retina, optic nerve, and sclera. Uveitis might be caused by an infectious or non-infectious etiology plus a variety of systemic diseases. Severe vision loss can occur, if uveitis is not treated in time, which is why uveitis is expected to be the cause of 5-10% of visual impairment or blindness worldwide[1-3]. In developed countries, up to 20% of officially registered cases of blindness can be attributed to complications of uveitis[1,4,5]. The socio-economic problem of the disease is significant since uveitis mainly involves patients of operating age (20-50 years)[4,5]. The prevalence and pattern of uveitis varies with gender, age, genetic factors, and ethnicity, plus ecological factors and the center of the study (private

clinics or university centers). There are no reports regarding uveitis patterns in Yemen, although there are other recent studies on eye problems and eye diseases in Yemen[6-13]. This is the first study to well define the uveitis etiology and epidemiology in Sana'a, Yemen. Knowing the clinical and demographic patterns of uveitis in different geographical areas will avoid unnecessary, wasteful of valuable and limited resources.

There are many clinical types of uveitis dependent on the site of infection, extent of association, inflammation pathological pattern, and etiologies. Various causative agents that cause uveitis have been recognized. Internal causes, together infectious and non-infectious, are very widespread. Infectious causes include fungal, bacterial, parasitic, viral, and other infections. Infectious and autoimmune-mediated uveitis causes may differ in different populations[14]. Widespread types of autoimmune uveitis include Behçet's disease, Vogt-Koyanagi Harada (VKH) syndrome and sarcoidosis. Infectious causes may contrast mostly depending on environmental factors. VKH is prevalent among pigmented races for instance African Americans, Orientals, Africans, Hispanics and Middle Easterners. The VKH prevalence is estimated to be high among the Saudi population. Behçet's disease is particularly widespread in Mediterranean countries and Far Eastern countries, and is more common between 30° and 40°N latitudes in European populations and Asian populations[1,3,15]. It is known that the disease is more prevalent in Turkey and Japan. In Saudi Arabia, a large number of patients suffer from Behçet's disease, as well as ocular toxoplasmosis and tuberculosis had uveitis. While the rate of these diseases decrease in Western European countries. The prevalence of tuberculous uveitis has decreased over the past two decades in the United States with one report describing a prevalence of tuberculous uveitis of 0.2% in a group of 445 patients in a Southern California clinic[16]. In a report from UK that integrated 368 patients, tuberculous uveitis was not identified[1,17]. Histoplasmosis and Toxocariasis are estimated to be less common as a result of the very low humidity in this part of Asia including Yemen as well as the scarcity of indoor pets. Chavis *et al.*, obtained a comprehensive picture of the Middle East in 1992[18]. The authors studied in this report, 282 uveitis cases and identification of widespread causes of uveitis. These causes were Behçet's disease, Vogt-Koyanagi Harada syndrome, idiopathic vasculitis, panuveitis, idiopathic intermediate and toxoplasmosis. This report also illustrated a comparatively high incidence of ocular tuberculosis compared to the Western countries[18]. Sequentially the study was conducted to assist in the development and design of preventive policies and diagnostic methods for uveitis in Yemen.

SUBJECTS AND METHODS

This cross-sectional, retrospective analysis integrated 65 uveitis patients who were referred to the Eye Consulting Center clinic, from January 2021 to the end of December 2021. Data regarding patient age, sex, and anatomical location of disease, pathological and clinical manifestations were collected then evaluated. After careful history taking, patients assumed of having uveitis received comprehensive eye inspections, considerable physical assessments, and laboratory tests for autoimmune markers, genetic markers as HLA-B27, infectious, inflammatory, or systemic etiology.

Based on defined standard criteria, the systemic diseases were diagnosis. The subsequent laboratory tests designed to examine the eye, associations of systemic symptoms and most potential differences were performed: complete blood picture and count, erythrocyte sedimentation rate (ESR), C-reactive protein level, venereal disease research laboratory test (VDRL), urinalysis, ELISA antibodies IgM for cytomegalovirus uveitis and herpes, chest x-ray (CXR) or high-resolution computerized tomography (CT) scan of the chest for TB and sarcoidosis. Also for TB sputum smear, culture, and tuberculin skin were done. For autoimmune diseases and genetic disorder antineutrophil cytoplasmic antibody testing, antinuclear antibody testing, angiotensin-converting enzyme level, and human leukocyte antigen (HLA) typing were done. In Behçet's disease, it is known that there is no specific pathological test or technique existing to diagnose the disease, even though the criteria of the international study group for the disease are very sensitive and specific, and include clinical criteria and the pathergy test[19].

