



TO STUDY OCULAR MANIFESTATIONS IN HIV POSITIVE PATIENTS AT TERTIARY CARE HOSPITAL

Ophthalmology

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ABSTRACT

Background: Ophthalmic presentations of HIV include micro-vasculopathy, neuro-ophthalmic disorders, neoplasms and opportunistic infections. It has been for the most part due to the opportunistic infections and neoplasias that accompany the syndrome. Early detection of the ocular manifestations of HIV/AIDS is critical since these ocular manifestations may be the primary presentation of the systemic infection. This study was done to evaluate the prevalence of various ocular manifestations and visual acuity in HIV seropositive patients attending the ophthalmology OPD of tertiary care centre. **Methodology:** The present Prospective observational study was conducted on 150 HIV seropositive patients attending the ophthalmology OPD. HIV seropositive patients referred to ophthalmology OPD irrespective of ocular complaints or treatment status to routine ophthalmology examination or for routine ophthalmology examination, were included. Detailed history of the patients was taken as per case record proforma followed by General and systemic examination. Detailed ophthalmic examination were done and findings like visual acuity, external eye examination, ocular motility, pupillary reflexes, anterior segment examination by slit lamp bi microscopy and dilated fundus examination by indirect ophthalmoscopy were noted. Also, CD4 count of each patient was done. **Results:** Out of 150 HIV positive patients, 37 (24.7%) were found to have Ocular manifestation which were associated with HIV infection. Prevalence of ocular manifestations was maximum in age groups 51 to 60 years (36.8%) (p value 0.402), in females (30%) (p value 0.216), in stage II (44.8%) and stage III (37.5%) (p value 0.010) and in patients with CD4 count ≤ 250 cells/mm³ (p value 0.000). In right eye, 40.5% patients with ocular manifestations had diminution of vision compared to only 8 (7.1%) without ocular manifestations (p value 0.000). In left eye, 35.1% patients with ocular manifestations had diminution of vision compared to only 4 (3.5%) patients without ocular manifestations (p value 0.000). Common ophthalmic lesions (Right Eye) associated with HIV were CMV Retinitis, Contagiosum Molluscum, Herpes Zoster Ophthalmicus and Viral Keratitis. In Left Eye, Posterior Blepharitis Contagiosum Molluscum and CMV Retinitis involving Macula were common. Blindness was observed in total 12 (8%) patients. Out of 12 patients, most common cause was Optic Atrophy in 3 (25%) and Severe Dry Eye in 2 (16.7%) cases. **Conclusion:** Ophthalmic manifestations affects commonly the reproductive age group. HIV associated blindness was observed 8% patients, most common being Optic Atrophy and Severe Dry Eye. Clinical stage, CD4 count, visual acuity, anterior and posterior findings were significant associated. However, most patients were unaware of their ophthalmic status and there is the need to emphasizes the importance of routine ophthalmic screening at the time of diagnosis of HIV seropositivity in adults.

KEYWORDS

Ocular Manifestations, HIV Positive Patients, CD4 Count, Anterior Segment, posterior Segment, CMV Retinitis, Herpes Zoster Ophthalmicus

INTRODUCTION:

Human Immunodeficiency Virus (HIV), is a retrovirus which causes Acquired Immune Deficiency Syndrome (AIDS)⁽¹⁾. Since its discovery in 1981, HIV/AIDS has emerged as a global health problem⁽²⁾. The prevalence rate of HIV/AIDS has been reported to be 0.8% globally, 5% in Sub-Saharan Africa and 18.8% in South Africa⁽³⁾. The impact of the HIV/AIDS pandemic has spurred much research into the disease and its various systemic and ocular complications. **Macleane et al**⁽⁴⁾ first described the ocular manifestations of HIV infection more than 20 years ago.

