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To Study Prevalence of Ocular Surface Diseases in Human Immunodeficiency Virus Positive Patients and its Correlation with CD4 Count – a Cross Sectional Observational Study

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Abstract

To determine prevalence of ocular surface diseases in Human Immunodeficiency Virus positive patients and its correlation with CD4 count a cross sectional observational study. A cross sectional observational study. The present observational study was conducted at a tertiary health care institute in Central India. There was a total of 233 Human Immunodeficiency Virus positive patients who were enrolled in this study and their prevalence was calculated for Ocular Surface Diseases which was also compared with their CD4+ cell count. Permission to conduct the study on Human Immunodeficiency Virus positive patients was taken from Maharashtra State Acquired Immunodeficiency Disease Control Society and National Acquired immunodeficiency disease Control Organisation. Statistical analysis done using MSExcel2019 and Graph pad prism. The overall prevalence of OSD was 36.5% and that most common OSD found were DED, Blepharitis, and Conjunctivitis. Most of study participants with ocular surface diseases had CD4 cell count which was statistically significant. The present study determines the prevalence of ocular manifestations in the enrolled study participants who are Human Immunodeficiency Virus positive, where CD4 cell counts were found to be between low and very low for most of the study participants.

Keywords: *Human immunodeficiency virus positive participants, ocular surface diseases, CD4 cell count, dry eye disease.*

Introduction

Background: Human Immunodeficiency Virus (HIV) continues to be a significant global health issue, affecting millions worldwide. As of 2022, approximately 39 million people were living with HIV, of which 1.3 million became newly infected in 2022.[1] The immunosuppressive nature of HIV, particularly its effect on CD4+ T-lymphocytes, predisposes patients to a range of opportunistic infections and other complications, including ocular surface diseases (OSDs).Ocular surface diseases encompass a spectrum of conditions affecting the cornea, conjunctiva, and eyelids, potentially leading to significant morbidity and a reduction in quality of life[2]. These conditions include keratoconjunctivitis sicca (dry eye syndrome), herpes simplex and zoster infections, blepharitis , uveitis, ocular surface neoplasms like kaposi sarcoma and opportunistic infections such as cytomegalovirus retinitis, this prevalence and severity of OSDs are often linked to the degree of immunosuppression, typically measured by CD4 count.

Rationale for study

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 Conditions such as dry eye syndrome are prevalent among HIV-infected individuals, often resulting from the chronic inflammatory state induced by the virus. India, home to the third-largest population of people living with HIV globally, faces unique challenges in managing the epidemic [3]The correlation between ocular surface diseases and CD4 count in individuals living with HIV is well-documented. This study specifically indicated that individuals with CD4 counts below 200 cells/mm³ were more likely to experience severe ocular surface diseases compared to those with higher CD4 counts.[4]

Objectives of study

The study aims to determine the prevalence of ocular surface diseases in HIV positive and its correlation with CD4 count.

1. Primary objective**:** To know the prevalence of ocular surface diseases in HIV positive patients
2. Secondary objective**:** To study relation of CD4 count and ocular surface diseases in HIV positive patients

Materials and Methods

Study setting: this study was conducted in HIV care centre of Tertiary health care hospital of Central India over a period of 18 months (from December 2022 to May 2024).

Study design: This prospective observational cross sectional study was conducted on 233 patients.

Ethic statement: Study was conducted after getting approval from institutional ethics committee, and as per the guidelines of declaration of Helsinki.

Written informed consent was been taken from all participants enrolled in study.

Permission to conduct the study on HIV positive patients was taken from Maharashtra State AIDS Control Society (MSACS) and National AIDS Control Organisation (NACO).

Sampling Strategy

Inclusion Criteria

- HIV positive patients of all sexes in the age group of 18-60 years.
- All patients with co-existent anterior and posterior segment where included.
- Patients willing to sign informed consent form.

Exclusion Criteria

- With age less than 18 years and more than 60 years
- Patients with similar ocular manifestations secondary to

immunosuppressant, occupational hazards or environmental causes were excluded.
- Preexisting anterior segment diseases.
- Preexisting corneal degenerations and dystrophies.
- HIV positive patients not willing to be a part of study.

Sample Size: Sample Size of 233 patients was calculated to determine the prevalence of ocular surface diseases in HIV positive patients with a precision of 5% by taking prevalence as 19% from previous study.