It is known that Behçet's disease has a high degree of similarity with diseases that cause muco-cutaneous lesions such as herpes simplex labialis, and consequently the diagnosis was made by maintaining clinical suspicion until all ordinary causes of oral lesions were excluded from the differential diagnosis. The diagnosis of infectious uveitis was based on typical clinical findings (for most cases of cytomegalovirus (CMV) retinitis, toxoplasmosis and herpes simplex virus [HSV] uveitis). Seroconfirmation of these infections was also done by, in addition to toxoplasmosis, and leishmaniasis using ELISA. In conditions where the etiology cannot be determined through the above stated actions, the disorder is considered idiopathic, and incomplete features and uveitis due to trauma or surgery were excluded.

Uveitis classification: Based on the criteria of the Uveitis Nomenclature Working Group, the anatomic site was classified into four groups:

1. Anterior (the anterior chamber is the primary site of inflammation).
2. Intermediate (the major site of inflammation is the vitreous cavity).
3. Posterior uveitis (intraocular inflammation primarily involving the retina and/or choroid).
4. Panuveitis (diffuse inflammation without a predominant site of involvement)[20].

Ethics considerations: Following a commitment to the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee of Sana'a University.

Statistical analysis: Using the statistical software Epi Info version 6 (CDC, Atlanta, USA) data analysis was performed. The quantitative data were expressed as

mean values, standard deviation (SD), when the data were normally distributed. Qualitative data were also expressed as percentages.

RESULTS

The results of the study are illustrated in Table 1 to Table 4. Mean patient age at the onset of uveitis was 36.3±13.4 (range: 9-75) years. The ratio of females to males was 2.6: 1. Sixty-seven percent had bilateral involvement.

Table 1: Sex and age distribution of uveitis patients.

Characters	Number (%)
Sex	
Male	18(27.7)
Female	47(72.3)
Age groups	
≤ 20 years	5(7.7)
21-30 years	21(32.3)
31-40 years	18(27.7)
41- 50 years	13(20)
≥51 years	8(12.3)
Total	65(100)
Mean age	36.3 years
SD	13.4 years
Median	34 years
Mode	50 years
Min	9 years
Max	75 years

The predominant type was Pan-uveitis (46.2%), anterior acute uveitis (36.9%), intermediate acute uveitis (12.3%) while posterior acute uveitis was less common (4.6%). Considering medical conditions, 53.8% of the patients were suffering from acute uveitis and 46.2% with chronic uveitis.

Table 2: Distribution of different type of uveitis, medical conditions and laterality of infected eye.

Type of uveitis	Number (%)
Anterior acute uveitis	24(36.9)
Intermediate acute uveitis	8(12.3)
Posterior acute uveitis	3(4.6)
Panuveitis	30(46.2)
Total	65(100)
Medical conditions	
Acute uveitis	35(53.8)
Chronic uveitis	30(46.2)
Laterality	
Unilateral	25(38.5)
Bilateral	40(61.5)

Laterality, 38.5% had unilateral while most o the patients had bilateral uveitis. Also 53.8% of the patients developed complications. Considering possible causes, the most common diagnoses were "idiopathic" (32.3%), HLA-B27 positive (21.5%), Behçet's syndrome (13.8%), Granulomatous uveitis (TB) (9.2%), Seronegative spondyloarthropathy (6.2%), Fuchs' uveitis (6.2%), followed by less common as Vogt-Koyanagi-Harada (4.6%), Herpetic uveitis (3.1%), and Toxoplasmosis (3.1%).

DISCUSSION

In the present study, the mean of patient ages at onset of uveitis was 36.3±13.4 (range: 9-75) years, females were 2.6 times more expected to have uveitis than males, and panuveitis was the majority common type of uveitis (46.2%). These results confirmed that uveitis may involve people of different ages but that young adults are further commonly affected by uveitis, which imposing a massive economic influence on persons plus society. The mean age and sex ratio of uveitis patients in the current study is in harmony with other studies in which most young adults and females are more expected to be affected[1,2,21-29]. The most common type of uveitis in the current study was panuveitis (46.2%), conclusion panuveitis as the majority common type of uveitis is reliable with the results of studies by Hosseini *et al*., Islam and Tabbara, Merrille, Gregoire, and Al Dhahri[1,2,30-32]. However, the majority of studies discovered that anterior uveitis is the most prevalent uveitis,[25,33-37] while Wakabayashi[38] and Al-Shakarchi[39] accounted posterior uveitis as the predominant type.

Table 3: Diagnostic etiologies of uveitis among patient group.

Uveitis entity	Number (%)
Idiopathic	21(32.3)
Behçet syndrome	9(13.8)
Seronegative spondyloarthropathy	4(6.2)
HLA-B27 positive	14(21.5)
Fuchs uveitis	4(6.2)
Granulomatous uveitis (TB)	6(9.2)
Vogt-Koyanagi-Harada (VKH)	3(4.6)
Herpetic uveitis	2(3.1)
Toxoplasmosis	2(3.1)
Total	65(100)

Many of the current research, including this research, has a high rate of undiagnosed cases (idiopathic= 32.3%), despite the developments in different diagnostic methods globally, which must reduce the number of cases of unknown cause (idiopathic). Therefore, a patient history, review of systems, and a careful physical examination are useful in choice and minimizing diagnostic tests for this group. Regardless of international efforts to standardize the international given name system for uveitis and its diagnostic tests, ophthalmologists have not up till now come to a consensus on this issue.

