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ORIGINAL RESEARCH

Prevalence and Risk Factors for Ocular Complications in New-Onset Uveitis: A Study From a Tertiary Referral Center in Northern Thailand

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Purpose: To determine the prevalence and identify risk factors of ocular complications in patients with uveitis.

Methods: This retrospective study reviewed of 340 consecutive patients with a first episode of active uveitis from January 2015 to December 2019. Demographic and clinical data, including ocular complications were analyzed.

Results: The mean age of the cohort was 47 years. Among them, 75 patients were HIV-positive (74% male), and 265 were HIV-negative (53% male). An Infectious etiology was identified in 52% of cases. Ocular complications, developed in 151 patients (44%), with their type strongly correlate to the anatomical location of uveitis. Multivariate analysis revealed chronic inflammation (risk ratio [RR]=18.9; 95% confidence interval [CI] 6.1–58.8), recurrent inflammation (RR=20.4; 95%; CI 6.5–64.3), and poor visual acuity (VA) at presentation (RR=3.6; 95% CI 1.4–9.2) as significant risk factors for complications.

Conclusion: Nearly half of the patients with uveitis developed ocular complications, highlighting the importance of identifying risk factors. Understanding the relationship between the location of inflammation and specific complication patterns is essential for early detection and targeted prevention strategies.

Keywords: uveitis, ocular complication, risk factors, blindness, Thailand

Introduction

Uveitis is a leading cause of multiple ocular complications associated with temporary and permanent visual loss, and approximately 10–15% of preventable blindness is due to this ocular disorder.[1,2] Numerous ocular complications related to uveitis have been reported; some are reversible, while others result in permanent vision loss. The most commonly reported complications of uveitis included cataract, macular edema, and glaucoma.[3–8] The complications of uveitis are heterogeneous and challenging to categorize, with previous reports offering varying definitions. Our study focused specifically on complications that lead to visual loss, whether reversible or irreversible.

Previous studies, mainly from the US and Europe showed that a significant proportion of uveitis patients developed at least one ocular complication, though the reported prevalence varied from 29.5% to 46% across studies.[3–6] The prevalence of complications is associated with the causes of uveitis, which vary by geographic location depending on genetic and environmental factors. Access to medical care and types of medical treatment are also of significant influence. Most previous studies investigated the risk factors for the development of ocular complications in specific subtypes of uveitis (for example, a high prevalence of complications was found in juvenile idiopathic uveitis, sympathetic ophthalmia, and acute retinal necrosis in contrast to human leucocyte antigen [HLA] B27-associated uveitis).

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However, the prevalence of complications in the uveitis population in its totality was not frequently studied.[9–11] Previously identified risk factors for complications included age above 65 years, intermediate uveitis, topical steroid use, and chronic course.[5,10,11]

Few studies in Asia have assessed the prevalence and predictors of complication of uveitis. Early identification of ocular complications is crucial for timely treatment, which helps retain visual function. Our study aims to assess the prevalence and risk factors associated with ocular complications in patients with uveitis in Northern Thailand.

Materials and Methods

Consecutive patients presenting with new-onset uveitis to the Department of Ophthalmology at Chiang Mai University hospital, Thailand from January 2015 to December 2019 were included and retrospectively reviewed. Patients were excluded if they had ocular complications at baseline including cataracts, prior episodes of uveitis, no perception of light (total blindness) at baseline, were younger than 18 years, had masquerade syndromes, or had a follow-up of fewer than three months. Average follow-up was 18 months.

