

PATTERN OF ANTERIOR UVEITIS IN KMN EYECARE

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Abstract

Introduction: Anterior uveitis is the most common form of uveitis, but there are relatively few anterior uveitis studies in Indonesia. The purpose of this study is to analyze the pattern of anterior uveitis in KMN EyeCare.

Methods: This is a retrospective analytic descriptive study. The samples are new patients diagnosed with anterior uveitis in KMN EyeCare between 2019 – 2021. Data collected from medical records are age, gender, clinical manifestation, etiology, and visual outcome.

Result: Two hundred fifty-three (253) patients are included in this study. The most common manifestations of anterior uveitis are keratic precipitates (34%), posterior synechiae (23.3%), hypopyon (7.9%), increased IOP (7.1%), and secondary cataract (6.3%). Visual outcome more than 0.5 in 90.1% of patients and below 0.5 in 9.9% of patients. The etiology is non-infectious autoimmune-related (46.7%) consists of HLA-B27 related, and rheumatoid arthritis; followed by infectious etiology (36%) consisting of herpetic, tuberculosis, cytomegalovirus, and idiopathic (17.3%). HLA-B27 anterior uveitis is more likely to affect males than females with a statistically significant $p < 0.05$.

Conclusion: The most common etiology of anterior uveitis is non-infectious autoimmune-related, especially HLA-B27-related anterior uveitis. The HLA-B27-related anterior uveitis is predominantly in males. Keratic precipitates, posterior synechiae, and hypopyon are common clinical manifestations of anterior uveitis. The visual outcomes are good in this study.

Keywords: anterior uveitis, infectious disease, autoimmune disease

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INTRODUCTION

Uveitis is a sight-threatening inflammatory ocular disease and leads to 5 – 10 % of visual impairment

worldwide. Uveitis and its associated complications account for up to 25% of blindness in developing countries and vary from 3 – 10% in developed countries.¹ Anterior uveitis is the most common form of uveitis encountered by ophthalmologists.²

Generally, anterior uveitis can be divided into infectious or non-infectious etiology in which most cases of non-infectious anterior uveitis are idiopathic and associated with systemic diseases especially autoimmune disorders. A study by Wakefield et al even showed that up to half of all cases of anterior uveitis are associated with HLA – B27.³ There are relatively few studies on the clinical features and etiology of anterior uveitis in Indonesia. One study in Indonesia showed

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That infectious uveitis was the most common type of uveitis in Indonesia (33% of all cases) with leading etiology were toxoplasmosis and uveitis associated with active pulmonary TB.⁴ The purpose of this study is to describe the clinical features, etiology, and visual outcome of anterior uveitis patients in KMN EyeCare for three years between 2019 – 2021.

METHODS

This is a retrospective descriptive study of all patients with anterior uveitis seen in the infection and immunology department between 2019 – 2021 in KMN EyeCare. The data were collected from medical records of patients with anterior uveitis who are being taken care of by one uveitis specialist (RLU). Naming and meshing of all patients done as guidelines of Standardization of Uveitis Nomenclature (SUN). The inclusion criteria were: first, new anterior uveitis patients who need uveitis management that have been referred by an internist or rheumatologist. Second, anterior uveitis patients who have been completed an ancillary examination and diagnosed as either non – infectious or infectious uveitis by our uveitis specialist. Exclusion criteria of this study are other types of uveitis patients like intermediate uveitis, posterior uveitis, and panuveitis, or patients who have incomplete examinations.

The physical examination in these patients includes visual acuity, anterior segment examination with slit-lamp, posterior segment examination with indirect lens and retinal photography. The ancillary test including laboratory tests like erythrocyte sedimentation rate (ESR), interferon -gamma release assay (IGRA), viral markers for Toxoplasma, Herpes Simplex, and Cytomegalovirus, Human Leukocyte antigen (HLA – B27), C-reactive protein, Rheumatic factor (Rh factor), serum nuclear antibody (ANA),

anti-dsDNA antibodies. The term idiopathic uveitis was used when a specific etiological cause could not be determined despite laboratory and imaging investigations.

Data collected for clinical features were determined by keratic precipitates (KPs), hypopyon, fibrin exudate, transient increase of IOP, iris atrophy, posterior synechiae, secondary glaucoma, iris neovascularization, hypotony, complicated cataract, and cystoid macular edema. Etiology of the anterior uveitis was determined as infectious, non – infectious or idiopathic. Visual outcome was determined by the visual acuity of the patients.

Ethics Statement

This study was conducted following the Declaration of Helsinki and approved by the Medical Committee of KMN EyeCare.

Statistical Analysis

Data presented in this paper were analyzed using SPSS ver 25.0 (SPSS Inc., Chicago, USA). Data shown in the table were frequency and percentage based on the type of the data. Statistical analysis was calculated to determine the association between gender with the etiology of anterior uveitis analyzed with a chi-square test, with $P < 0.05$ being statistically significant.