Table 4: Ocular complications in uveitis patient.

Ocular complications	Number (%)
Cataract formation	27 (41.5)
Cataract formation + secondary glaucoma	8 (12.3)
Total complication	35 (53.8)
No complication	30 (46.2)
Total	65 (100)

For example, there were significant contradictions concerning the diagnostic tests using in a recent study

by uveitis professionals, underscoring the requirement for evidence-based guidelines[40]. In the present study, there were 9 different causes of uveitis. The most common was idiopathic cases (32.3%), followed by HLA-B27-positive (21.5%), Behçet's syndrome (13.8%), and Granulomatous uveitis (TB) (9.2%). Behçet's disease (13.8%) was the most common systemic disease. In a study performed by Soheilian *et al.*,[21] in Iran, 45.5% of uveitis cases were idiopathic, with Behçet's disease, Fuchs uveitis, Eale's disease and Toxocariasis being the most prevalent causes of uveitis[26]. An Iranian study by Hosseini *et al.*,[1] the most common diagnoses were 'idiopathic' in anterior and intermediate uveitis, toxoplasmosis in the posterior uveitis group, and Behçet's and Vogt Koyanagi Harada's diseases in panuveitis. Also, obtained results are similar to that done by Kianersi in Iran which indicated that 35.5% of uveitis cases were idiopathic, and Behçet's disease and Fuchs' uveitis were the main known causes[41]. In a study by Khairallah *et al.*, in France, Behçet's syndrome, toxoplasmosis and VKH were the most common causes of posterior uveitis and panuveitis[42]. Behçet's disease was reported to be the main known cause of uveitis in a Turkish study by Sengun *et al.*,[35] in which 28.3% of patients developed idiopathic uveitis. In the current study, HLA-B27-positive ankylosing spondylitis was elevated (21.5%), and this result is similar to that reported by Cimeno's[36] and Guney's[43] studies in which HLA B27-associated uveitis was a major cause of anterior uveitis[43]. Anterior uveitis, is the second type in current study in compare to previous studies in which anterior uveitis is the most common type of uveitis[26,30-32] and is usually treated by ophthalmologists in the clinic and most cases are not referred to tertiary center. This type of uveitis can happen again or expand to more posterior parts of the eye, warranting referral. Consequently, these cases have a lower prevalence in studies conducted in centers of higher education.

In the present study, toxoplasmosis cases constituted a small portion of cases (3.1%) compared to tuberculosis (9.2%), which was more prevalent and this reflects the high prevalence of this infection in Yemen[44,45]. These differences may be due to genuine differences in their epidemiology or, since most toxoplasmosis cases are certainly diagnosed by eye examination and initiation of treatment, patients are less likely to be referred to tertiary referral centers. Despite the high prevalence of infectious and non-infectious causes of uveitis in Yemen such as brucellosis[46-49], leptospirosis[50], kala-azar[51], cytomegalovirus[52,53], celiac disease[54,55]. There were no cases diagnosed with the previously mentioned infectious and autoimmune disorders. This may be because appropriate laboratory tests normally used to diagnose certain underlying diseases, including rheumatic tests (such as antinuclear antibody and rheumatoid factor) and serology for infectious diseases such as syphilis, toxoplasmosis, brucellosis and leptospirosis were not used by clinicians and together with some of the cases in the current study. Based on the results of the present study and further epidemiological studies of uveitis, a specific screening for uveitis should be designed based on a exhaustive history and comprehensive eye examination. Para-clinical tests should be limited to the most likely differential diagnoses provided by careful examination.

CONCLUSIONS

In conclusion, ocular imaging can be of value in reduction differential diagnoses, particularly in posterior intervention. The major limits of this study are the retrospective design and hospital construction for the study, where it cannot express the status of the disease among the entire population. The study duration was short. Some diagnoses may change during follow-up, and some cases of idiopathic uveitis may get a specific diagnosis. Finally, in contrast to most epidemiological studies of uveitis, clinical phenotypes of uveitis differ in the clinic of the Eye Consultation Center and Referral Center tertiary in Sana'a, Yemen, where panuveitis was the most common clinical phenotype in this study. The most common systemic disease was Behçet's disease. More future studies are required.

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AUTHOR'S CONTRIBUTION

Al-Shamahi EY: clinical examinations, writing original draft. **Muhsin NM:** methodology, data interpretation. **Al-Shamahi EH:** investigation, conceptualization. **Al-Shamahy HA:** critical review, supervision. The final manuscript was read and approved by all authors.

DATA AVAILABILITY

The datasets generated during this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

There is no conflict of interest associated with this study.

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