Diagnosis of uveitis was made by the presence of inflammation according to the criteria of the Standardization of Uveitis Nomenclature Workgroup.[12] All patients underwent uveitis work-up, which included complete blood counts, urine analysis, serologic tests for HIV and syphilis. Radiologic chest examination and tuberculin skin test were also performed. In addition, HLA B27 determination was performed in all patients with anterior uveitis. The investigations were further extended according to the probability of specific diagnoses (tailored approach). They included fluorescein and indocyanine green angiography, ultrasonography, polymerase chain reaction (PCR) in patients with a suspicion of infections caused by HSV-1, HSV-2, VZV, or CMV, cytology and flow cytometry, and microbial cultures of aqueous and vitreous fluids as well as cerebrospinal fluid examinations. Chest computed tomography (CT) was performed in patients with a suspicion of tuberculosis and/ or sarcoidosis. Consultations were also performed with an internist, rheumatologist, and neurologist. Regarding the management of active uveitis, the treatment modalities were performed according to current recommended guidelines. Treatment of non-infectious uveitis was determined by the severity of inflammation using a step-up approach with topical anti-inflammatory therapy, mydriatics and/or systemic therapy with non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and/or immunosuppressive/immunomodulatory agents. This study was reviewed and approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (No: OPT-2564-07869), with a waiver for written informed consent due to its retrospective nature. This study was conducted in accordance to the Declaration of Helsinki and the patient data was maintained with confidentiality.

Demographic and ophthalmic data were collected, including age, gender, human immunodeficiency virus (HIV) infection status, laterality of ocular involvement, the site of inflammation (anterior, intermediate, posterior, panuveitis, scleritis), disease course (acute, chronic, recurrent), etiology (infectious or non-infectious), initial and final VA, duration of follow-up and ocular complications.

All uveitis-related complications were recorded as well as all cases of intraocular surgery during our follow-up. Course of uveitis (acute, recurrent and chronic) was determined according to the Standardization of Uveitis Nomenclature Workgroup.[12] Best-corrected visual acuities (BCVAs) were scored at initial visit and last follow-up using the Snellen chart.

Patients were categorized into two groups based on the development of ocular complications during follow-up. Ocular complications of uveitis encompassed band keratopathy, corneal opacity, cataract, glaucoma, hypotony maculopathy, epiretinal membrane, cystoid macular edema, retinal detachment (rhegmatogenous, tractional, exudative), macula scar, optic neuropathy, and secondary choroidal neovascularization. Temporary high ocular pressure that was resolved with no permanent damage and posterior synechiae, which do not affect VA were not registered.

Statistical Analysis

A binary assessment of ocular complications was performed. Data was expressed as mean and standard deviation (SD) for continuous variables with normal distribution, median and interquartile range (IQR) for skewed data, and proportion for categorical variables. Comparisons were performed using the Student's *t*-test (parametric) or the Mann–Whitney

U (non-parametric) test depending on the data distribution for continuous variables and the Fisher's exact test for categorical variables.

Univariate and multivariate logistic regression analyses were used to explore and identify factors associated with ocular complications of uveitis and to calculate risk ratios (RRs), and 95% confidence intervals (CIs). The logistic regression analysis was chosen for risk factor analysis to predict the likelihood of a binary outcome. The model included gender, age, HIV infection status, site of inflammation, disease course, etiology, and initial VA. P-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using Stata Statistical Package version 16.1 (StataCorp, College Station, TX, USA).

Results

Table 1 shows demographic and ophthalmic data. Our study included 196 males and 144 females (male-to-female ratio was for HIV-positive patients 2.8 and for HIV-negative patients 1.1). Most patients (52%) had an infectious cause of uveitis, including cytomegalovirus, herpes simplex type 1 and 2, varicella zoster, toxoplasmosis, toxocariasis, and tuberculosis. The infectious causes of anterior uveitis included HSV1, HSV2, VZV, CMV proved by aqueous PCR. Panuveitis (41%) was most common anatomical location. Of total, 151 patients (44%) developed at least one ocular complication.

