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ORIGINAL RESEARCH ARTICLE

# SYSTEMIC ASSOCIATION OF UVEITIS IN NEPALESE POPULATION

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## ABSTRACT

Background: Infectious diseases are very common in Nepal and almost all infections are capable of causing uveitis. Parasitic infestations affect large number of Nepalese population and any parasitic infestation can potentially lead to development of uveitis. Local and systemic viral infections, immunological disorder like autoimmune diseases and malignancies can lead to uveitis. All these emphasize the necessity of proper systemic evaluation and investigation to identify the underlying systemic illness causing uveitis in order to see the pattern of systemic illness and determine the commonest associated systemic disease with uveitis. Methods: A prospective study was conducted at BP Koirala Lions Centre for Ophthalmic Studies from November 2008 to April 2010. All the patients underwent a standard diagnostic protocol when indicated by special tests and procedures performed in order of likelihood. Results: A total of 308 patients with uveitis was seen during the study period. For 146 (47.4%) patients, a specific diagnosis was established based on history, ocular examination and laboratory investigations. A definite association with systemic disease was determined for 82 (26.6%) patients. A well established clinical uveitis entity without a recognizable systemic disorder was present in 64 (20.8%) cases. A diagnosis could not be established in 162 (52.6%) cases. Toxoplasmosis was found to be most frequently associated with uveitis accounting for 5.8 % of the total cases followed by tuberculosis (3.6%), herpes infections (3%), ankylosing spondylitis (2.9%), leprosy (2.3%), sarcoidosis (1.6%) and parasitic infestations (1.3%). Conclusion: The importance of relevant systemic work up in uveitis cases in our set up has been reemphasized by the present study.

***Key words:*** *Infection, Systemic association, Uveitis*

## INTRODUCTION

Uveitis is one of the major causes of severe visual impairment all over the world. Uveitis is relatively confusing term since it implies primary inflammation of the uveal tract. However it has become clear during the last few decades of research into the causes of uveitis, the uveal tract acts primarily as a conduit for the inflammatory cells and the increased blood flow that accompany inflammation targeted to other sites in the eye such as the aqueous, vitreous, retina and optic nerve. Uveitis is therefore, better referred to as intraocular inflammation (IOI).

Despite the advances made in various areas of diagnostic medicine, causes of a large number of uveitis are still undetermined and hence we find that a good percentage of uveitis cases are classified as idiopathic group. On the other hand, uveitis may also be the first presenting feature in certain cases of systemic diseases or may form part of multi systemic involvement of many disease processes such as tuberculosis, sarcoidosis, leprosy, Behcet's disease, AIDS etc.

Uvea being high in protein content and highly vascular structure, modification in its antigenecity by factors such as trauma or infections or predetermined genetic makeup may precipitate immune mediated reaction leading to uveitis, some of which are fulminant. Many uveitis entity are curable or at least controllable in the sense that ocular damage can be prevented or limited with the early diagnosis and proper therapy. In order to know

the etiology of uveitis, proper evaluation of the patient is necessary, for which we must consider a list of infections, autoimmune diseases, inflammatory conditions, masquerade syndrome that might cause uveal inflammation and the patients are to be investigated as indicated by the physical appearance of the ocular lesions in the context of their racial origins and systemic symptoms. There are not many literatures originated in Nepal regarding uveitis. To strengthen and upgrade the management facilities for the cases of uveitis, it is important to have baseline data on systemic profile of the disease. Therefore, a prospective study was designed to find out the systemic profile of the uveitis cases.

## MATERIAL AND METHODS

All the cases attending the uveitis clinic were evaluated in prospective manner except those who were excluded from the study due to unwillingness for investigations, treatment initiated prior to our consultation and uveitis following trauma, cataract and intraocular surgery. The study period extended from November 2008 to April 2010.

Every patient was evaluated in detail by external examination and slit lamp biomicroscopy. Fundus examination was done by slit lamp using 90- D lens and with indirect ophthalmoscope using 20-D lens after full dilatation of pupil. Patients were classified according to the current International Uveitis Study Group (IUSG); classification based on the localization of intraocular inflammation.[1] Ancillary tests included B scan ultrasound, fundus fluorescein angiography in selected cases and tailored laboratory investigations in each case. Standard diagnostic criteria were employed for all syndromes or entities of uveitis.[2,3] Consultation was done with the concerned medical specialist whenever needed. The final etiological diagnosis was made based on clinical features, laboratory investigations and systemic evaluation.

