

OCULAR FINDINGS OF HIV/AIDS PATIENTS AND THEIR CORRELATION WITH CD4 COUNT*Vishwanath Bannikuppe Narasimhaiah¹, Shruti Prakash Naik², Shashidhar Swamy³, Lekha Lakshmikanth⁴*¹Associate Professor, Department of Ophthalmology, Bangalore Medical College and Research Institute, Bangalore.²Postgraduate Student, Department of Ophthalmology, Bangalore Medical College and Research Institute, Bangalore.³Professor, Department of Ophthalmology, Bangalore Medical College and Research Institute, Bangalore.⁴Postgraduate Student, Department of Ophthalmology, Bangalore Medical College and Research Institute, Bangalore.

ABSTRACT

BACKGROUND

Ocular involvement in HIV/AIDS includes various clinical presentations including both anterior and posterior segment, most of the manifestations are those of the posterior segment. The severity of these posterior segment changes increases with decreased CD4 count. Aim of the study is to look for severity of ocular manifestations in correlation with CD4 count.

MATERIALS AND METHODS

A cross sectional study of ocular changes in 360 cases of HIV/AIDS patients between October 2016-May 2018. All patients underwent thorough ophthalmic evaluation including BCVA, Anterior segment examination with slit lamp biomicroscopy and posterior segment examination with Indirect ophthalmoscopy, CD4 count was noted and patients were categorised based on CD4 count and correlation of severity of ocular manifestations with CD4 count done with statistical software SPSS.

RESULTS

Out of 360 patients, 267 were on HAART. 54.4 % were males and 45.6% females. Maximum number of patients were in the age group of 31-40 years. Ocular manifestations were present in 252(70%) patients. Most common manifestation was HIV retinopathy (18.8%) followed by dry eye (6.9%), cataract (5.5%), CMV retinitis (5.2%), choroiditis (3.6%).

CMV retinitis, choroiditis and orbital cellulitis were common in patients with CD4+count<50. Severity of ocular manifestations involving posterior segment and orbital cellulitis increased with decrease in CD4 count. There was statistically significant association between severity of ocular manifestations with CD4 count ($P<0.001$), and vision with CD4 count ($P<0.001$).

CONCLUSION

Patients with low CD4 count are at increased risk of acquiring severe manifestations such as posterior segment changes and orbital cellulitis. Complete ocular evaluation is must in all patients with HIV/AIDS for early diagnosis and treatment of sight threatening complications.

KEYWORDS

HIV/AIDS; CD4 Count; Ocular manifestations; HAART.

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BACKGROUND

HIV (Human immune deficiency virus) infection is the first major pandemic of twentieth century faced by mankind. This is caused by a retrovirus HIV belonging to Lentivirus subfamily.¹ HIV causes a wide spectrum of diseases including an acute mononucleosis like syndrome and Acquired Immunodeficiency Syndrome (AIDS) related complex.²

World Health Organization (WHO) estimate of total HIV burden in the world is approximately 33.2 million.³ The life

time cumulative rate of developing ocular lesions in HIV patients is 52-100% in various studies.¹

Ocular involvement in AIDS is very common and includes various clinical presentations including both anterior and posterior segment, most of the manifestations are those of the posterior segment like HIV retinopathy, opportunistic infections, neuro ophthalmic lesions and unusual neoplasms. Immune recovery uveitis and drug reactions are associated with drugs like nevirapine and indinavir in Highly Active Antiretroviral Therapy (HAART).^{3,4}

Even in the HAART era many patients with HIV infection have visual symptoms in the absence of active opportunistic infection.⁵ The main mode of transmission being sexual transmission^{6,7,8} and the diagnosis was made with ELISA /WESTERN BLOT.⁹

Ocular lesions were more common when CD4+ cell count was less than 200 cells/mm.³ There seemed significant correlation between low CD4 and severe ocular manifestations.¹⁰ CMV retinitis, progressive outer retinal