Table 1 Demographic and Ophthalmic Data of Uveitis Patients With and Without Ocular Complications

	Total N = 340 N (%)	**Patients with Ocular Complications N = 151 N (%)**	**Patients without Ocular Complications N = 189 N (%)**	**P-value**
Gender				0.83
- Females	144 (42.4)	65 (43.0)	79 (41.8)	
- Males	196 (57.6)	86 (57.0)	110 (58.2)	
Age (years, mean ± SD)	46.8 ± 17.7	49.0 ± 17.6	44.3 ± 16.9	0.99
Laterality				0.50
- Unilateral disease	207 (60.9)	95 (62.9)	112 (59.3)	
- Bilateral disease	133 (39.1)	56 (37.1)	77 (40.7)	
HIV infection	75 (22.1)	35 (23.2)	40 (21.2)	0.69
Site				<0.001
- Anterior	108 (31.8)	33 (21.9)	75 (39.7)	
- Intermediate	32 (9.4)	5 (3.3)	27 (14.3)	
- Posterior	57 (16.8)	6 (4.0)	51 (27.0)	
- Panuveitis	140 (41.1)	107 (70.9)	33 (17.5)	
- Scleritis	3 (0.9)	0	3 (1.6)	
Course of disease				<0.001
- Acute disease	177 (52.1)	4 (2.7)	173 (91.5)	
- Chronic disease	125 (36.8)	110 (72.9)	15 (7.9)	
- Recurrent disease	38 (11.1)	37 (24.5)	1 (0.5)	

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Table 1 (Continued).

	Total N = 340 N (%)	**Patients with Ocular Complications N = 151 N (%)**	**Patients without Ocular Complications N = 189 N (%)**	**P-value**
Etiology				0.012
- Non-infectious	164 (48.2)	61 (40.4)	103 (54.5)	
- Infectious	176 (51.8)	90 (59.6)	86 (45.5)	
Initial visual acuity				
- VA ≥ 6/18	115 (33.8)	4 (2.7)	111 (58.7)	<0.001
- VA <6/18-6/60	78 (22.9)	16 (10.6)	62 (32.8)	
- VA <6/60-3/60	26 (7.6)	25 (16.6)	1 (0.5)	
- VA <3/60-1/60	29 (8.5)	25 (16.6)	4 (2.1)	
- VA <1/60-Perception to light	92 (27.1)	81 (53.6)	11 (5.8)	
- No perception to light	0	0	0	
Follow-up duration [months, median (IQR)]	17.7 (10.0–28.4)	20.1 (12.0–30.3)	15.6 (9.3–25.7)	<0.001
Ocular surgery*	91 (26.8)	91 (60.3)	0	<0.001
Final VA				
- VA ≥ 6/18	202 (59.4)	40 (26.5)	162 (85.7)	<0.001
- VA <6/18-6/60	62 (18.2)	39 (25.8)	23 (12.2)	
- VA <6/60-3/60	6 (1.8)	5 (3.3)	1 (0.5)	
- VA <3/60-1/60	2 (0.6)	2 (1.3)	0	
- VA <1/60-Perception to light	57 (16.8)	54 (35.8)	3 (1.6)	
- No perception to light	11 (3.2)	11 (7.3)	0	

Note: *Ocular surgery included laser peripheral iridotomy, phacoemulsification with or without intraocular lens implantation, pars plana vitrectomy, trabeculectomy, glaucoma drainage device.
Abbreviations: HIV, human immunodeficiency virus; IQR, interquartile range; SD, standard deviation; VA, visual acuity.

Among HIV-positive patients, 48% had posterior uveitis and 42% had panuveitis, with 84% of these cases attributed to infectious causes (53% due to CMV retinitis, 20% syphilis, 5% tuberculosis, 3% fungi, and 3% toxoplasmosis). In contrast, 18% of non-HIV patients had posterior uveitis and 31% had panuveitis, with infectious causes accounting for 26% of these cases (10% due to CMV, 5% HSV/VZV, 7% toxoplasmosis, 2% syphilis, 1% Toxocara, and 1% tuberculosis). However, neither univariate nor multivariate analyses identified HIV status as a significant risk factor. While infectious causes were more prevalent in HIV-positive patients and showed statistical significance in the univariate analysis (RR = 1.37; 95% CI, 1.08–1.76), this significance did not hold in the multivariate analysis.

