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Supplemental Issue: Spectrum of Uveitis in Asia Pacific

ORIGINAL ARTICLE

Epidemiology of Uveitis in a Tertiary Eye Center in Myanmar

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ABSTRACT

Purpose: To identify the characteristics of uveitis in a tertiary eye center in Myanmar.

Methods: A retrospective study was undertaken to obtain the characteristics of uveitis in a tertiary eye center in Myanmar from September 2013 to September 2014, using a standard clinical protocol and tailored laboratory investigations.

Results: A total of 139 patients were included in this epidemiologic study; 71 (51.1%) men and 68 (48.9%) women. The mean age of onset was 36.3 ± 15.5 years. Infectious uveitis constituted 76/139 (54.7%) cases and non-infectious etiologies accounted for 63/139 (45.3%) cases. The most common non-infectious etiologies were idiopathic, followed by HLA-B27-associated anterior uveitis and multifocal choroiditis with panuveitis, while tuberculosis was the most common infectious etiology.

Conclusions: Tuberculosis was the most frequent cause of uveitis among the infectious group of patients in this tertiary eye center as a result of endemic disease in Myanmar.

Keywords: Epidemiology, idiopathic, Myanmar, tuberculosis, uveitis

Uveitis is a general term describing a group of intraocular inflammatory diseases[1] and a major problem of severe visual deterioration globally,[2,3] including in Myanmar. The definitive diagnosis of uveitis remains challenging, as some patients present with confusing ocular and systemic signs and symptoms.[1] Uveitis can occur due to a variety of infectious and non-infectious causes. Although thorough laboratory investigations are used to determine the cause of uveitis, the number of idiopathic uveitis patients is increasing.[4] The etiology of the disease varies according to genetic, ethnic, geographic, and socioeconomic conditions,[1,5,6] for instance, infectious diseases such as tuberculosis are common in India and developing countries, whereas idiopathic uveitis and seronegative spondyloarthropathy are leading causes in developed countries.[1,7,8] The authors of this article aimed to determine the main causes of intraocular infection and inflammation in the Yangon Eye Hospital, Myanmar.

MATERIALS AND METHODS

A total of 139 consecutive patients were analyzed thoroughly in this retrospective study, which was conducted by the uveitis service at the Yangon Eye Hospital/Department of Ophthalmology, University of Medicine (1), Yangon, Myanmar, from September 2013 to September 2014. The institution review board approved data collection and the study complied with the tenets of the Declaration of Helsinki.

A standard clinical proforma, which included a standardized clinical history, systemic review, complete ophthalmic examination, tailored laboratory investigations and ancillary tests such as ultrasonography, fundus fluorescein angiography, and optical coherence tomography, were used to collect data in all cases. Cases of uveitis were classified according to the Standardization of Uveitis Nomenclature (SUN) criteria[9] on the basis of the primary anatomic site of inflammation, namely

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anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis. The onset of uveitis was identified as sudden or insidious, and the duration of uveitis was classified as limited (<3 months' duration) or persistent (>3 months' duration). The course of the uveitis was described as acute (sudden onset and limited duration); recurrent (repeated episodes separated by periods of inactivity without medication for >3 months); and chronic (persistent uveitis with relapse in <3 months without medication). Uveitis was morphologically identified as granulomatous when large, mutton-fat keratic precipitates, Koeppe and/or Bussaca nodules on the iris, and/or choroidal and optic disc granulomas were identified.[10] Assessment of a patient began with a detailed questionnaire form; including information on the current history, thorough review of organ systems, family history, exposure to pets, occupation, social and travel history, followed by detailed eye examination and laboratory investigations. A short differential diagnosis was achieved by the method of exclusion. Investigations for infectious causes included: the Mantoux test; QuantiFERON-TB Gold test; Venereal Disease Research Laboratory (VDRL) test; *Treponema pallidum* hemagglutination (TPHA) test; toxoplasma and *Toxocara* antibodies testing; *Bartonella* antibody test; human immunodeficiency virus (HIV) antibody test; and viral antibodies testing. Investigations for non-infectious causes included testing for autoantibodies such as antinuclear activity (ANA), rheumatoid factor, anti-ds-DNA, c-ANCA, p-ANCA, HLA-B27, and level of serum angiotensin-converting enzyme (ACE). Radiologic investigations included: chest X-ray; computed tomography (CT) for chest or brain; brain magnetic resonance imaging (MRI); sacroiliac joints and knee joints X-rays. Some invasive procedures such as aqueous and vitreous tap for cytologic examination and polymerase chain reaction (PCR) were performed whenever necessary. Consultation with an internist, rheumatologist, pulmonologist, or neurologist was sought whenever required. Other diagnostic tests, such as fluorescein angiography, visual field testing and ocular ultrasonography examinations were undertaken as needed.