Results: A total of 308 patients having uveitis were included in this study. Out of these, 191 were male and 117 were female, showing predominance of male over female. Uveitis was seen most frequently between the age groups of 16 and 40 accounting for 73% out of total cases.

Of the 308 cases, a specific diagnosis of uveitis could be established in 146 (47.4%) cases and 162 (52.6%) still remained in idiopathic group. Among the diagnosed 146 cases, 82 of them had some or other systemic involvement accounting for 26.6% out of total. Remaining 64 cases were found to have specific entity of diseases accounting for 20.8% of total. Of the 82 cases that had systemic involvement, 18 were found to have Toxoplasmosis accounting for 5.8% of total uveitis cases. Toxoplasmosis being recognized as the commonest systemic disease causing uveitis followed by tuberculosis (3.6%), herpes infection (3%), ankylosing spondylitis (2.9%), leprosy (2.3%), Vogt-Koyanagi-Harada (VKH) syndrome (1.9%) , sarcoidosis(1.6%) and parasitic infestations (1.3%). Those diagnosed under specific entity of disease, Eales' disease (9.1%) was commonly encountered followed by pars planitis (6.5%), seasonal hyperacute panuveitis (SHAPU) (2.6%), and sympathetic ophthalmia (1.3%) (Table 1).

**Table 1: Types of infection and uveitis**

| Etiology | | No. of cases | % |
|---|---|---|---|
| Idiopathic | | 162 | 52.6 |
| Infectious uveitis: | | 55 | 17.9 |
| Bacterial | Tuberculosis | 11 | 3.6 |
| | Syphilis | 1 | 0.3 |
| | Leprosy | 7 | 2.3 |
| Viral | Herpes (Zoster/ Simplex) | 9 | 3.0 |
| | HIV | 4 | 1.3 |
| | ARN | 1 | 0.3 |
| Parasitic | Toxoplasmosis | 18 | 5.8 |
| | Other parasitic | 4 | 1.3 |
| Non infectious: | | 27 | 8.7 |
| Ankylosing spondylitis | | 9 | 2.9 |
| Reiter's syndrome | | 3 | 1.0 |
| Rheumatoid arthritis | | 2 | 0.6 |
| Juvenile rheumatoid arthritis | | 1 | 0.3 |
| Sarcoidosis | | 5 | 1.6 |
| Behcet's disease | | 1 | 0.3 |
| VKH syndrome | | 6 | 1.9 |
| Specific entity: | | 64 | 20.8 |

| | | |
|---|---|---|
| Eales' disease | 28 | 9.1 |
| Sympatheic ophthalmia | 4 | 1.3 |
| MEWDS | 2 | 0.6 |
| SHAPU | 8 | 2.6 |
| Parsplanitis | 20 | 6.5 |
| AMPPE | 1 | 0.3 |
| Serpiginous choroiditis | 1 | 0.3 |
| Total | 308 | 100 |

In the present study, according to the anatomical localization, anterior uveitis was seen in 183(59.4%) cases, posterior uveitis in 69 (22.4%), panuveitis in 32 (10.4%) and intermediate uveitis in 24 (7.8%) cases (Table 2). Idiopathic uveitis was seen in 162 (52.6%) cases, 64 (20.8%) cases were of specific syndromes of uveitis (specific uveitis entity), 55 (17.9%) cases were secondary to systemic infection and 27 (8.7%) were related to non infectious etiology. (Figure 1).

**Table 2: Systemic disease in uveitis patients**

| Systemic disease | All uveitis patients N=308 | Anterior uveitis N= 183 (59.4%) | Intermediate uveitis N= 24 (7.8%) | Posterior uveitis N= 69 (22.4%) | Panuveitis N= 32 (10.4%) |
|---|---|---|---|---|---|
| Tuberculosis | 11 | | 4 | 6 | 1 |
| Syphilis | 1 | 1 | | | |
| Leprosy | 7 | 7 | | | |
| Herpes | 9 | 6 | | | |
| HIV | 1 | | | 1 | |
| ARN | 1 | | | 1 | |
| Toxoplasmosis | 18 | | | 18 | |
| Other parasitic | 4 | | | 1 | 3 |
| Sarcoidosis | 5 | | | | 5 |
| Behcet's disease | 1 | | | | 1 |
| VKH | 6 | | | 4 | 2 |
| Ankylosing spondylitis | 9 | 9 | | | |
| Reiter's syndrome | 3 | 3 | | | |
| Rheumatoid arthritis | 2 | 2 | | | |
| Juvenile rheumatoid arthritis | 1 | 1 | | | |
| Total | 76 (24.7%) | 29 (9.4%) | 4(1.3%) | 31(10.1%) | 12(3.9%) |