Reference Study: A cross-sectional study on Ocular manifestation of HIV/AIDS and correlation with CD4+ cells count among adult HIV/AIDS patients in Jimma town, Ethiopia: a cross sectional study, 2013 by Bekele, Gelaw, and Tessema.

Study Procedure:
- Detailed demographic profile of the patients including age, gender, ethnic group and residence of diagnosed HIV patients were undertaken.
- Screening: Symptoms like redness, pain, itching, dryness, foreign body sensation, diminution of vision, lesions over eyelids or face or nose. This was done using dry eye disease questionnaire and ocular surface disease index.
- Ocular examination and evaluation protocol: A careful and detailed ocular examination was carried out which includes- Best corrected visual acuity assessed by using Snellen's distant vision chart and Snellen's near vision chart.
- Examination of adnexa and extra ocular structures included the examination of face, orbits ,eyebrows, eyelids, palpebral fissure using pen torch and slit lamp biomicroscopy.
- Examination of anterior segment – conjunctiva, cornea, anterior chamber, iris, pupil, lens was carried out by slit lamp biomicroscopy.
- Fundus examination with indirect and direct ophthalmoscope and +90D lens on slit lamp biomicroscopy.
- Specific investigations – especially for dry eye disease done were tear film breakuptime(TBUT),Schirmer's test,staining procedures using fluorescein , rose Bengal and Lissamine staining strips
- Laboratory investigations: like complete hemogram, serum creatinine, blood urea, blood sugar was performed, CD_{4+} T lymphocyte count was performed.

Statistical Analysis: % of patients provisionally diagnosed as ocular surface diseases will be recorded. Correlation of CD4 count with ocular surface diseases of any will be evaluated using appropriate statistical tests .All statistical analysis will be done using MSExcel2019 and Graph pad prism.

Data Management: Collected data was checked, edited at the end of every day during the period of data collection. Data was entered in Microsoft Excel 2019 then rechecked and cleaned after entry to ensure the quality of data.

Data analysis plan and methods: Data analysis was done using Epi Info™ 7.2.6.0
- **Continuous variables:** Summarized as mean with standard deviation.
- **Categorical variables:** Summarized as proportion.
- **Association:** Pearson chi-square test and Fisher's exact test were applied to find out the significant association between the final outcome of retina maturity and various factors associated with it.
- **Significance level was kept at $p<0.05$**

Results

- In the present study, the study participants were mostly young adults and middle aged with highest frequency belonging to 36-45 years age group and median age of 40±10.15 years.
- The gender distribution in our study slightly favoured females to males, females 122 (52.4%) and males 111 (47.6%) respectively.
- Maximum study subjects resided in urban areas201 (86.3%) and the remaining 32(13.7%) resided in rural region.
- Their visual acuity in right eye as measured by Snellen's chart. 39.1% study subjects had normal 6/6 vision in their right eye, 20.2% had 6/12 vision, 12% had 6/9 vision, 11.6% had 6/36 vision and very few had debilitating vision , visual acuity in left eye was found to be of 6/6 (43.3%) followed by 6/18 (12.9%), then 6/36 (11.6%) and 6/24 (11.2%).
- Among them 68.7% had normal anterior segment whereas 31.8% had abnormal findings in right eye and 67.8% and 32.2% in left eye respectively.
- At least one ocular manifestation were present in 36.5% of study subjects and in 63.5% there were no manifestations.
- Most of the adnexal manifestations were seen with CD4 cell count 200-499 cells/mm^3, with 56.5% having one or the other adnexal manifestation like Blepharitis, Conjunctivitis, Dry eye disorder (DED).
- There were 40% study subjects showing adnexal manifestations with CD4 cell count between 0-199 cells/mm^3 and only 3.5% study subjects having adnexal manifestations had CD4 cell count ≥500 mm^3.
- It can be gleaned from this that ocular manifestations were seen more in study subjects having less CD4 cell count and this has shown to be statistically significant with a p value of <0.001.