The diagnosis of specific uveitis diseases was made according to international criteria. Vogt–Koyanagi–Harada (VKH) was diagnosed according to the revised diagnostic criteria for VKH disease.[11] Ocular toxoplasmosis was diagnosed in patients who had typical localized retinochoroiditis with positive toxoplasma antibody test results. Diagnosis of ocular toxocariasis was made in the presence of identifiable *Toxocara* granuloma with inflammation and vitreous bands or tractional retinal detachment with positive *Toxocara* antibody test results.[12] Diagnosis of acute retinal necrosis was made according to the standard diagnostic criteria for acute retinal necrosis syndrome.[13] Herpetic anterior uveitis was diagnosed in patients with suggestive clinical signs, such as herpetic keratitis, reduced corneal sensation, sectoral iris atrophy, and raised intraocular pressure.[14] Ocular tuberculosis diagnosis was based on positive Mantoux or QuantiFERON-TB Gold test results with or without positive chest radiography and positive response to anti-tuberculosis drugs at the end of follow-up.[15] Other systemic and ocular diseases were diagnosed according to current guidelines. Cases were identified as idiopathic when a specific diagnosis, in terms of ocular or systemic disease, could not be identified. For statistical analyses, data were collected using a standard proforma. Data entry, data clean-up, data summarization and data analyses were carried out by computer, using the Statistical Package for the Social Sciences (SPSS software, version 16.0 for Windows). Descriptive and summary statistics were carried out. Frequency and percentage were calculated for the categorical data, whereas means and standard deviations (SD) were calculated for the continuous variables.

RESULTS

In total, 139 patients fulfilled the selection criteria and were analyzed systematically. Ethnically, the majority of patients were from Myanmar 122 (87.8%), followed by Chinese 10 (7.2%) and Indian 7 (5%). Table 1 describes the demographic and clinical characteristics of patients on presentation. There were 7 (51.1%) male and 68 (48.9%) female patients, with a mean age of 36.3 ± 15.5 years at the onset of uveitis. The youngest age of onset was 1 year and the oldest was 67 years.

In terms of laterality, unilateral disease was frequently found in anterior uveitis, whereas bilateral involvement was more common in posterior uveitis and panuveitis. Regarding the course of uveitis, chronic uveitis was seen most often 89/139 (64%) followed by acute uveitis 25/139 (18%) and recurrent uveitis 25/139 (18%). Non-granulomatous uveitis occurred more frequently 71/139 (51%) than granulomatous uveitis 68/139 (49%).

Table 2 demonstrates the etiology of uveitis based on anatomic areas. Among the 139 patients, anterior uveitis was the most common presentation in 63/139 (45.3%) cases, followed by posterior uveitis 33/139 (23.7%), panuveitis 29/139 (20.9%), and intermediate uveitis 14/139 (10.1%). Infectious uveitis constituted 76/139 (54.7%) cases and non-infectious uveitis etiologies accounted for 63/139 (45.3%) cases. The etiology of uveitis was identified in 91/139 (65.5%) of the patients. Among non-infectious cases, idiopathic uveitis was the most common form in 48/63 (76.2%) cases, followed by HLA-B27-positive anterior uveitis and multifocal choroiditis with panuveitis. On the other hand, the most common infectious forms of uveitis in this study were tuberculosis in 45/76 (59.2%) cases, followed by uveitis due to HIV 6/76 (7.9%) cases, and endophthalmitis 6/76 (7.9%) cases.

TABLE 1. Demographic and general characteristics of 139 uveitis patients in dependence of anatomic involvement in a tertiary eye center in Myanmar.