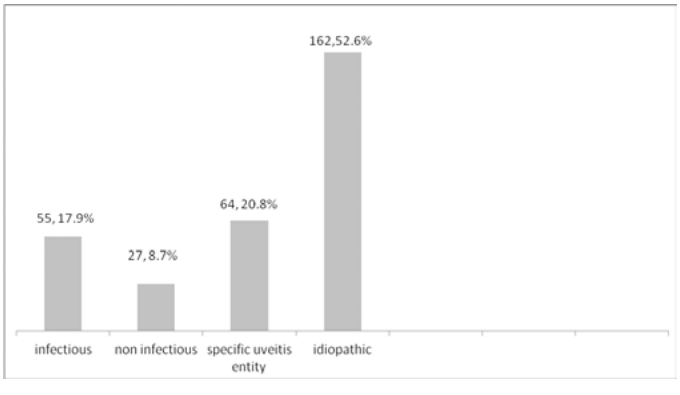


**Figure 1: Etiological diagnosis of uveitis**

Anterior uveitis (59.4%) was most commonly observed of all cases. In anterior uveitis, specific diagnosis could be established in 29 cases (15.8%). The most common underlying causes were ankylosing spondylitis and other arthritic diseases (8.2%), leprosy (3.8%) and herpes infections (3.3%) (Table 2). Diagnosis could not be made in 154 cases (84.2%).

In posterior uveitis group (69, 22.4%), a specific diagnosis could be made in 91 % (n=63) of cases. Eales' disease was present in 9.1%, MEWDS in 0.6%, APMPPE in 0.3% and serpiginous choroiditis in 0.3%. Posterior uveitis was associated with systemic infections in 10.1%, ocular toxoplasmosis in 26.1%, tuberculosis in 8.7%, HIV in 1.4%, ARN in 1.4% and parasitic infestation in 1.4 %.

In intermediate uveitis, the etiology was idiopathic pars planitis in 20 cases (83%) and 4 patients were found to have systemic tuberculosis.

In panuveitis group (32 cases, 10.4%), a specific diagnosis could be established in 50% (n=16) .

Seasonal hyperacute panuveitis (SHAPU) was present in 25% and sympathetic ophthalmia in 12.5%. Panuveitis was associated with systemic infection in 3.9 % (n=12), sarcoidosis in 15.6%, parasitic infestation in 9.4 %, VKH in 6.3 %, tuberculosis in 3.1%, and Behcet's disease in 3.1 %.

Discussion: In this prospective study of 308 patients, the specific diagnosis for an intraocular inflammation was established in 47.4% of all cases. The cause of uveitis remained unknown in 52.6% cases. This result correlates with other studies where they have reported the cause of uveitis being unknown in approximately 30-60% of patients.[4-12] Systemic disease, which could be considered to be related to the intraocular inflammation, was determined in 26.6% of all cases on the basis of history, ocular examination and laboratory investigations. It was similar to the study done by Rothova et al where systemic disease related to intraocular inflammation was diagnosed in 26%.[13] The reported frequency of a systemic disease causing uveitis varies from less than 19% to 46%.[2, 14-18]

Comparison of uveitis statistics from various countries is very difficult. Several factors may attribute to the variation in reported incidence of the various systemic diseases underlying intraocular inflammation. The true geographical differences as well as the true location of patients, author's interest, diverse diagnostic investigations and criteria influence the study.

In the current study, age at presentation ranged from 3-65 years. The peak age of onset was observed in 16-40 years of age (73%). Findings from our study is consistent with those from previous reports.[1, 19-21] This shows that majority of patients are students and of working age and so the condition may cause potentially serious economic consequences with many days off work as well as interfere with education.