HIV-AIDS was discovered in the early 1970's. Amongst the various communicable diseases that have been well controlled with the advancing sciences, HIV- AIDS⁽⁵⁾ has been a major challenge. It poses a challenge not just to the doctors treating the disease but also to the patient subjected to social stigma. Eye with its adnexa is no exception to HIV infection. Ophthalmic⁽⁶⁾ presentations of HIV include micro-vasculopathy, neuro-ophthalmic disorders, neoplasms and opportunistic infections. Mainly seen and examined by the treating physician it becomes a necessity that all HIV infected patients undergo routine ophthalmic evaluations irrespective of symptoms for early identification of manifestations and prompt initiation of treatment to prevent visual loss.

The ocular manifestations of HIV/AIDS have been for the most part due to the opportunistic infections and neoplasias that accompany the syndrome⁽⁷⁾. The evolution of HIV and the appearance of new strains of the virus have however, changed the incidence of the disease with resultant changes in AIDS-related eye diseases and blindness. Research has indicated that anti-retroviral therapy has also modified the clinical progression of the disease⁽⁸⁾. The HIV virus has been found in the tear film and other ocular structures such as the cornea, vitreous and chorioretinal tissue. Ocular manifestations have been reported in 70 to 100% of individuals infected with HIV⁽⁹⁾. The ocular

manifestations may involve the adnexae and anterior and posterior segments of the eye. In addition, HIV/AIDS also presents with orbital and neuro-ophthalmic manifestations⁽⁹⁾. Anterior segment involvement usually results in tumours and external infections while posterior segment involvement usually results in HIV-retinopathy and a number of opportunistic infections of the retina and the choroid.

Early detection of the ocular manifestations of HIV/AIDS is critical since these ocular manifestations may be the primary presentation of the systemic infection⁽⁹⁾. This has implications for the prognosis of the disease. It is difficult to review this topic in one article considering the huge body of literature that exists on the ocular manifestations of HIV/AIDS. This study was done to evaluate the prevalence of various ocular manifestations and visual acuity in HIV seropositive patients attending the ophthalmology OPD of tertiary care centre.

OBJECTIVES:

1. To evaluate the prevalence of ocular manifestations in HIV seropositive patients attending the ophthalmology OPD of tertiary care centre.
2. To study various ocular manifestation and causes of blindness in HIV seropositive patients.

MATERIAL AND METHODS

The present Prospective observational study was conducted on 150 HIV seropositive patients attending the ophthalmology OPD of Shri Chatrapati Shivaji Maharaj General Hospital, Solapur from December 2020 to October 2022. HIV seropositive consented patients referred to ophthalmology OPD irrespective of ocular complaints or treatment status to routine ophthalmology examination or for routine ophthalmology examination, were included. Patients with other previous history of ocular disease were excluded.

After getting approval from ethics committee, study was started.

Written informed valid consent was taken from the patients in English and local language (Marathi) as perform approved by IEC. All patients were given Standard of Care during their participation in the study. Patients were selected based on inclusion criteria. Detailed history of the patients was taken as per case record proforma followed by General and systemic examination. Detailed ophthalmic examination were done and findings like visual acuity, external eye examination, ocular motility, pupillary reflexes, anterior segment examination by slit lamp bi microscopy and dilated fundus examination by indirect ophthalmoscopy were noted. Also, CD4 count of each patient was done.

Statistical/ Data Analysis:

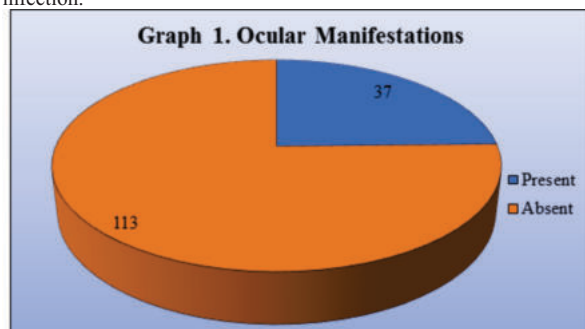
Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi square test, Fisher Exact tests were used as test of significance for qualitative data continuous data was represented as mean and standard deviation. Unpaired t test was used as test of significance to identify the mean difference between two quantitative variables for comparison. p value (Probability that the result is true) of 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

OBSERVATIONS AND RESULTS:

The present study was conducted on 150 HIV seropositive patients attending the ophthalmology OPD of tertiary care hospital from December 2020 to October 2022 to evaluate the prevalence of various ocular manifestations in HIV seropositive patients attending the ophthalmology OPD of tertiary care centre.