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necrosis, acute retinal necrosis and orbital cellulitis were seen if CD4 was less than 200.¹¹⁻¹⁵ Adnexal and anterior segment manifestations include blepharitis, molluscum contagiosum, dry eye, uveitis and cataract.¹⁶⁻²¹

CD4⁺ T-lymphocyte count is proved to be a reliable predictor of immune status of patient for the risk of various infections. Hence the need for study of severity of ocular manifestations in correlation with CD4 counts.¹

MATERIALS AND METHODS

This is a cross sectional study, conducted on 360 HIV/AIDS patients. The study was conducted in Minto ophthalmic hospital and Bowring and Lady Curzon hospital attached to Bangalore Medical College and Research Institute, Bangalore. Study period was from October 2016 to May 2018.

Inclusion Criteria

1. All HIV positive patients coming to Minto and Bowring Lady Curzon hospital for ocular evaluation.
2. HIV positive patients giving written informed consent.

Exclusion Criteria

1. Patients not willing for ocular evaluation
2. HIV positive patients with diabetic retinopathy changes

An informed consent was obtained from every patient. Cases were collected according to piloted proforma meeting the objectives of the study.

Vision was recorded with the help of Snellen's Chart. Torch light examination was done to look for anterior segment grossly and pupillary reactions both direct as well indirect. Slit lamp biomicroscopy evaluation was done to document any anterior segment pathology, the size of the pupil and its dilatation with mydriatic was evaluated. Based on the slit lamp findings other tests such as s tonometry, lacrimal syringing, and Schirmer's test was done to confirm the slit lamp findings.

Standard mydriatic drops were used to dilate the pupils and the detailed posterior segment evaluation done with Indirect Ophthalmoscope with 20D lens. In cases of macular changes slit lamp examination with 78/90 D lens was done. In case if the media was hazy B Scan ultrasonography was done. OCT and FFA were done if indicated. All the patients underwent general physical examination, and systemic examination CD4 count was noted, and was ordered for CD4 if not done in past 3 months. The patients were categorised into one of the 4 categories depending on CD4 count such as-

- a. CD4 count >500 cells/mm³
- b. CD4 count between 200-499 cells/mm³
- c. CD4 count 50-199 cells/mm³
- d. CD4 count between <50 cells/mm³. Correlation between CD4 counts and severity of ocular manifestations were studied using statistical software SPSS 18.0

RESULTS

In our study out of 360 patients 54.4% were males, 45.6% were females. The mean age was 31-40 years. The major mode of transmission of HIV was sexual 87.8%. In our study family history was found to be positive in 34.7% patients as the main mode of transmission was heterosexual transmission. Chief complaint at the diagnosis of HIV was fever 41.9% followed by cough, diarrhoea, weight loss and pain abdomen. In our study out of 360 patients 74.2% were on antiretroviral therapy (ART). The mean duration of ART was 36 months. Majority of ocular complaint at the time of evaluation was diminution of vision which was mainly due to posterior segment lesions and cataract.

Ocular Findings	No. of Patients	%
Absent	108	30.0
Posterior Segment	120	33.3
Anterior Segment	110	30.6
Neuro-ophthal	18	5.0
Orbit	4	1.1
Total	360	100.0

Table 1. Various Ocular Manifestations in Patients with HIV/AIDS Patients

In our study posterior segment manifestations were 33.3% in which HIV retinopathy was 18.8% could be due to the reason that many of our patients 74.2% were on ART.

Post Segment	No. of Patients (n=360)	%
• Within Normal Limits	240	66.6
• HIV Retinopathy	68	18.8
• CMV Retinitis	19	5.27
• Choroiditis	13	3.6
• Vasculitis	4	1.11
• Others	16	4.4

Table 2. Distribution of Posterior Segment Manifestations in HIV/AIDS Patients

CD4 Category	No. of Patients	%
≤50	81	22.5
51-199	141	39.2
200-499	96	26.7
>500	42	11.7
Total	360	100.0

Table 3. CD4 Count Category Distribution

In our study majority of patients with ocular manifestations had CD4 count in the range of 51-199 (<200).