Ocular complications according to the location of uveitis are shown in Table 2. In the whole series, the most common complication was cataract (29%), followed by retinal detachment (12%), macular scars (12%), and glaucoma (6%). Based on the site of uveitis, patients with panuveitis had the highest rate of ocular complications (76%), followed by anterior uveitis (31%). Cataract and glaucoma were exclusive to anterior uveitis, and none with anterior uveitis developed retinal detachment and/or macular scar. Posterior uveitis exhibited predominantly macular scars and retinal detachment, while cataract development was lower than other anatomical entities. Conversely, cataract was mostly found in panuveitis (44%), followed by anterior uveitis (26%) and intermediate uveitis (16%). Retinal detachment was mostly

Table 2 Ocular Complications in Uveitis

Complications	Number of Patients N = 340 N (%)	Anterior Uveitis N = 108 N (%)	Intermediate Uveitis N = 32 N (%)	Posterior Uveitis N = 57 N (%)	Panuveitis N = 140 N (%)	Scleritis N = 3 N (%)
At least one complication present	151 (44.4)	33 (30.6)	5 (15.6)	6 (10.5)	107 (76.4)	0
Cataract	98 (28.8%)	28 (25.9%)	5 (15.6%)	2 (3.5%)	61 (43.6%)	0
Retinal detachment	42 (12.4%)	0	0	5 (8.8%)	37 (26.4%)	0
- Rhegmatogenous	29 (8.5%)	0	0	4 (7.0%)	25 (17.9%)	0
- Tractional	4 (1.2%)	0	0	0	4 (2.9%)	0
- Exudative	9 (2.6%)	0	0	1 (1.8%)	8 (5.7%)	0
Macular scar	40 (11.8%)	0	0	6 (10.5%)	34 (24.3%)	0
Glaucoma	21 (6.2%)	12 (11.1%)	2 (6.3%)	0	7 (5.0%)	0
Epiretinal membrane	12 (3.5%)	1 (0.9%)	2 (6.3%)	1 (1.8%)	8 (5.7%)	0
Optic neuropathy	12 (3.5%)	0	0	1 (1.8%)	11 (7.9%)	0
Corneal opacification	10 (2.9%)	6 (5.6%)	0	0	4 (2.9%)	0
Cystoid macular edema	8 (2.4%)	0	1 (3.1%)	2 (3.5%)	5 (3.6%)	0
Choroidal neovascularization	3 (0.9%)	0	0	0	3 (2.1%)	0
Hypotony maculopathy	1 (0.3%)	0	0	1 (1.8%)	0	0
Band keratopathy	1 (0.3%)	0	0	0	1 (0.7%)	0

found in panuveitis (26%), followed by posterior uveitis (9%), while glaucoma developed predominantly in anterior uveitis (11%) followed by intermediate uveitis (6%). During follow-up, 60% of those with complications had at least one ocular surgery compared to none of those without complications.

Development of ocular complications was in univariate analysis associated with age older than 50 years, intermediate uveitis, posterior uveitis, panuveitis, chronic and recurrent inflammation, infectious etiology, and initial VA less than 6/18. In multivariate analysis, we identified three independent risk factors related to the occurrence of ocular complications, ie, chronic disease (RR 18.93, CI 6.09–58.84; $p < 0.01$), recurrent disease (RR 20.44, CI 6.49–64.28; $p < 0.01$) and initial VA less than 6/18 (Table 3). Age, gender, laterality, and HIV infection status were not significantly different. The median follow-up time was longer in those with complications [20.1 months (IQR 12.0–30.3 months)] than in those without [15.6 months (IQR 9.3–25.7 months)].

Almost all patients without ocular complications (92%) had an initial VA 6/60 or better. In contrast, most patients with complications (87%) had an initial VA of 6/60 or worse. With treatment, patients with complications gained

Table 3 Univariate and Multivariate Logistic Regression Analysis of Factors Associated With Ocular Complications of Uveitis

	Univariate Analysis		Multivariate Analysis	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Male (vs female)	0.97 (0.76–1.23)	0.82	1.04 (0.74–1.47)	0.81
Age > 50 years	1.01 (1.00–1.02)	< 0.01	1.00 (0.99–1.01)	0.99
Unilateral (vs bilateral)	1.09 (0.85–1.40)	0.5	1.11 (0.77–1.60)	0.58
HIV infection	1.07 (0.81–1.41)	0.65	0.97 (0.62–1.53)	0.91

(*Continued*)

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Table 3 (Continued).