Prevalence of Ophthalmic Manifestations Associated with HIV Infection:

In the present study, out of 150 HIV positive patients, 37 (24.7%) were found to have Ocular manifestation which were associated with HIV infection.



Correlation Between Demographic Variables, Clinical Characteristics And Ophthalmic Manifestations Associated With HIV Infection:

Majority of the patients, 51 (34%), belong to age group 41 to 50 years followed by 36 (24%) were aged ≤ 30 years. Mean age of the patients was 41.1 ± 13.2 years ranging from 9 to 80 years. Prevalence of ocular manifestations was maximum in age groups 51 to 60 years (36.8%) and 41 to 50 years (27.5%). But the association was not significant (p value 0.402).

90 (60%) were males and 60 (40%) were females. Male to female ratio

was 1.5:1. Prevalence of ocular manifestations was more in females (30%) compared to males (21.1%). But the association was not significant (p value 0.216).

Table 1. Correlation between Demographic variables, clinical Characteristics and Ophthalmic Manifestations associated with HIV Infection:

		Ophthalmic Manifestations Associated with HIV Infection		Total	Chi square & p-value
		Present	Absent		
Age group	≤ 30 Years	5 (13.9%)	31 (86.1%)	36 (100%)	4.03, 0.402
	31 to 40 Years	9 (25.7%)	26 (74.3%)	35 (100%)	
	41 to 50 Years	14 (27.5%)	37 (72.5%)	51 (100%)	
	51 to 60 Years	7 (36.8%)	12 (63.2%)	19 (100%)	
	> 60 Years	2 (22.2%)	7 (77.8%)	9 (100%)	
Gender	Male	19 (21.1%)	71 (78.9%)	90 (100%)	1.53, 0.216
	Female	18 (30%)	42 (70%)	60 (100%)	
Clinical Staging	Stage I	21 (18.6%)	92 (81.4%)	113 (100%)	9.30, 0.010
	Stage II	13 (44.8%)	16 (55.2%)	29 (100%)	
	Stage III	3 (37.5%)	5 (62.5%)	8 (100%)	
Cd4 count (cells/mm ³)	≤ 250	4 (100%)	0 (0%)	4 (100%)	42.09, 0.000
	251 to 500	10 (83.3%)	2 (16.7%)	12 (100%)	
	501 to 750	15 (42.2%)	47 (75.8%)	62 (100%)	
	751 to 1000	7 (10.3%)	61 (89.7%)	68 (100%)	
	> 1000	1 (25%)	3 (75%)	4 (100%)	
Total	37 (24.7%)	113 (75.3%)	150 (100%)		

Most of the patients, 113 (75.3%) were belong to Stage I, 29 (19.3%) in Stage II and 8 (5.3%) were belong to Stage III. Prevalence of ocular manifestations was maximum in stage II (44.8%) followed by stage III (37.5%) and the association was also significant (p value 0.010).

68 (45.3%) patients had CD4 count between 751 to 1000 cells/mm³ and 62 (41.3%) patients had CD4 count between 501 to 750 cells/mm³. Only 18 (10.7%) patients had CD4 count less than 500 cells/mm³. Prevalence of ocular manifestations was maximum in patients with CD4 count ≤ 250 cells/mm³ (100%, all the patients had manifestations) and in patients with CD4 count between 251 to 500, it was 83.3%. As the CD4 count increases, prevalence decreases and this association was also significant (p value 0.000).