Vision	CD4 levels				Total (n=360)	P value
	>500 (n=42)	200-499 (n=96)	51-199 (n=141)	≤50 (n=81)		
Right Eye						
• 6/6-6/9	34(81%)	67(69.8%)	78(55.3%)	36(44.4%)	215(59.7%)	<0.001**
• 6/12-6/18	4(9.5%)	18(18.8%)	33(23.4%)	6(7.4%)	61(16.9%)	
• 6/24-6/36	3(7.1%)	4(4.2%)	14(9.9%)	7(8.6%)	29(8.1%)	
• 6/60	0(0%)	2(2.1%)	9(6.4%)	9(11.1%)	20(5.6%)	
• <6/60	1(2.4%)	5(5.2%)	7(5%)	22(27.2%)	35(9.7%)	
Left Eye						
• 6/6-6/9	34(81%)	66(68.8%)	77(54.6%)	41(50.6%)	218(60.6%)	<0.001**
• 6/12-6/18	5(11.9%)	18(18.8%)	35(24.8%)	5(6.2%)	64(17.8%)	
• 6/24-6/36	2(4.8%)	6(6.3%)	15(10.6%)	10(12.3%)	32(8.9%)	
• 6/60	0(0%)	1(1%)	6(4.3%)	10(12.3%)	17(4.7%)	
• <6/60	1(2.4%)	5(5.2%)	8(5.7%)	15(18.5%)	29(8.1%)	

Table 4. Vision Distribution of Patients Studied in Relation to CD4 Levels

Chi-Square/Fisher Exact Test.

Table 4 correlation between vision and CD4 count. In both eyes vision <6/60 was found to be majority in category 4 where CD4 count was < 50. The correlation between vision and CD4 was statistically significant $p < 0.001\%$ with chi square / Fisher Exact Test.

In our study we found correlation between age and CD4 count in which maximum cases were in the age group range of 31-40 years and maximum cases with CD4 <50 were in the same group with a significance of $p = 0.025$.

Ocular Findings	CD4 levels				Total
	>500	200-499	51-199	≤50	
Absent	32(76.2%)	44(45.8%)	29(20.6%)	4(4.9%)	109(30.3%)
Posterior Segment	0(0%)	13(13.5%)	57(40.4%)	50(61.7%)	120(33.3%)
Anterior Segment	10(23.8%)	39(40.6%)	48(34%)	13(16%)	110(30.6%)
Neuro Ophthal	0(0%)	0(0%)	7(5%)	11(13.6%)	18(5%)
Orbit	0(0%)	0(0%)	0(0%)	3(3.7%)	3(0.8%)
Total	42(100%)	96(100%)	141(100%)	81(100%)	360(100%)

Table 5. Ocular Findings in Relation to CD4 Levels

$P < 0.001$, Significant, Chi-Square Test.

Table-5 There is significant correlation between severity of ocular manifestations such as posterior segment findings and opportunistic infections which increased with decrease in CD4 count with $p < 0.001$.



Figure 1. Fundus picture Showing CMV Retinitis



Figure 2. Fundus picture of HIV Retinopathy



Figure 3. Clinical Picture of Left Eye Ocular Surface Squamous Neoplasm

DISCUSSION

Since its first report in 1981, AIDS had spread rapidly across the continents. The incidence of HIV is increasing in India since 1986, when first case of HIV was reported from Chennai. The life time cumulative rate of developing ocular lesion in HIV patients is 52-100% in various study.¹

The prevalence of ocular manifestation in this study was found to be 70% which is much higher than previous studies could be due to the reason that this study was done in tertiary care centre where screening ocular evaluation was done at the time of diagnosis of HIV itself and due to many patients who were referred from peripheries to our centre as it is a tertiary centre.

In our study out of 360 patients 54.4% were males, 45.6% were females. The mean age was 31-40 years which is similar to previous studies by D K Sahu et al² where mean age was 34 years, Ram Sharma et al¹ mean age was 21-40 years, Sisay Bekele et al¹⁰ mean age was 30-34 years.