	Univariate Analysis		Multivariate Analysis	
	RR (95% CI)	**P-value**	**RR (95% CI)**	**P-value**
Site of inflammation				
- Anterior	Reference		Reference	
- Intermediate	0.51 (0.22–1.20)	0.12	0.91 (0.33–2.47)	0.86
- Posterior	0.34 (0.15–0.78)	0.01	0.69 (0.28–1.68)	0.41
- Panuvetities	2.52 (1.87–3.40)	<0.01	1.03 (0.65–1.62)	0.91
- Scleritis	NA		NA	
Course of disease				
- Acute disease	Reference		Reference	
- Chronic disease	38.94 (14.75–102.82)	<0.01	19.00 (6.40–56.45)	<0.01
- Recurrent disease	43.09 (16.33–113.69)	<0.01	20.51 (6.67–63.03)	<0.01
Infection (vs non-infection)	1.37 (1.08–1.76)	0.01	0.98 (0.66–1.50)	0.98
Initial visual acuity				
- VA ≥ 6/18	Reference		Reference	
- VA <6/18-6/60	5.90 (2.05–17.00)	<0.01	2.58 (0.84–7.97)	<0.05
- VA <6/60-3/60	27.64 (10.51–72.73)	<0.01	3.59 (1.15–11.22)	<0.05
- VA <3/60-1/60	24.78 (9.35–65.72)	<0.01	3.76 (1.21–11.66)	<0.05
- VA <1/60-Perception to light	25.31 (9.62–66.58)	<0.01	3.56 (1.18–10.71)	<0.05

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; RR, risk ratio; VA, visual acuity.

improvement in their VA, and half of them (52%) recovered to VA 6/60 or better. Final VA ≥ 6/18 was observed in 86% of patients without complications whereas only 27% of patients with complications reached this range.

Discussion

Our study revealed that almost half of the patients with uveitis (44%) developed one or more complications, even despite our limited average follow-up duration of 18 months. Three independent risk factors for the development of complications were identified, ie, chronic and recurrent course of uveitis as well as a poor initial VA. The type of complications was strongly associated with the anatomic location of uveitis, with panuveitis exhibiting the highest prevalence of complications.

A limited number of studies on this topic, mainly from the US and Europe, show a variable prevalence of uveitis complications in the general uveitis population (29.5–45.8%).[3–6] A single-center study from Europe reported a complication rate of 44%,[5] which is very similar to our findings. A high complication rate of 66% was found in the study assessing the insurance claims data in a population of patients with non-infectious intermediate uveitis, posterior uveitis, or panuveitis.[11] Based on an extensive database, this study had a potentially longer follow-up duration (5.6 years) and did not contain data for anterior and infectious uveitis, which explains its high complication rates.

Most previous studies exhibited a slight majority of female patients, ranging from 52% to 61.5%.[5,6,11,13,14] In our study a majority of males was observed, which can be explained by a high percentage of HIV-positive patients, who were predominantly male. The male-to-female ratio in our non-HIV uveitis population is in line with previous reports. Of note, in 2023, the HIV prevalence rate in Thailand was 1.1–1.3%.[15]

Panuveitis is defined as the inflammation of all uveal components of the eye without a specific site of inflammation. The widespread nature of this inflammation, which affects nearly all tissue within the eye globe, makes treatment and control more challenging compared to localized inflammation. Prolonged, uncontrolled inflammation can lead to permanent damage to ocular tissue, resulting in lasting visual impairment. Anterior uveitis specifically refers to an inflammatory condition that affects the iris and the anterior portion of the ciliary body. Since the retina and choroid located in the posterior segment are not involved, retinal detachment is rarely observed in these cases.

