

Prevalence and Associated Factors of Ocular Manifestations of Acquired Immune Deficiency Syndrome Among Adults at University of Gondar Hospital, North West Ethiopia, 2021

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Introduction: Acquired immune deficiency syndrome is a disease with common clinical ocular manifestations. Ocular manifestations lead to blindness, which has a common social and economic impact.

Purpose: This study aimed to assess the prevalence and associated factors of ocular manifestations of acquired immune deficiency syndrome among adults at the University of Gondar Hospital, North West Ethiopia, 2021.

Patients and Methods: A cross-sectional study was conducted on 401 patients from June to August 2021. Samples were selected based on a systematic random sampling technique. Data collection was done using structured questionnaires. Data extraction format was used to collect the clinical characteristics of patients including ocular manifestations. Data entry was done by EpiData version 4.6.0.6 and exported to the Statistical Package for the Social Sciences version 26 for data analysis. Associated factors were analyzed by binary logistic regression. P-value <0.05 with a 95% confidence level was used to declare a significant association.

Results: A total of 401 patients were involved with a response rate of 91.5%. The overall prevalence of ocular manifestations of acquired immune deficiency syndrome was 28.9%. The common ocular manifestations were seborrheic blepharitis at 16.4% and squamous conjunctival growth at 4.5%. Age >35 years (AOR=2.52, 95% CI: 1.19, 5.35), Clusters of differentiation 4 count <200 cells/ μ L (AOR=4.76, 95% CI: 2.50, 9.09), World Health Organization stage II (AOR=2.60, 95% CI: 1.23, 5.50), history of eye disease (AOR=3.05, 95% CI: 1.38, 6.72), and duration of Human Immunodeficiency Virus >5 years (AOR=2.79, 95% CI: 1.29, 6.05) were statistically associated with the ocular manifestation of acquired immune deficiency syndrome.

Conclusion and recommendations: In this study, the prevalence of ocular manifestation of acquired immune deficiency syndrome was high. Age, CD4 count, duration of HIV, eye disease history, and WHO clinical staging were the significant factors. Early eye checkups and regular ocular examinations of HIV patients would be helpful.

Keywords: ocular manifestation, HIV/AIDS, Gondar, Ethiopia

Introduction

Acquired immune deficiency syndrome (AIDS) is the most common cause of death in many parts of the United States, Europe, and sub-Saharan Africa.¹ Globally, 38.4 million people were living with Human Immune Virus (HIV) and from those 28.7 million were accessing antiretroviral therapy (ART) in 2021.² In eastern and southern Africa, 20.6 million people live with the virus.² In sub-Saharan Africa, more than 16 million people have been negatively affected by the spread of infectious diseases.³ Ethiopia has the lowest prevalence rate of HIV/AIDS in East Africa. There are more than one million people who have the virus and are surviving with it.⁴

Ocular manifestations of HIV infection have been common worldwide. Globally, 70–80% of the people with HIV have been treated for an eye condition related to their HIV infection at some point during their illness.⁵ In the pre-Highly

Active Antiretroviral Therapy (HAART) period, 50% to 75% of the HIV-infected individuals had HIV-related ocular problems.⁶ The total possibility that an HIV-positive person will have at least one abnormal ocular lesion (eye abnormality) over their lifetimes ranges from 52% to 57%.⁷

HIV-infected individuals presented with various ocular conditions that are directly attributed to HIV/AIDS and its effect on the human immune response.^{8,9} The disease can have an adnexal, anterior segment, posterior segment, orbital, and neuro-ophthalmic manifestations.¹⁰ Cytomegalovirus retinitis (CMV), Kaposi sarcoma, and squamous cell carcinoma remain the most common ocular disorder among HIV-infected population.^{8,11} The pattern of ocular conditions in HIV infection is related to the history of eye problems, WHO stage of HIV/AIDS, CD4 count, age, and duration of HIV/AIDS.^{8,10,12}

People living with HIV/AIDS in developing countries who lose their vision typically have a short life expectancy.⁶ In developing countries, 5–25% of all the HIV patients become blind due to ocular complications of HIV/AIDS.¹³ HIV-related blindness has a significant impact, leading to a loss of economic independence, social standing, and family decision-making process, and productivity loss leads to a deterioration of quality of life.^{14,15}

At present, antiretroviral therapy (ART) becomes more available in developing countries like Ethiopia; however, life expectancy and the prevalence of blindness related to HIV/AIDS are expected to go up.