Characteristics	Total (n = 139)		Anterior uveitis (n = 63)		Intermediate uveitis (n = 14)		Posterior uveitis (n = 33)		Panuveitis (n = 29)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Age at onset (years) (mean ± SD)	36.3 ± 15.5	37.2 ± 16.6	37.8 ± 14.7	35.8 ± 14.8	33.5 ± 14.3					
0–10	9	6.5	1	1.6	–		3	9.1	5	17.2
11–20	12	8.6	5	7.9	–		2	6.1	5	17.2
21–30	33	23.7	14	22.2	7	50	7	21.2	5	17.2
31–40	30	21.6	14	22.2	1	7.1	8	24.2	7	24.1
41–50	29	20.9	13	20.6	2	14.3	9	27.3	5	17.2
51–60	20	14.4	13	20.6	3	21.4	3	21.4	1	3.4
>60	6	4.3	3	4.8	1	7.1	1	3	1	3.4
Gender										
Male	71	51.1	28	44.4	11	78.6	18	54.5	14	48.3
Female	68	48.9	35	55.6	3	21.4	15	45.5	15	51.7
Laterality										
Unilateral	79	56.8	44	71.6	7	50	14	42.42	14	48.3
Bilateral	60	43.2	19	28.4	7	50	19	57.58	15	51.7
Onset of uveitis										
Sudden	53	38.1	39	61.9	2	14.3	3	9.1	9	31
Insidious	86	61.9	24	38.1	12	85.7	30	90.9	20	69
Duration of current episode										
Limited (<3 months)	41	29.5	35	55.6	–		–		6	20.7
Persistent (>3 months)	98	70.5	28	44.4	14	100	33	100	23	79.3
Course of uveitis										
Acute	25	18	19	30.2	–		–		6	20.7
Recurrent	25	18	22	34.9	–		2	6	1	3.4
Chronic	89	64	22	34.9	14	100	31	93.9	22	75.8
Type of inflammation										
Granulomatous	68	49	36	57.1	3	21.4	7	21.2	22	75.9
Non-granulomatous	71	51	27	42.9	11	78.6	26	78.8	7	24.1

SD, standard deviation.

TABLE 2. Etiological classification of anterior, intermediate, posterior, and panuveitis in patients attending a tertiary eye center in Myanmar.

Etiology	Total (n = 139)		Anterior (n = 63)		Intermediate (n = 14)		Posterior (n = 33)		Panuveitis (n = 29)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Idiopathic	48	34.5	32	50.8	6	42.9	7	21.2	3	10.3
PSS	1	0.7	1	1.6	–		–		–	
FHI	1	0.7	1	1.6	–		–		–	
HSV keratouveitis	3	2.2	3	4.7	–		–		–	
HZV keratouveitis	1	0.7	1	1.6	–		–		–	
CMV retinitis	5	3.6	1	1.6	–		4	12.1	–	
TB uveitis	45	32.4	12	19	8	57.1	13	39.4	12	41.4
Syphilis	4	2.9	2	3.2	–		1	3	1	3.4
Toxoplasmosis	4	2.9	–		–		4	12.1	–	
Endogenous endophthalmitis	6	4.3	–		–		–		6	20.7
HLA-B27-associated anterior uveitis	5	3.6	5	8	–		–		–	
VKH	2	1.4	–		–		–		2	6.9
SLE	2	1.4	1	1.6	–		1	3	–	
HIV	6	4.3	4	6.3	–		1	3	1	3.4
Multifocal choroiditis with panuveitis	4	2.9	–		–		–		4	13.8
Bartonellosis	1	0.7	–		–		1	3	–	
Toxocariasis	1	0.7	–		–		1	3	–	

PSS, Posner–Schlossman syndrome; FHI, Fuchs heterochromic iridocyclitis; HSV, *Herpes simplex* virus; HZV, *Herpes zoster* virus; CMV, cytomegalovirus; TB, tuberculosis; HLA, human leukocyte antigen; VKH, Vogt–Koyanagi–Harada syndrome; SLE, systemic lupus erythematosis; HIV, human immunodeficiency virus.