Table 1: Distribution of study subjects according to age

Age group (in years)	Number	Percent
18-25	17	7.3
26-35	69	29.6
36-45	78	33.5
46-55	55	23.6
56-65	14	6.0
Total	233	100.0

Minimum= 19 years Maximum= 60 years
Median= 40±10.15 years

Chart 1: Distribution of study subjects according to age

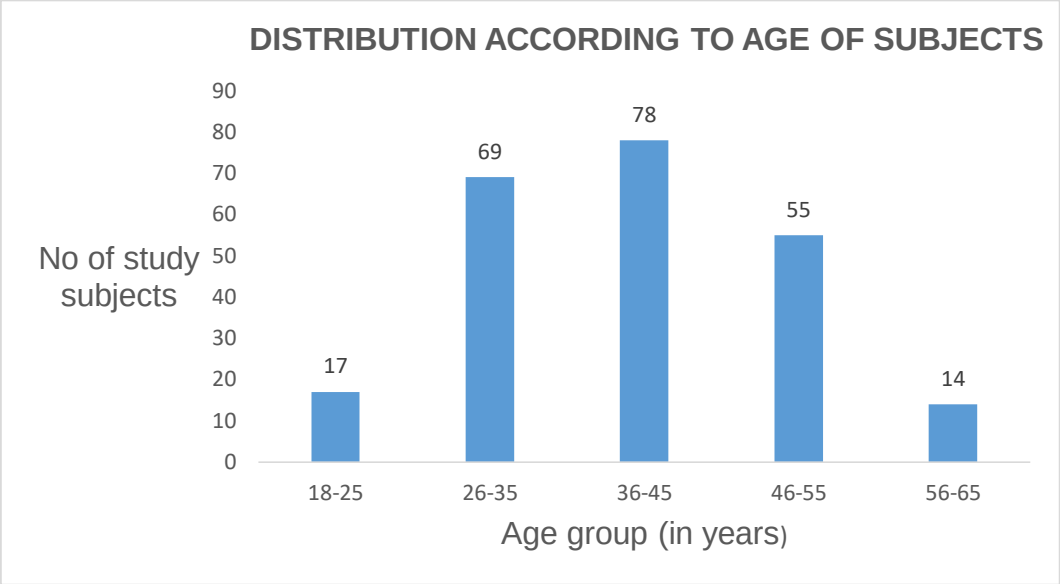

Table 2: Distribution of study subjects according to presence of ocular surface diseases

Ocular surface diseases	Number	Percent
Absent	148	63.5
Present	85	36.5
Total	233	100.0

Chart 2: Distribution of study subjects according to presence of ocular surface diseases