Even though different studies have been done on the prevalence of ocular manifestations of HIV/AIDS in developing countries like Ethiopia, there is not much information about the factors associated with ocular manifestations in the study area. Therefore, the purpose of this study was to further determine the prevalence of ocular manifestation of HIV/AIDS and the associated factors among adult HIV patients.

Methods and Materials

Study Design, Setting, and Study Period

A hospital-based cross-sectional study was conducted among adult HIV patients attending at University of Gondar Comprehensive Specialized Hospital ART clinic from June to August 2021. Gondar Town is located 750 kilometers from the capital city of Ethiopia Addis Ababa. University of Gondar Comprehensive Specialized hospital is a tertiary health care center and teaching hospital. The hospital started offering (ART) service in 2005. At the beginning, more than 7500 adults were enrolled in care and counseling programs. Currently, the hospital is providing ART service for more than 5000 HIV patients.

Sample Size Calculation

The sample size for the first objective was 398 based on single population proportion formula using evidence from a study conducted in Ethiopia Gondar hospital,¹⁶ with the assumptions²=21.4% ($p = 0.214$) CI=95% and margin of error=4%.

$$n = (Z^2 pq) / d^2 = 1.96 * 1.96 * 0.21 * 0.79 / 0.04 * 0.04 = 398$$

For the second objective, the power approach, stat Calc (EPIinfo7) was used. Based on the reviewed literature, CD4 count and HAART use were the factors repeatedly associated with the ocular manifestation of HIV/AIDS. The sample size was determined based on the study conducted in Jimma, Ethiopia¹⁷ (Table 1).

By taking the largest of all, the final sample size was 438.

Sampling Technique

A systematic random sampling technique was used with an interval of 5 to select the study participants at ART clinic of University of Gondar Comprehensive Specialized hospital. Using a lottery method, a single number was taken from 1 to 5 to determine the first subject and continue with every fifth interval. There were 50 cases per day who visited the ART clinic. The interval was calculated by dividing the expected number of patients who attend to the center within 2 months by the total sample size ($N=2000$; $n=438$; $K=(2000/438)=4.5=5$).

Table I Sample Size Calculation for the Second Objective

Variables	Assumptions
CD4 count	High CD4 count-to-low CD4 count ratio=3.3:1 (95% CI, power=80%) Unexposed with outcome=20.9 Exposed with outcome=39.7 Odds ratio=2.49, n=278
HAART use	No HAART use-to-HAART use ratio=0.98:1 (95% CI, power=80%) Unexposed with outcome=17.9 Exposed with outcome=32.5 Odds ratio=2.21, n=303

Source and Study Population

All adult HIV patients who are receiving regular service at the University of Gondar Hospital ART clinic and patients attending during the data collection period.

Inclusion and Exclusion Criteria

All adult HIV patients attending at University of Gondar Hospital ART clinic were enrolled in the study, and patients who had additional medical problems of diabetes, hypertension, and ocular trauma were excluded from the study.

Operational Definition

CD4 count – CD4 count of the patients within the last 6 months during the data collection time.

Ocular manifestation of HIV/AIDS – If the patients had at least one of the following ocular findings: Herpes zoster ophthalmicus, CMV retinitis, HIV retinopathy, molluscum contagiosum, seborrheic blepharitis, ocular squamous neoplasia, and neurophthalmic disorder.^{10,13,18,19}

Adnexal manifestations – Herpes zoster ophthalmicus, molluscum contagiosum and Kaposi's sarcoma.¹⁹

Anterior segment manifestations – Ocular surface squamous neoplasia, seborrheic blepharitis.¹⁹

Posterior segment manifestations – Retinal microvasculopathy, CMV retinitis, or HIV retinopathy.¹⁹

Neuro-ophthalmic manifestations – Papilledema, optic neuritis, optic atrophy and cranial nerve palsy.¹⁹

Data Collection Procedure and Tools

A structured questionnaire was used to collect sociodemographic data. Selected patients were examined for possible HIV-related ocular problems. Visual acuity was taken by using the Snellen E- chart. External eye examination was done by torch and magnifying loop. The posterior segment was examined after dilation of the eye by using a direct ophthalmoscope. Data extraction format was used to record CD4 counts, viral load, WHO staging, HIV confirmation date from the medical record, and also the ocular findings.