Among patients presenting with all forms of uveitis, idiopathic causes were found to be most commonly associated with anterior uveitis in 48/139 (34.5%) cases. Of these 48 idiopathic cases, 32/48 (66.7%) were anterior; 7/48 (14.6%) posterior; 6/48 (12.5%) intermediate; and 3/48 (6.2%) panuveitis. There were 63/139 (45.3%) anterior uveitis cases. The most common cause was idiopathic, 32/63 (50.8%); followed by tuberculosis 12/63 (19%); HLA-B 27-positive anterior uveitis 5/63 (8%); anterior uveitis due to HIV 4/63 (6.3%); *Herpes simplex* keratouveitis 3/63 (4.7%); and syphilitic anterior uveitis 2/63 (3.2%). There were five single cases of Posner–Schlossman syndrome, Fuchs uveitis, *Herpes zoster*-associated keratouveitis, cytomegalovirus-induced anterior uveitis, and systemic lupus erythematosis-associated anterior uveitis representing 1/63 (1.6%) patients in each case. All cases of the Herpes virus group-associated anterior uveitis had an anterior chamber tap (PCR for HSV, HZV, and CMV) and three had a positive result for HSV; one was positive for HZV; and another one had a positive result for CMV. Among HLA-B27-positive anterior uveitis, one case was associated with ankylosing spondylitis.

In intermediate uveitis, specific diagnosis was established in 8/14 (57.1%) patients, of which all were tuberculosis-associated uveitis. No specific cause was found in the remaining 6/14 (42.9%) intermediate uveitis cases.

Among patients presenting with posterior uveitis, tuberculosis was the most common diagnosis, 13/33 (39.4%); followed by idiopathic uveitis 7/33 (21.2%); CMV retinitis 4/33 (12.1%); and toxoplasma retinitis 4/33 (12.1%). Other causes of posterior uveitis were syphilis, SLE, HIV, bartonellosis, and toxocariasis with 1/33 (3%) each.

In panuveitis patients, the most common etiology was tuberculosis 12/29 (41.4%) followed by endogenous endophthalmitis 6/29 (20.7%) and multifocal choroiditis with panuveitis 4/29 (13.8%). Vogt–Koyanagi–Harada syndrome was seen in 2/29 (6.9%) cases and syphilis and HIV-induced panuveitis were identified with 1/29 (3.4%) each. There were 3/29 (10.3%) idiopathic panuveitis cases.

DISCUSSION

This study provides detailed information about the epidemiology of uveitis in a tertiary eye center in Myanmar. In our uveitis study, the results compare well with other reported uveitis epidemiology studies in Asia and worldwide, where men and women were almost equally affected and the most common age group on presentation was the second and third decade.[4] The mean age of onset in our study was 36.3 ± 15.5 years (see Table 1). This figure was similar to a previous study, which found the mean age of onset to be between 30 and 40 years.[16] In contrast, in the two studies by Grajewski et al.[4] and Achrya et al.,[17] the mean age of onset was 45 years.

The population in the study under discussion had a fairly homogenous background as many patients were Myanmar and came from different regions of Myanmar. Etiology could be identified in 91/139

TABLE 3. Etiologies of uveitis according to age at onset in a tertiary eye center in Myanmar.

Etiology	Total (n = 139)		Age (years)					
			≤16 (n = 12)		17–60 (n = 121)		>60 (n = 6)	
	n	(%)	n	(%)	n	(%)	n	(%)
Idiopathic	48	34.5	5	41.7	40	33.1	3	50.0
PSS	1	0.7	–		1	0.8	–	
FHI	1	0.7	–		1	0.8	–	
HSV keratouveitis	3	2.2	–		3	2.5	–	
HZV keratouveitis	3	0.7	–		1	0.8	–	
CMV retinitis	5	3.6	1	8.3	4	3.3	–	
TB uveitis	45	32.4	–		44	36.4	1	16.7
Syphilis	4	2.9	–		3	2.5	1	16.7
Toxoplasmosis	4	2.9	3	25	1	0.8	–	
Endogenous endophthalmitis	6	4.3	1	8.3	4	3.3	1	16.7
HLA-B27-associated anterior uveitis	5	3.6	–		5	4.1	–	
VKH	2	1.4	–		2	1.7	–	
SLE	2	1.4	1	8.3	1	0.8	–	
HIV	6	4.3	–		6	5.0	–	
Multifocal choroiditis with panuveitis	4	2.9	1	8.3	3	2.5	–	
Cat-scratch	1	0.7	–		1	0.8	–	
Toxocariasis	1	0.7	–		1	0.8	–	

PSS, Posner–Schlossman syndrome; FHI, Fuchs heterochromic iridocyclitis; HSV, *Herpes simplex* virus; HZV, *Herpes zoster* virus; CMV, cytomegalovirus; TB, tuberculosis; HLA, human leukocyte antigen; VKH, Vogt– Koyanagi–Harada syndrome; SLE, systemic lupus erythematosis; HIV, human immunodeficiency virus.