RESULT

There were 253 anterior uveitis patients included in this study. Table 1. shows that male (52.6%) are more than females (47.4%) and the age most common is over 50 years old (50.6%). Table 2 shows that the most common clinical characteristic was keratic precipitate in 34% of patients, followed by posterior synechiae 23.3%, hypopyon 7.9%, increased IOP 7.1%, and complicated cataract 6.3%.

Table 1. Demographic data

Variables	Frequency	Percentage
Gender	n=253	
Male	133	52.6%
Female	120	47.4%
Age (years)	n=253	
<30	20	7.9%
31-50	105	41.5%
>50	128	50.6%
Laterality	n=253	
Unilateral	132	52.2%
Bilateral	121	47.8%

Table 2. Clinical characteristic of study subjects

Clinical characteristic	Frequency	Percentage
Keratic precipitates	86	34%
Posterior Synechiae	59	23.3%
Hypopyon	20	7.9%
Fibrin	13	5.1%
Mutton Fat	5	2%
Iris Pigment	6	2.4%
Pupil seclusion	2	0.8%
Corneal edema	4	1.6%
Iris atrophy	4	1.6%
Increased IOP	18	7.1%
Secondary glaucoma	14	5.5%
Secondary cataract	16	6.3%
Neovascular glaucoma	1	0.4%

Table 3. Etiological Classification of Uveitis

Etiology	Frequency	Percentage
<u>Infection</u>	91	36%
TB	33	13%
CMV	20	7.9%
HSV	26	10.2%
VZV	9	3.5%
Rubella	1	0.4%
Dental infection	2	0.8%
<u>Non-infection</u>	118	46.7%
HLA – B27	86	34%
Rheumatoid Arthritis	16	6.3%
Posner Schlossman Syndrome	7	2.7%
Sjogren Syndrome	5	1.9%
SLE	4	1.5%
<u>Idiopathic</u>	44	17.3%

Table 3. shows that the most common cause of anterior uveitis in KMN EyeCare is the non-infection etiology, 46.7% of all cases. The most common etiology of non-infectious anterior uveitis are HLA-B27 34%. Meanwhile the most common cause of anterior uveitis from the infection group is TB 13% of

all cases, followed by viral infection (HSV 10.2%, CMV 7.9%, VZV 3.5%, and rubella 0.4%).

Table 4. shows that the good visual outcome > 0.5 in 90.1% and < 0.5 in 9.9% of patients.

Table 4. Visual outcome after treatment

Visual Outcome	Frequency	Percentage
>0.5	228	90.1%
<0.5	25	9.9%

Table 5. shows the calculation of the association between gender with the etiology of anterior uveitis analyzed with a chi-square test, with $P < 0.05$ being statistically significant. In this table, we can see that HLA – B27 is significantly more in males than females with a P-value of 0.000.

uveitis and then followed by HLA-B27.⁹ The difference of etiology in different studies depend on the geography and racial differences between countries where the study conducted.

In our study, the most common cause was HLA – B27-related anterior uveitis. This result may be

Table 5. Gender related to Etiology Anterior Uveitis

Etiology of Anterior Uveitis	Male	Female	Total	P-value (Chi-Square test)
HLA B-27	60	26	86	0.000
TB	14	19	33	0.148
HSV	13	13	26	0.630
VZV	6	3	9	0.197
CMV	9	11	20	0.342
Idiopathic	23	21	44	0.895
RA	9	7	16	0.682

DISCUSSION

The most common causes of anterior uveitis in this study were non-infection uveitis related to HLA B-27 (34%) and idiopathic uveitis (17%). Meanwhile, infection anterior uveitis was caused by TB (13%), HSV (10.2%), and CMV (7.9%). A study in Taiwan by W. Chiang et al and Pascual et al in Spain showed that the most common etiologies are idiopathic, and then followed by HLA–B27-related uveitis.^{5,6} Our study was also different from the study of Yalçındağ et al in Turkey which showed that idiopathic was the most common cause of anterior uveitis and HSV was the main etiology of infection anterior uveitis.⁷ Study in India by Sabhapandit et al showed that idiopathic uveitis was still the main etiology of non-infectious anterior uveitis but the most common cause of infectious anterior uveitis was TB.⁸ Meanwhile a study by Sonoda et al in Japan showed that herpetic uveitis was the most common etiology of anterior

related to the fact that the majority of our positive HLA – B27 patients had undergone the allele study by a rheumatologist before being referred to our clinic. Our study is also the same with a study in Chongqing, China by Yang P et al who showed that more than 61.5% of anterior uveitis patients were HLA-B27 positive.¹⁰ HLA B-27 is a major histocompatibility complex (MHC) class 1 antigen present in approximately 8% of the population in the US. About 40%-50% of patients with anterior uveitis are HLA-B27 positive, but the precise trigger for anterior uveitis in HLA-B27 positive persons remains unclear. Several autoimmune diseases known as *seronegative spondyloarthropathies* are strongly associated with both anterior uveitis and HLA-B27. *Seronegative spondyloarthropathies* mean the patients do not test positive for rheumatoid factor, this group of diseases includes ankylosing spondylitis (AS), reactive arthritis syndrome, inflammatory bowel disease, and psoriatic arthritis.¹¹ HLA-B27 was reported to be positive in 7.7% of the

healthy Taiwanese population. Approximately 50%–75% of patients with HLA-B27-associated anterior uveitis have seronegative spondyloarthropathy, with ankylosing spondylitis (AS) being the most common diagnosis.⁵