Table 2. Correlation between Visual Acuity and Ophthalmic Manifestations associated with HIV Infection:

Visual Acuity		Ophthalmic Manifestations Associated with HIV Infection		Total	Chi square & p-value
		Present	Absent		
Right Eye	6/6 to 6/18	18(48.65%)	93(82.30%)	111(74%)	49.52, 0.000
	6/24 to 6/60	4(10.81%)	12(10.62%)	16(10.67%)	
	< 6/60 to 1/60	5(13.51%)	0(0%)	5(3.33%)	
	FC* + (Close to face)	6(16.22%)	0(0%)	6(4%)	
	PL Present	1(2.70%)	8(7.08%)	9(6%)	
	No PL	3(8.11%)	0(0%)	3(2%)	
Left Eye	6/6 to 6/18	25(67.57%)	94(83.18%)	119(79.33%)	30.6, 0.000
	6/24 to 6/60	0(0%)	13(11.50%)	13(8.67%)	
	< 6/60 to 1/60	5(13.51%)	2(1.77%)	7(4.67%)	
	FC* + (Close to face)	4(10.81%)	0(0%)	4(2.67%)	
	PL present	1(2.70%)	4(3.54%)	5(3.33%)	
	No PL	2(5.41%)	0(0%)	2(1.33%)	
Total	37(100%)	113(100%)	150(100%)		

* Finger Count

Most of the patients (111, 74%) had normal vision (6/6 to 6/18), 16 (10.7%) patients had vision 6/24 to 6/60 and vision of < 6/60 to 1/60 observed in 5 (3.3%) patients. In 6 (4%) patients fingers count present close to face, 9 (6%) had perception to light. 3 (2%) didn't have perception to light. 15 (40.5%) patients with ocular manifestations were found to have diminution of vision (visual acuity < 6/60) compared to only 8 (7.1%) patients without ocular manifestations had diminution of vision. The difference was statistically significant (p value 0.000).

Table 3. Correlation between Anterior and posterior segment findings and Ophthalmic Manifestations associated with HIV Infection:

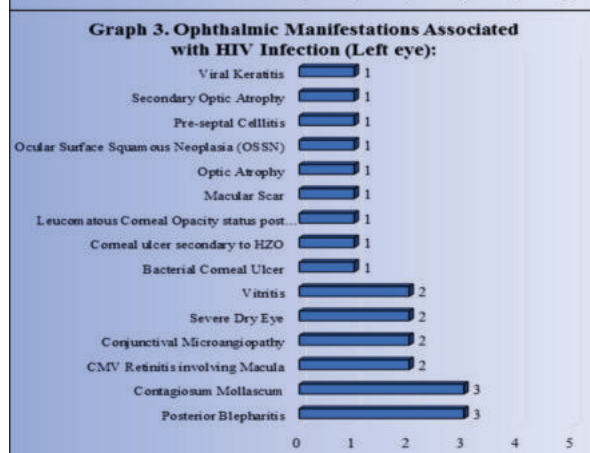
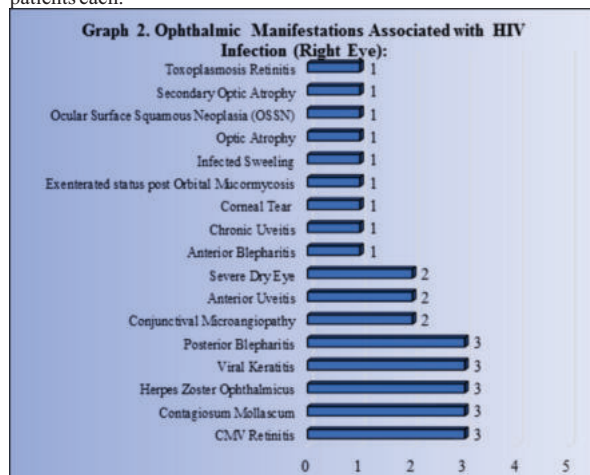
Anterior and Posterior Segments		Ophthalmic Manifestations Associated with HIV Infection		Total	Chi square & p-value
		Present	Absent		
Anterior Segment (Rt Eye)	Abnormal	24(64.86%)	1(0.88%)	25(16.67%)	77.6, 0.000
	Normal	13(35.13%)	112(99.11%)	125(83.33%)	
Posterior Segment (Rt Eye)	Abnormal	8(21.62%)	0(0%)	8(5.33%)	29.6, 0.008
	Normal	26(70.27%)	105(92.92%)	131(87.33%)	
	Can't be assessed	3(8.11%)	8(7.08%)	11(7.33%)	
Anterior Segment (Lt Eye)	Abnormal	14(37.83%)	0(0%)	14(9.33%)	42.8, 0.000
	Normal	23(62.16%)	113(100%)	136(90.67%)	
Posterior Segment (Lt Eye)	Abnormal	6(16.22%)	0(0%)	6(4%)	22.9, 0.000
	Normal	27(72.97%)	109(96.46%)	136(90.67%)	
	Can't be assessed	4(10.81%)	4(3.54%)	8(5.33%)	
Total		37(100%)	113(100%)	150(%)	