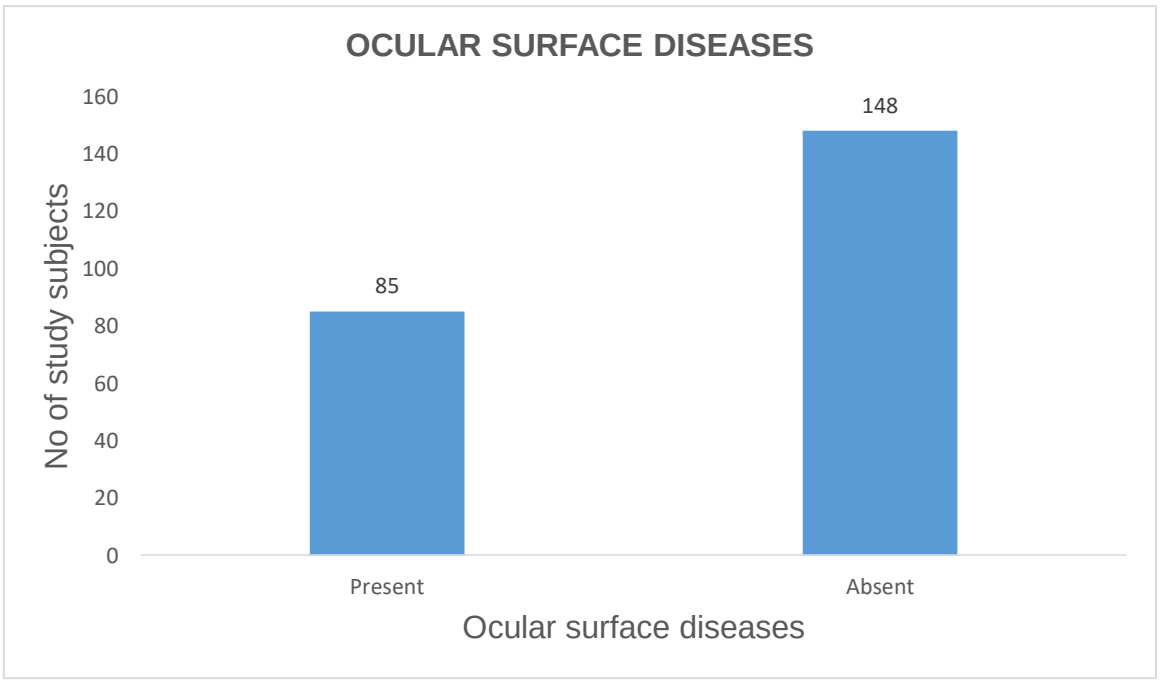

Table 3: Distribution of subjects having ocular surface disease according to CD4 cell count

CD4 cell count (cells/mm^3)	Number	Percent
0-199	34	40.0
200-499	48	56.5
≥500	3	3.5
Total	85	100.0

Chart 3: Distribution in subjects having ocular surface diseases according to CD4 count

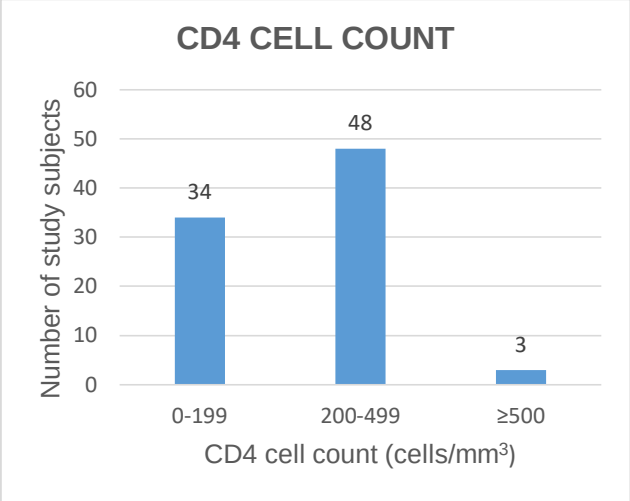

Table 4: Distribution of ocular surface diseases and CD4 cell count in study subjects

Ocular surface diseases	CD4 Cell count (cells/mm^3)			Total (%)
	0-199 (%)	200-499 (%)	≥500 (%)	
Blepharitis	7 (8.2)	13 (15.2)	0	20 (23.5)
Conjunctivitis	2 (2.3)	19 (22.3)	3 (3.5)	24 (28.2)
DED	11 (12.9)	14 (16.4)	0	25 (29.4)
MGD	4 (4.7)	0	0	4 (4.7)
Keratitis	5 (5.8)	0	0	5 (5.8)
Molluscum contagiosum	1 (1.2)	1 (1.2)	0	2 (2.3)
HZO	2 (2.3)	1 (1.2)	0	3 (3.5)
OSSN	2 (2.3)	0	0	2 (2.3)
Total	34 (40)	48 (56.5)	3 (3.5)	85 (100)

Chart 4: Distribution of ocular surface diseases and CD4 cell count in study subjects