In our study, anterior uveitis occurs most frequently in patients over 50 years old, in contrast with other studies like the study by Sabhapandit et al in India which shows that uveitis occurs more frequently in young and middle-aged patients despite the anatomical location of uveitis.⁸ Study by W. Chiang et al in Taiwan showed that uveitis occurs frequently in younger patients.⁵ Study by Gevorgyan et al in the US also showed that the mean age of uveitis patients was 45.9 years old.¹² Most of the epidemiology studies about uveitis in several countries showed that anterior uveitis tends to affect patients between 20-50 years old.^{9,13-15} The contradiction of earlier studies with our study can be caused by most of the patients who came to our clinic being above 50 years old.

Male were more likely to suffer anterior uveitis, especially the HLA-B27 related in our study. We analyzed with a chi-square test to see the significance between gender and the etiology of anterior uveitis. From the analysis, we found that males were more statistically significant than women to have HLA-B27-related anterior uveitis with a P-value of 0.000. This finding is following many earlier studies which also showed the male prevalence of HLA-B27-related anterior uveitis.^{5,6,9-11,16}

Keratic precipitates were the most common clinical characteristics in our study followed by posterior synechiae, hypopyon, increased IOP, complicated cataract, and fibrin. The study by Tugal-Tutkun et al in Turkey shows that the most common clinical features of herpetic anterior uveitis are keratic precipitates and increased IOP.¹⁷ However in our study, these clinical features are also found in other etiology of anterior uveitis, especially the HLA-

B27-related anterior uveitis. Our study was in contrast with the meta analysis by D'Ambrosio et al which showed that hypopyon and fibrinous reaction were the predominant clinical characteristic of HLA-B27-related anterior uveitis.¹⁶ Study by Yang P et al also showed that corneal endothelium wrinkling was also frequently seen in HLA-B27-related anterior uveitis patients which we did not find in our study.¹⁰

There was 1 patient of anterior uveitis with neovascular glaucoma. This uncommon finding was like two previous studies in Nigeria and China which showed that uveitis could be a rare etiology of neovascular glaucoma although there was no known direct correlation between these two.^{18,19}

In our study, alternating bilateral involvement was the most common following a higher percentage of non-infectious anterior uveitis especially the HLA-B27 related. These findings are the same as many studies which showed that HLA-B27-related anterior uveitis was more likely to involve bilateral eyes alternately.^{5,6,9-11,16} Meanwhile unilateral involvement was more predominant in the herpetic and CMV anterior uveitis in our study, this is in accordance with the study by Tugal-Tutkun and Hsiao YT et al.^{11,13}

There were increased IOP and secondary glaucoma in some patients in our study. The increased IOP and secondary glaucoma were more common in HSV uveitis, CMV uveitis, and PSS. These findings were the same as other previous studies which showed that viral uveitis were tend to have increased IOP.^{2,20,21} Some patients with HLA-B27-related uveitis and idiopathic uveitis also had increased IOP and secondary glaucoma in our study due to the side effect of long term steroid therapy.

Visual outcomes of the patients in our study were good, 90.1% of all the anterior uveitis patients in our clinic had the visual acuity >0.5, this is due to the clinical course of the diseases did not involve the posterior segment of the eyes, and also they had

minimal complications because their systemic conditions were also treated by the internists and rheumatologists. Collaboration between ophthalmologists and rheumatologists in managing uveitis patients was the most important factor in having a good prognosis of visual outcome. In our study, the bad visual outcome in 9.9% of our patients was due to complications like complicated cataract and secondary glaucoma as many previous earlier studies have shown.^{9,11,12}

Our study has limitations. We chose a retrospective design, and although retrospective studies can be completed within a relatively short time, the potential bias cannot be controlled by the identification of confounding factors in advance. The most reliable survey will be "prospective" and simultaneously designed to guarantee a certain "patient follow-up duration" to achieve definite diagnoses.

CONCLUSION

The most common etiology of anterior uveitis in our study is non-infectious anterior uveitis, especially HLA-B27-related anterior uveitis and idiopathic. HLA-B27-related anterior uveitis is predominantly in males. Keratic precipitates, posterior synechiae, and hypopyon are the most common clinical manifestations of anterior uveitis. The visual outcomes are good in this study

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