Ophthalmic Manifestations Associated with HIV Infection (Right Eye):

Common ophthalmic lesions (Right Eye) associated with HIV infection were CMV Retinitis, Contagiosum Molluscum, Herpes Zoster Ophthalmicus, Viral Keratitis and Posterior Blepharitis in 3 (2.0%) patients each, Conjunctival Microangiopathy, Anterior Uveitis and Severe Dry Eye were observed in 2 (1.3%) patients each.

Ophthalmic Manifestations Associated with HIV Infection (Left Eye):

Common ophthalmic lesions (Left Eye) associated with HIV infection were Posterior Blepharitis Contagiosum Molluscum in 3 (2.0%) patients each, CMV Retinitis involving Macula, Conjunctival Microangiopathy, Severe Dry Eye and Vitritis observed in 3 (2%) patients each.



Most of the patients (119, 79.3%) had normal vision (6/6 to 6/18), 13 (8.7%) patients had vision 6/24 to 6/60 and vision of < 6/60 to 1/60 observed in 7 (4.7%) patients. In 4 (3.7%) patients fingers count present close to face, 5 (3.3%) had perception to light. 2 (1.3%) didn't have perception to light. 13 (35.1%) patients with ocular manifestations were found to have diminution of vision compared to only 4 (3.5%) patients without ocular manifestations had diminution of vision. The difference was statistically significant (p value 0.000).

Table 4: Causes Of Blindness In HIV Positive Patients:

Causes of Blindness	Frequency	Percentage (n=12)
Optic Atrophy	3	25
Severe Dry Eye	2	16.7
Corneal Ulcer Secondary to HZO	1	8.3
Secondary Optic Atrophy	1	8.3
Complicated Cataract with Chronic Uveitis	1	8.3
CMV Retinitis 3	1	8.3
HZO	1	8.3
Orbital Mucormycosis	1	8.3
Toxoplasma Retinitis	1	8.3
Total	20	100

Blindness was observed in total 12 (8%) patients. Out of 12 patients, most common cause was found to be Optic Atrophy in 3 (25%) and Severe Dry Eye in 2 (16.7%) cases.

DISCUSSION:

The present study was conducted on 150 HIV seropositive patients attending the ophthalmology OPD of tertiary care hospital from December 2020 to October 2022 to evaluate the prevalence of various ocular manifestations in HIV seropositive patients attending the ophthalmology OPD of tertiary care centre.

Prevalence of Ocular manifestation which were associated with HIV infection

In the present study, out of 150 HIV positive patients, 37 (24.7%) were found to have Ocular manifestation which were associated with HIV infection. There are many studies correlating the prevalence of Ophthalmic manifestations with HIV infection.

There is a study done by *Sophia Pathai et al*⁽¹⁰⁾ who determined the ophthalmic manifestations of HIV at the time of enrolment into ART Centre i.e., naïve to ART which proved the prevalence of ophthalmic manifestations to be 17.5%. However, prevalence rate was higher in the *Gururaj et al*⁽¹¹⁾ study which had 54%. In a study by *Wangting Li et al*⁽¹²⁾, prevalence of Ocular manifestation in HIV patients was 8% which was less than our study.