Cataracts formed the most frequent complication (29%), which is in accordance with previous reports. Retinal detachment and macular scars were typically found in panuveitis and posterior uveitis, consistent with previous studies.[16,17] Our results confirm that glaucoma commonly develops in anterior uveitis, where local inflammation and inflammatory mediators frequently induce anatomic alterations of the anterior chamber, angle, and trabecular meshwork[18] and topical corticosteroids are nearly always used. Our study is characterized by a high frequency of retinal scars, which might partly explain a high prevalence of infections. Most previous studies report a higher prevalence of macular edema than our results. The reason for this discrepancy needs to be clarified. First, patients in a referral center are often seen later in their disease course when macular atrophy is more often present than edema itself. Second, our cohort predominantly consisted of infectious uveitis, in contrast to previous studies that reported non-infectious causes. Each etiology is associated with specific complications. In infectious uveitis, inflammation can be more aggressive and progress rapidly, triggering a specific immune response that may result in severe tissue damage, including retinal or macular scarring. In non-infectious uveitis, the immune response tends to be more regulated; however, prolonged inflammation can lead to complications such as cystoid macular edema, glaucoma, and epiretinal membrane formation. Two previous retrospective studies from Asia (Thailand and China) reported complication rates of approximately 70%.[13,14] These two studies had a longer follow-up duration (33 and 37 months, respectively) and differed in anatomical types, causal diagnoses, and registration of complications from our series. In the study from China,[14] the most common uveitis causes were non-infectious, such as Vogt–Koyanagi–Harada disease (21%) and Behcet's disease (15%), whereas in our study, majority of the patients had infectious etiology. Moreover, the study from China included a broader spectrum of complications (steroid-induced ocular hypertension and Seclussio-pupillae).

We identified three major risk factors for the development of complications in uveitis, ie, chronic and recurrent course of uveitis and a poor VA at first presentation to ophthalmologist. Our findings highlight the importance of early and effective treatment for these groups of patients.[5,6] The follow-up schedule and treatment plan are determined by the specific cause of uveitis. Infectious causes should be identified quickly, and prompt administration of antimicrobial agents, along with early follow-up, is essential. The lack of necessary laboratory evaluations can delay diagnosis and lead to significant damage to ocular tissue. For non-infectious uveitis, it is crucial to effectively manage inflammation to prevent eye damage. Advanced age and anatomical location of uveitis were previously reported as factors associated with complications of uveitis but did not reach level of significance in our multivariate analysis. We cannot exclude that these factors could become significant if more patients were included. The poor VA at presentation was a crucial factor in developing complications. This finding suggests that early presentation of patients with uveitis to ophthalmologists specialized in uveitis care is crucial. The availability of medical care undoubtedly plays an important role here. In addition, the acute onset of infectious uveitis, which formed most of our population might also play a role, though we did not find a clear difference in complication rates between infectious and non-infectious uveitis.

Several limitations apply to our study. First, our series is retrospective and from a tertiary referral center, undoubtedly subject to a referral bias and various confounders. Our follow-up is limited due to the referral character of our center; once the disease activity is under control, the patients are referred to their original institutions. A higher complication rate is likely found with a longer follow-up duration. Lastly, a clear comparison with other studies is not always feasible since the causes of uveitis vary enormously by geographic location and depend on genetic, ethnic, environmental, and cultural factors. The availability and accessibility of treatment modalities vary strongly among the diverse institutions, and the level of medical care differs. These phenomena affect the generalizability of the data of individual studies. However, our study focused on Asian patients with new-onset uveitis in a tertiary care to limit the variability.

In conclusion, ocular complications of uveitis are both frequent and potentially sight-threatening. This study identified chronic and recurrent uveitis, along with poor visual acuity (VA) at presentation, as key risk factors for developing such

complications. Additionally, the patterns of complications were strongly correlated with the anatomical location of inflammation. These findings underscore the importance of early recognition, tailored treatment, and close monitoring to mitigate the risk of vision loss in affected patients.

Ethical Approval

This study was approved by the Ethics Committee of Chiang Mai University.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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