Data Quality Control

Data were collected by three optometrists. To maintain the quality of the data, the recruited data collectors were trained about the aim of the study and how to retrieve data. Questioners were prepared from reviewed pieces of literature Jimma (Ethiopia),¹⁷ Jakarta (Indonesia),²⁰ Ghana,²¹ South Korea,²² and Taiwan.²³ Structured questionnaires were first prepared in English, then translated to Amharic and back-translated to English by an independent translator. A pretest test was done on 21 patients at Debre Tabor hospital to check the consistency and completeness of the data item. The data collection process was monitored by the investigator throw-out the data collection period. Completed questionnaires were checked regularly for completeness of the information. In addition, double-entry of data was done in about 5% of the data collected.

Data Processing and Analysis

Data were entered into EpiData version 4.6.0.6 and exported to IBM Statistical Package for the Social Sciences (SPSS) version 26 software for data analysis. Both descriptive and analytical statistical procedures were performed. Descriptive statistics were used for the presentation of sociodemographic data and prevalence of ocular manifestations. Tables and figures were used for the presentation of data. Binary logistic regression was used to identify associated factors for ocular manifestations of HIV/AIDS. Bivariable and multivariable binary logistic regression models were used. Variables with a p-value less than 0.25 at bivariable logistic regression were entered into a multivariable logistic regression to identify significant variables for the ocular manifestation of HIV/AIDS. A p-value of less than 0.05 with a 95% confidence interval was used to declare a significant association between variables. Model fitness was checked by using Hosmer and Lemeshow's goodness of fit ($p=0.45$).

Ethical Considerations

Ethical clearance was obtained from the University of Gondar College of Medicine and Health Sciences Ethical Review Board (ERB 688/06/2021). A permission letter was also obtained from the clinical director of Gondar Hospital and the ART clinic focal person. The risks and benefits of the study were clarified for the patients. Written informed consent was also taken from study patients. Personal identifiers were not included to maintain confidentiality. This study also complies with the Declaration of Helsinki principles on medical research involving human subjects. The health, rights and confidentiality of the study subjects during the data collection were the first consideration and everything done during the data collection on study participants were on patient's interest. Patients with ocular manifestations of HIV/AIDS were advised and linked to the eye clinic for further diagnosis and management.

Results

Sociodemographic Characteristics of Study Participants

A total of 401 study participants were involved in the study with a response rate of 91.55%. The majority 79.1% (317) of participants were in the age group >35 years, with a median age of 45 and interquartile range (IQR, 37–50 years). More than half of 65.1% (261) were female participants. About 93.8% (376) were urban residents and 29.4% (118) of patients had a secondary school education level. About 35.9% (144) were housewives and 42.9% (172) of participants were married (Table 2).

Table 2 Sociodemographic Characteristics of Study Participants Among Adult HIV Patients in Gondar University Comprehensive Specialized Hospital ART Clinic, 2021

Variable	Frequency	Percentage
Age		
18–35 years	84	20.9
>35 years	317	79.1
Sex		
Male	140	34.9
Female	261	65.1
Residence		
Rural	25	6.2
Urban	376	93.8
Religion		
Orthodox	350	87.3
Muslim	46	11.5
Protestant	3	0.7
Catholic	2	0.5

(Continued)

Table 2 (Continued).

Variable	Frequency	Percentage
Marital status		
Single	82	20.4
Married	172	42.9
Divorced	69	17.2
Widowed	78	19.5
Educational status		
Unable to read and write	92	22.9
Read and write	15	3.7
Primary school	113	28.2
Secondary school	118	29.4
College and above	63	15.7
Occupation		
Farmer	13	3.2
Housewife	144	35.9
Employed	92	22.9
Daily laborer	140	34.9
Student	12	3.0

Clinical Profile of Study Participants

Of the total 401 participants, the majority (98.5%) of them had received HAART. About 83.8% of the patients had CD4+ count ≥ 200 cells/ μL with interquartile range (IQR, 264–585.50 cells/ μL). No single participant was in WHO clinical stage IV, while 11.5% (46) of the participants were in WHO clinical stage II. Most (99%) of the patients had a viral load lower than 10,000. The majority 70.8% (284) of them had no history of eye disease and only 86 (21.4%) of patients had an eye checkup history. The prevalence of visual impairment was 13.96% (Table 3).