Like in other studies, we have higher incidence of males (62%) as compared to females (38%). (Male: Female ratio was 1.6:1).[1-3,6,15,22,23]

Anterior uveitis was the most common form of intraocular inflammation followed by posterior, pan and intermediate uveitis. Likewise, the anatomical entity most frequently associated with systemic disease was anterior uveitis ( 9.4%), posterior (10.1%) and panuveitis ( 3.9%). The results are comparable to other published reports.[1,8,9,12,13,20,24]

The majority of anterior (84%) and intermediate (83%) uveitis were idiopathic than are posterior and panuveitis, similar to the the study by Rathinam et al.[23]

Infectious uveitis occurs in a higher frequency in developing world, constituting from 11.9% to 50%.[23] Infectious uveitis in the present study accounted for 16.4% of total uveitis. The most common infectious forms of uveitis seen in this study included toxoplasmosis, tuberculosis, leprosy, herpetic uveitis and other parasitic diseases, comparable to published reports from other parts of world.[4,6,9,20,25-27]

The diagnosis of tuberculosis, leprosy, ankylosing spondylitis, and other uveitis associated with arthritis was established before the onset of uveitis. The patients with toxoplasmosis, herpes, HIV and parasitic infestations were not known to have these systemic diseases prior to the ocular symptoms and the diagnosis was made during the uveitis work up.

In anterior uveitis, ankylosing spondilytis, leprosy and herpes infections were the major cause in our study which is comparable to the report by Das et al. [29] However remarkably higher number (152, 84%) of idiopathic anterior uveitis is contradictory to study done by same author.[29]

In posterior uveitis, ocular toxoplasmosis was the commonest etiological cause (26.1%) which is similar to reports by Biswas et al, Rathinam el al, Das et al and Talin et al.[1,23,28,29]

In the intermediate uveitis group, the etiology was idiopathic pars planitis in 83% and a specific diagnosis was made in the remaining 4 cases of which tuberculosis was the primary cause.

In panuveitis group, Seasonal hyperacute panuveitis (SHAPU) was the leading etiological cause (25%). All were seen in pediatric population. The seasonal hyperacute panuveitis entity was first reported in Nepal in 1975 and this type of unusual uveitis has not been reported from anywhere else till date.[30] The etiology of uveitis is unknown. The condition is marked by severe exudation into vitreous causing leucocoria in a red eye. Fibrinous exudation with

or without hypopyon is almost a constant finding in the anterior chamber, which, in the presence of invariably occurring hypotony, has been called malignant hypotension. The end result is a white pupil in a white phthisical eye. Because of seasonal occurrence, extremely fulminant course and clinical feature of panuveitis, this has been named seasonal hyperacute panuveitis (SHAPU). Other systemic association detected with panuveitis included sarcoidosis, parasitic infestations, Behcet's disease and tuberculosis.

Overall, the largest diagnostic group comprised patients with specific uveitis entity (20.8%), followed by those with infectious diseases (17.9%), arthritic diseases (4.9%) and, lastly, non-infectious systemic diseases (3.9%). The finding in this study is consistent with Talin et al report.[30]

Among the patients with ocular tuberculosis, all were known to have this disease before the onset of uveitis. One of the patients was suffering from military tuberculosis. The other had pulmonary tuberculosis with exudative detachment in one eye. Rest (n=9) had ocular tuberculosis in the past and was released from treatment and had recurrence.

A case of syphilitic uveitis had VDRL test positive with 1:8 titre. Other confirmatory tests like FTA-ABS, TPHA could not be performed because of the lack of laboratory techniques available during the study period. The case improved with antisyphilitic therapy.

The diagnosis of leprosy was established before the onset of uveitis. The diagnosis of HIV retinopathy was made during the uveitis work up. All cases of uveitis associated with arthritis were known to have these diseases before the onset of uveitis. Toxoplasmosis accounted for 18 (5%) of total uveitis cases. It was the most common cause of uveitis in this study occurring in 18 of 340 patients. Among the parasitic uveitis, in one case a parasite could be seen roaming in and out of the macular hole. The parasite was taken out by anterior chamber paracentesis and sent for histopathological examination, which revealed it as microfilaria worm.

## CONCLUSIONS

The present study revealed many systemic disorders were found to give rise to uveitis in our set up and hence this aspect should be given due importance during the work up of a case of uveitis, mere ocular management in many of such cases can not improve the condition and systemic morbidity may lead to other serious physical problems to the cases, apart from the ocular one that he or she has. In some cases, the presence of a systemic disease was not suspected prior to eye involvement and was only recognized during the course of work up for uveitis. This has been of great benefit for such cases, as some potential complications of these systemic diseases could be prevented by timely detection and treatment of systemic disorders.

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