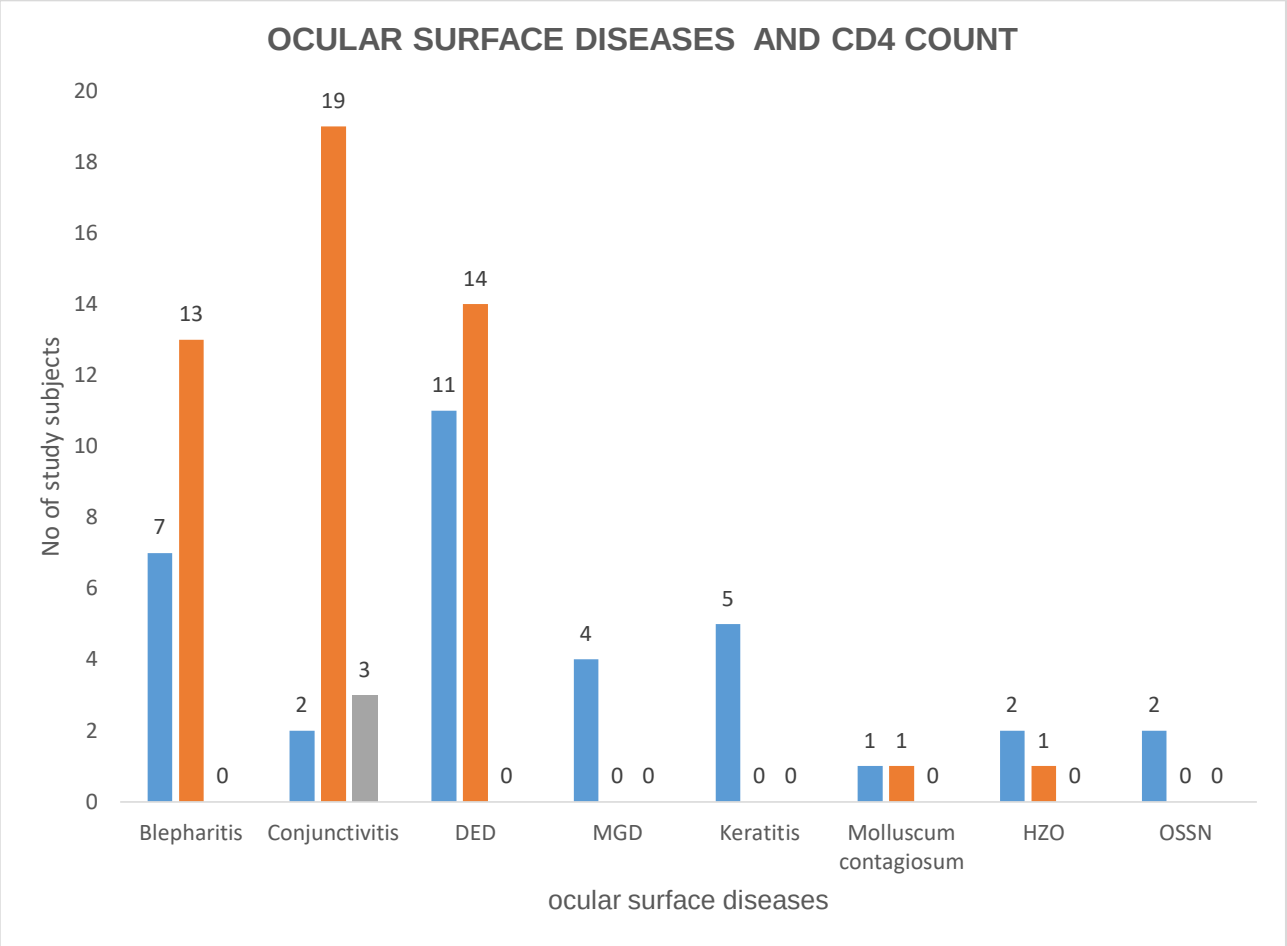

Table 5: Association of ocular surface diseases with CD4 cell count

		Ocular surface diseases		Total
		Absent	Present	
CD4 cell count (cells/mm^3)	0-199	1	33	34
	200-499	96	48	144
	≥500	54	1	55
Total		151	82	233

ChiSq = 82.66 P value <0.001

Discussion

The prevalence of ocular surface diseases is higher in individuals with HIV compared to the general population. This is likely due to the underlying immune dysfunction caused by HIV which leads to deranged CD4 counts, this makes the ocular surface more vulnerable to infections and other diseases.[5]

In addition, HIV-positive individuals often have other systemic infections and comorbidities that can further increase the risk of ocular surface disease.

In the present study, the study participants were mostly young adults and middle aged with highest frequency belonging to 36-45 years age group and median age of 40±10.15 years. The gender distribution in our study slightly favoured females

to males. This was similar to the study conducted at an HIV clinic by Ismail I et al. [7], where the mean age of study participants was 48.9 years and females were more than males. In a study conducted by Bekele et al. [4], the mean of study subjects was 31.9 years (SD± 8.96) and most of them were in the age group of 20–34 years. As in our current study, majority of the subjects were females here.

In the current study, most of the study subjects had 6/6 visual acuity and very few had debilitating vision. Similar results were also noted by Bekele S et al.[4], where majority had visual acuity >6/18 and only 2.6% having monocular blindness. The same results were also reported by Labh R et al.[8], where <10% had severe visual impairment or blindness.