The major mode of transmission of HIV was sexual 87.8% which was similar to study by Ram Sharma et al.¹ where it was 94%. In our study family history was found to be positive in 34.7% patients as the main mode of transmission was heterosexual transmission.

In this study main complaints at the diagnosis of HIV was fever 41.9% followed by cough, diarrhoea, weight loss and pain abdomen

In our study out of 360 patients 74.2% were on antiretroviral therapy. The mean duration of ART was 36 months which was similar to study by Sisay Bekele et al¹⁰ where the mean duration was 27 months.

Majority of ocular complaint at the time of evaluation was diminution of vision which was mainly due to posterior segment lesions and cataract. In our study posterior segment manifestations were 33.3% in which HIV retinopathy was 18.8% which is much less than the previous study by Ram Sharma et al¹ where it was 46% could be due to the reason that many of our patients 74.4% were on ART. CMV retinitis in our study was 5.27% which was much less than previous studies by Ram Sharma et al¹ could be because their study was done in pre HAART era when the rate of prevalence of CMV opportunistic infection was high

due to decreased CD4 count and hence decreased immunity. Tubercular choroiditis in our study was 3.6% which was less than the study by D. K. Sahu et al² where it was 11% but almost similar to Ram Sharma et al¹ 5% due to the effect of both HAART and anti-tubercular therapy.

In our study the anterior segment manifestations were 30.6% of which dry eye was majority with 6.9% which is similar to previous studies by Sisay Bekele et al. where it was 11%. Ocular surface squamous neoplasia in our study was 1.9% which was similar to previous studies by Sisay Bekele et al in which it was 2.3%. Blepharitis was 2.2% molluscum contagiosum was 1.3% which were similar to previous studies and by Sisay Bekele et al. where these were 3.2% and 2.6% respectively, this could be because both the studies were done in HAART era.¹⁰

In this study neuro ophthalmic manifestations were 5% which was more than previous study by Sisay Bekele¹⁰ 2.6% this could be because most of our patients had CD4 count <200.

In our study majority of patients with ocular manifestations had CD4 count in the range of 51- 199 i.e < 200 which is less than previous study by Sisay Bekele et al¹⁰ where mean CD4 count was 308 this could be because most of our patients were diagnosed to be having HIV in the late stage when the CD4 count was <200.

In our study majority had a vision in the range of 6/9-6/6 which was 60% in both the eyes which was much less than the previous studies could be because most of the patients were with CD4 count <200 and screened early at the time of diagnosis of HIV.

We found correlation between vision and CD4 count in our study which was significant with $p < 0.001$, where majority patients with vision <6/60 were in the category 4, CD4 count of <50.

In our study we found correlation between age and CD4 count in which maximum cases were in the age group range of 31-40 years and maximum cases with CD4 < 50 were in the same group with a significance of $p = 0.025$.

In this study we found significant correlation between severity of ocular manifestations such as posterior segment, neuro ophthalmic, orbital manifestations increased with decrease in CD4 count with $p < 0.001$ which is similar to

previous study by Sisay Bekele¹⁰ where they got $p = 0.001$, this is because most of our patients were with CD4 count <200 and were more prone for opportunistic infections. Opportunistic infections such as CMV retinitis, orbital cellulitis and cryptococcal meningitis with papilloedema and neoplasia i.e. ocular surface squamous neoplasia were seen in patients with CD4 <50.

CONCLUSION

This is a cross sectional study to look for the ocular manifestations and their correlation with CD4 count in patients with HIV/AIDS. This study demonstrated significant correlation between ocular manifestations and low CD4 count. Detailed ophthalmic evaluation including fundus examination is must in all cases of HIV/AIDS patients as it may help in early diagnosis, treatment and prevention of

sight threatening complications due to opportunistic infections. We acknowledge that this study is limited as it is done in tertiary centre and a larger prospective randomised control trial should be performed to further assess the severity of ocular manifestations and their correlation with CD4 count.

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