SOCIODEMOGRAPHIC STATISTICS:

Age of the patients and Ophthalmic Manifestations Associated with HIV Infection:

In the present study, prevalence of ocular manifestations was maximum in age groups 51 to 60 years (36.8%) and 41 to 50 years (27.5%). But the association was not significant (p value 0.402). This pattern was similarly noticed in *Biswas et al*⁽¹³⁾ and *Gururaj et al*⁽¹¹⁾ study. Also comparable with the Gururaj et al study was the increase in prevalence with increase in age. Similar pattern was also seen in study by *Lamichhane G et al*⁽¹⁴⁾.

Gender of the patients and Ophthalmic Manifestations Associated with HIV Infection

Prevalence of ocular manifestations was more in females (30%)

compared to males (21.1%). But the association was not significant (p value 0.216). This finding was similarly noted in **Biswas et al**⁽¹³⁾ and **Lamichhane G et al**⁽¹⁴⁾ study. As previously mentioned, the age gender distribution in our study was not significant, $p=0.3$. This was also the finding in **Lamichhane G et al**⁽¹⁴⁾ study.

Clinical Staging and Ophthalmic Manifestations Associated with HIV Infection:

Prevalence of ocular manifestations was maximum in stage II (44.8%) followed by stage III (37.5%) and the association was also significant (p value 0.010). The findings were similar in the **Gururaj et al**⁽¹¹⁾ and **Amare et al**⁽¹⁵⁾ study. With p value of 0.010 we can conclude that prevalence of ocular manifestation increases with the clinical staging of disease. And this is probably due to the increase in the opportunistic infection in these stages. This was observed both in **Gururaj et al**⁽¹¹⁾ and the **Amare et al**⁽¹⁵⁾ study as well.

Association between CD4 Count and Ophthalmic Manifestations Associated with HIV Infection:

Prevalence of ocular manifestations was maximum in patients with CD4 count ≤ 250 cells/mm³ (100%, all the patients had manifestations) and in patients with CD4 count between 251 to 500, it was 83.3%. As the CD4 count increases, prevalence decreases and this association was also significant (p value 0.000). This was comparable to the Ethiopian study by **Amare et al**⁽¹⁴⁾. However, the prevalence of ocular manifestations in the range < 250 cells/mm³ fell drastically in comparison **Gururaj et al**⁽¹⁵⁾ and **Sophia Pathai et al**⁽¹⁶⁾, and significantly with **Amare et al**⁽¹⁴⁾. P value in our study was 0.000, which was significant. In the study by **Sophia Pathai et al**⁽¹⁶⁾, the prevalence of ophthalmic manifestations in patients with CD4 count less than 200 cells/mm³ was 23.8%.

There was significant association found between visual acuity and ocular manifestations (both p values 0.000). Among the 37 patients, 18 had normal visual acuity on right side and 25 had normal visual acuity on left side. Hence the prevalence of visual impairment due to HIV associated ocular manifestation is around 30.2% on right side and 32.4% on left side. **Sophia Pathai et al**⁽¹⁶⁾ in their study found that prevalence of any visual impairment (including blindness) was low (8.5%) compared to our study. **Pratik Y. Gogri et al**⁽¹⁶⁾ found 25% patients with visual acuity $< 6/60$ similar to our study.

Anterior and posterior Segment findings and Ophthalmic Manifestations Associated with HIV Infection: In both eyes, abnormal Anterior and Posterior Segment findings were observed significant more in patients with ocular manifestations due to HIV compared to patients without ocular manifestation due to HIV. Prevalence of anterior and posterior segment abnormalities in present study were similar to findings of a study by **Pratik Y. Gogri et al**⁽¹⁶⁾, total of 26 patients (65%) had anterior segment lesions and 40% patients had posterior segment lesions. The prevalence of anterior segment findings was significantly higher in comparison to the two Indian studies mentioned above (**Gururaj et al**⁽¹¹⁾ and **Sophia Pathai et al**⁽¹⁶⁾). In our study, the prevalence of posterior segment manifestations was more compared to anterior segment, which exactly matches with the study done by **Sophia Pathai et al**⁽¹⁶⁾.