In the study by Ghate M et al., [6] though 29.9% HIV infected study participants had refractive errors with 0.5% having blindness and 1.1% suffering from severe visual impairment. The participants in present study were evaluated for the condition of the anterior segment of their eye and it was seen that majority of participants had no abnormality in their anterior segment. The study done by Bekele S et al. [4], also reported similar findings with only 12.3% having anterior segment manifestations with keratoconjunctivitis sicca being most common.

Similarly, the study by Labh R et al.[8], also reported only a quarter of its study participants having anterior segment manifestations. The present study tries to determine the prevalence of ocular manifestations in the enrolled study participants who are HIV positive.

Out of all study participants, 36.5% reported at least one ocular manifestation. The most common manifestations were dry eye disease, conjunctivitis and blepharitis. The study conducted by Labh R et al.[8], reported nearly similar results to our study with 40% patients having ocular disease, with conjunctivitis being one of the commonest in their study also. The study conducted by Saini N et al. [9], also reported dry eye disease as the most common ocular manifestation in HIV positive patients. The second most common was HIV retinopathy followed by neuro ophthalmic complications.

CD4 cell count is an important prognostic parameter in HIV positive patients. In the present study, CD4 cell counts were found to be between low and very low for most of the study participants. Many of the other studies also reported lower CD4 cell counts when HIV patients suffered from ocular manifestations. Like, they study conducted by Hassan S et al.,[10] reported a mean CD4+ T- cells count was 410±281.65 with minimum to maximum was 6-1266 cells/µl.

A number of adnexal manifestations were seen in the participants of current study like dry eye disorder, blepharitis, conjunctivitis, keratitis etc. Most of these adnexal manifestations were seen in participants with CD4 cell count between 200-499 cells/mm^3 whereas very few adnexal manifestations were seen in participants with CD4 cell count ≥500 mm^3.

In the study conducted by Bekele S et al.,[4] similar results were seen with most of the study subjects having adnexal manifestation had CD4 cell count < 200 cells/µl and the most common adnexal manifestation seen was blepharitis followed by molluscum contagiosum and conjunctival squamous cell carcinoma.

Statistical analysis showed that in this study, there was seen a significant association between the occurrence of an ocular manifestation and CD4 cell count. The number of study participants having ocular manifestations were more when the CD4 cell count was less. This result is also documented in various studies around the world and in India also.

In the study conducted by Hassan S et al.,[10] CD4 cell counts had a highly significant relation with occurrence of ocular manifestation in HIV positive patients. Lower the CD4 cell count, more was the occurrence of ocular manifestations.

Statistically significant association between CD4 cell count and ocular manifestations was also seen in the study conducted by Bekele S et al.,[6], on adults HIV/AIDS patients.

Conclusion

Prevalence of OSDs in HIV positive patients in central India as found to be 36.5% in our study is similar to those reported in eastern and western parts of India, this overall prevalence of ocular manifestations of HIV/AIDS is higher than reported in previous studies. Prevalence was higher in females, patients with lower CD4 cell count and older patients. The commonest ocular surface disease were DED, Blepharitis, and Conjunctivitis. Age >35 years and CD4cell count of <200 cells/mm^3 were found to be independent risk factors for developing OSDs. Though OSDs of HIV/AIDS are low , HIV patients especially those with lower CD4 cell count , HIV positive for longer duration and older patients should have eye check-up and follow up regularly by an ophthalmologist and there should be concerned care with multidisciplinary approach, this may help in early diagnosis, treatment and prevention of sight threatening complications. Further prospective study should be carried out to investigate why some ocular findings are rare in our setting, so that real clinical picture and possible reasons will be known.

Limitations of the Study

In spite of every sincere effort my study has lacunae.

The notable short comings of this study are:

- The sample size was small. Only 233 cases are not sufficient for this kind of study
- The study has been done in a single centre
- Study being subjective assessment of all the parameters , subjective bias cannot be ruled out
- The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out
- The association between age and ocular surface diseases warrants further investigations

Strengths of Study

- Screening was done by a single ophthalmologist, hence ruling out any observer bias
- Prospective nature of the study
- Our study was performed in a tertiary health care centre with special HIV clinics and ART dispatch centres , thus the recruitment of patients were done easily and sincerely

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Author Contribution

Vaishnavi Awachat: Conceptualization, Methodology, Software Data curation, Writing-Original draft preparation. Visualization, Investigation. Minal Vyawahare: Conceptualization Validation, Writing- Reviewing and Editing. Piyush Madan: Supervision.

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