Table 3 Clinical Profiles of Adult HIV Patients Attending at University of Gondar Comprehensive Specialized Hospital ART Clinic, 2021

Variable	Frequency	Percentage (%)
Current CD4 cells		
<200 cells/ μL	65	16.2
≥ 200 cells/ μL	336	83.8
Viral load		
<10,000	397	99
$\geq 10,000$	4	1.0
Duration of HIV		
1–5 years	71	17.7
6–18 years	330	82.3
Current WHO stage		
Stage I	355	88.5
Stage II	46	11.5
HAART		
Yes	395	98.5
No	6	1.5

(Continued)

Table 3 (Continued).

Variable	Frequency	Percentage (%)
Eye disease history		
Yes	117	29.2
No	284	70.8
Eye checkup history		
Yes	86	21.4
No	315	78.6
Tuberculosis		
Yes	19	4.7
No	382	95.3
Visual impairment		
Yes	345	86.04
No	56	13.96

Prevalence and Pattern of HIV/AIDS-Related Ocular Manifestations

Of 401 adult HIV patients, 28.9% of them had HIV/AIDS-related ocular manifestations with 95% CI (24.9, 33.4) (Figure 1).

The most common ocular manifestations of HIV/AIDS were seborrheic blepharitis (16.4%) followed by squamous conjunctival growth (4.5%) (Figure 2).

Factors Associated with HIV/AIDS-Related Ocular Manifestations

In bivariable logistic regression, certain variables such as sex, age, WHO clinical stage of HIV, CD4 count, duration of HIV, history of eye disease, and eye checkup history were associated with the ocular manifestation of HIV/AIDS with a p-value <0.25.

In multivariable logistic regression analysis, age, CD4 count, WHO clinical stage of HIV/AIDS, eye disease history, and duration of HIV were statistically significant variables with p-value <0.05. Patients in the age group >35 years had 2.5 times higher odds of having ocular manifestation compared to patients ≤35 years of age (95% CI: 1.19, 5.35). Patients who had a CD4 count of fewer than 200 cells/μL had 4.7 times increased odds of having ocular manifestations compared with those having CD4 count ≥200 cells/μL (95% CI: 2.50, 9.09). HIV patients with a duration of higher than 5 years had 2.8 times more odds of having ocular manifestations than patients with a duration of ≤5 years (95% CI: 1.29, 6.05).

prevalence of ocular manifestation of HIV/AIDS

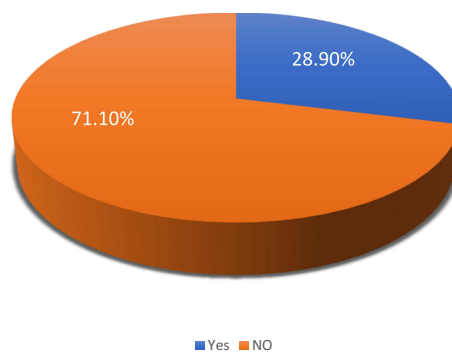


Figure 1 The proportion of ocular manifestation of HIV/AIDS among adult patients attending in University of Gondar Comprehensive Specialized Hospital ART clinic 2021.