Ophthalmic Manifestations Associated with HIV Infection:

Common ophthalmic lesions (Right Eye) associated with HIV infection were CMV Retinitis, Contagiosum Molluscum, Herpes Zoster Ophthalmicus, Viral Keratitis and Posterior Blepharitis in 3 (2.0%) patients each, Conjunctival Microangiopathy, Anterior Uveitis and Severe Dry Eye were observed in 2 (1.3%) patients each. And in Left Eye, Posterior Blepharitis Contagiosum Molluscum in 3 (2.0%) patients each, CMV Retinitis involving Macula, Conjunctival Microangiopathy, Severe Dry Eye and Vitritis observed in 3 (2%) patients each.

In the study done by **Sophia Pathai et al**⁽¹⁶⁾, CMV retinitis (8.7%) is the most common manifestation followed by HIV retinopathy (4.7%) which were higher as compared to our study. On comparing our study with **Biswas et al**⁽¹³⁾, we found a similar prevalence of blepharitis. They also mentioned in text both the lesion to be the most common anterior segment manifestation. **Pratik Y. Gogri et al**⁽¹⁶⁾ revealed that the most common finding was anterior uveitis (12.5%) followed by molluscum contagiosum and viral keratitis and blepharitis. CMV retinitis (12.5%) was the most common opportunistic infection of the retina/choroid followed by toxoplasmosis and tuberculosis.

CONCLUSION

The prevalence of Ophthalmic manifestations occurring in adults due to HIV infection was 24.7% which affects commonly the reproductive age group. It involves visual acuity, anterior segment and posterior segment. However, it's the posterior segment manifestations which were found to be more prevalent. HIV associated blindness was observed 8% patients, most common being Optic Atrophy (25%) and Severe Dry Eye (16.7%) cases.

No significant association was found with the age and gender. Though, significant association was found with clinical stage, CD4 count, visual acuity, anterior and posterior findings of the disease. Common ophthalmic lesions associated with HIV infection in right eye were CMV Retinitis, Contagiosum Molluscum, Herpes Zoster Ophthalmicus and Viral Keratitis and in left eye were Posterior Blepharitis, Contagiosum Molluscum, CMV Retinitis involving Macula and Conjunctival Microangiopathy.

However, most patients were unaware of their ophthalmic status and there is the need for screening. Hence, with the number of ocular findings observed, the present study strongly emphasizes the importance of routine ophthalmic screening at the time of diagnosis of HIV seropositivity in adults.

CLINICAL PICTURES:



Fig. 1: Conjunctival microangiopathy

Fig. 2: Ocular surface squamous neoplasia (OSSN)



Fig. 3: Leucomatous corneal opacity status post Herpes Zoster Ophthalmicus (HZO)

Fig. 4: Pre-septal cellulitis



Fig. 5: Severe dry eyes

Fig. 6: Rhino-orbital Mucormycosis



Fig. 7: Herpes Zoster Ophthalmicus (HZO) with corneal ulcer

Fig. 8: Viral keratitis

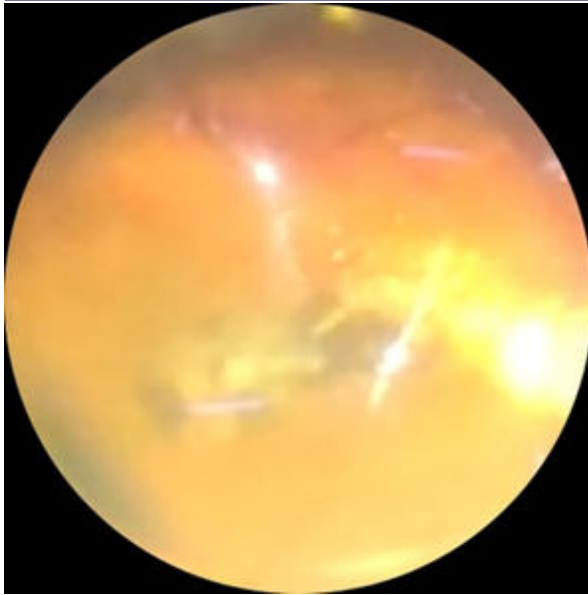


Fig. 11: CMV Retinitis

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