(65.5%) patients and no etiology could be established in the remaining 48/139 (34.5%). There were fewer idiopathic cases in our study compared with studies by Biswas et al.[18] and Singh et al.[1]

Anterior uveitis, 63/139 (45.3%), was the most common type of uveitis in our study. The second most common type of uveitis was posterior uveitis, 33/139 (23.7%), followed by panuveitis, 29/139 (20.9%), and intermediate uveitis, 14/139 (10.1%). Although the frequencies of intermediate, posterior, and panuveitis vary between different studies, anterior uveitis has been identified as the most frequent form.[1,8,19,20] However, in the two studies by Oruc et al.[21] and Henderly et al.[22] posterior uveitis was found to be the most common form of uveitis.

The most common non-infective etiology of anterior uveitis was HLA-B27-associated anterior uveitis 5/63 (8%), which was lower than reported in a study by Grajewski et al.[4] Among the infective etiologies of anterior uveitis, tuberculosis was the most common cause, accounting for 12/63 (19%) cases. A similar incidence was identified in North India.[1]

The result for intermediate uveitis in our study showed a high proportion of tuberculosis-associated uveitis, 8/14 (57.1%), and a relatively low frequency of idiopathic uveitis, 6/14 (42.9%), although idiopathic uveitis has been reported as the most common cause of intermediate uveitis in different studies.[1,4]

According to some studies, toxoplasmosis was the predominant form of posterior uveitis.[23–25] However, in our study, tuberculosis was the most common specific diagnosis of posterior uveitis, with 13/33 (39.4%). The proportion of toxoplasmosis cases, 4/33 (12.1%), was lower than in previous reports.[4,18,20,22,26] Cytomegalovirus (CMV) retinitis with underlying human immunodeficiency virus (HIV) accounted for 4/33 (12.1%) of posterior uveitis patients.

Among panuveitis patients, tuberculosis was the most frequent form, with 12/29 (41.4%). This was significantly higher than in previous studies by Singh et al. (26%),[1] Biswas et al. (2.16%),[18] Rodriguez et al. (2%),[20] and Mercanti et al. (5.8%).[26] Endogenous endophthalmitis was the second most common specific cause of panuveitis 6/29 (20.7%). This finding was also different from other studies by Singh et al.[1] Biswas et al.[18] and Henderly et al.,[22] where Vogt–Koyanagi–Harada syndrome (VKH) was the second most common etiology of panuveitis.

In this study, tuberculosis, affecting 45/139 (32.4%) cases, was the most common etiology in all anatomic forms of uveitis, especially in posterior uveitis cases. While this rate was high in comparison with most other studies, it was higher than reported in a study in North India, which showed tuberculosis and toxoplasmosis to be the most common forms of infectious uveitis.[1] There may be some limitations in making comparisons with other studies because of different genetic, ethnic, geographic, and environmental factors, as well as different lifestyles.

Anterior and posterior uveitis associated with rheumatoid arthritis and sympathetic ophthalmia were also identified, although these patients withdrew from our study and were not included. Although CMV retinitis was common in our region, not all CMV retinitis patients with underlying HIV infection were referred to our tertiary eye center, as many non-governmental organization clinics in our country were treating them with intravitreal ganciclovir injections.

In conclusion, our study found that anterior uveitis is the most common form of uveitis, which is compatible with the literature. Among cases of infectious uveitis, tuberculosis is the most frequent etiology, which may be due to Myanmar being one of several tuberculous-endemic countries globally. According to a 2011 WHO report, Myanmar is listed, along with 22 other high tuberculosis burdened countries in the world, with an estimated 180 000 new tuberculosis cases occurring in Myanmar at 2010.[27] The limitations of our study include referral bias, since the data were collected from a single tertiary eye center. Despite the limitations of our study, our results convey the general patterns of uveitis in Myanmar. Further study is warranted to establish the epidemiology of other important diseases, such as sarcoidosis, Behçet disease and juvenile idiopathic arthritis (JIA)-associated uveitis, which were not found in this study, in order to address the clinical features, complications, and management of uveitis in this tertiary eye center

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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