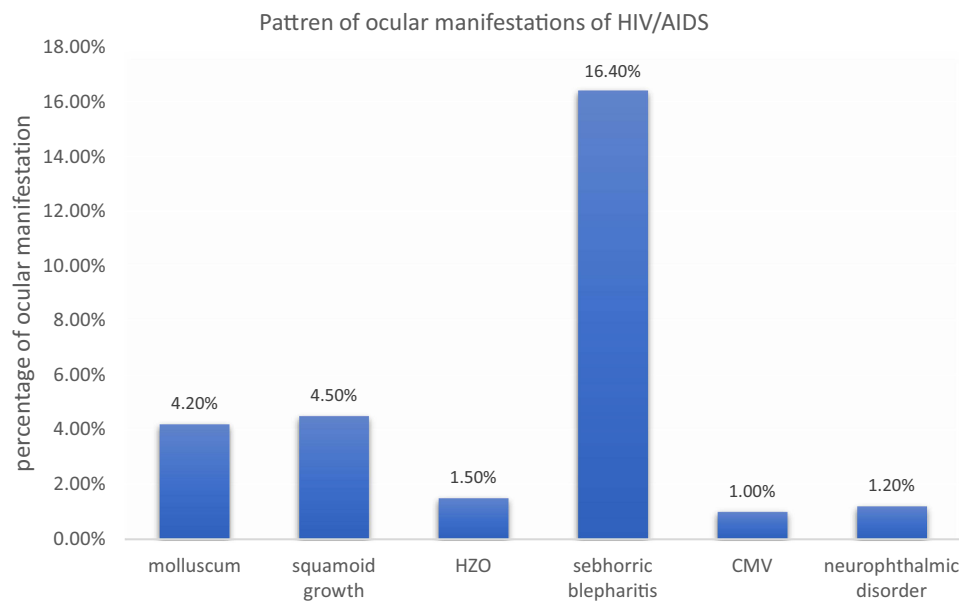


Figure 2 Pattern of HIV/AIDS-related ocular manifestations among adult patients attending at University of Gondar Comprehensive Specialized Hospital ART clinic, 2021.

Patients who were on WHO stage II had 2.6 times more odds of having ocular manifestation compared with WHO stage I (95% CI: 1.23, 5.50). Patients who had a history of eye disease had 3 times increased odds of having ocular manifestation compared with their counterparts (95% CI: 1.38, 6.72) (Table 4).

Table 4 Regression Analysis for Factors Associated with the Ocular Manifestation of HIV/AIDS Among Adult HIV Patients Attending at University of Gondar Comprehensive Specialized Hospital ART Clinic, 2021

Variables	Ocular Manifestations		COR (95% CI)	AOR (95% CI)	p-value
	Yes	No			
Sex					
Male	52	88	1.81 (1.16, 2.83)	1.63 (0.97, 2.75)	0.064
Female	64	197	1.00	1.00	
Age					
18–35 years	15	69	1.00	1.00	0.015
>35 years	101	216	2.15 (1.17, 3.94)	2.52 (1.19, 5.35)	
Residence					
Rural	6	19	0.76 (0.27, 1.96)	0.50 (0.14, 1.77)	0.28
Urban	110	266	1.00	1.00	
WHO stage					
Stage I	96	259	1.00	1.00	0.012
Stage II	20	26	2.07 (1.10, 3.89)	2.60 (1.23, 5.50)	
CD4count					
<200 cells/ μ L	34	31	3.39 (1.96, 5.86)	4.76 (2.50, 9.09)	<0.001
\geq 200 cells/ μ L	82	254	1.00	1.00	
HIV duration					
\leq 5 years	10	61	1.00	1.00	0.009
>5 years	106	224	2.88 (1.42, 5.85)	2.79 (1.29, 6.05)	

(Continued)

Table 4 (Continued).

Variables	Ocular Manifestations		COR (95% CI)	AOR (95% CI)	p-value
	Yes	No			
Eye checkup					
Yes	25	61	1.00	1.00	0.35
No	91	224	0.99 (0.58, 1.67)	0.97 (0.85, 156)	
History of eye disease					
Yes	41	76	1.50 (0.94, 2.38)	3.05 (1.38, 6.72)	0.006
No	75	209	1.00	1.00	

Abbreviations: CI, confidence interval; COR, crude odds ratio; AOR, adjusted odds ratio.

Discussion

This study assessed the prevalence and associated factors of ocular manifestations of HIV/AIDS among adult HIV patients. The prevalence of ocular manifestation of HIV/AIDS was 28.9% (95% CI: 24.9, 34.4). This finding was consistent with the studies done in Jimma (Ethiopia) 25.3%,¹⁷ Bahirdar (Ethiopia) 25.7%,¹² China 33.8%,²⁴ and Nepal 26.49%.²⁵

However, the result of this study was lower than the studies done in Gondar (Ethiopia), 60%,²⁶ Kenya 60.2%,²⁷ Ghana 48%,²¹ South Korea 48%,²² Nigeria 37.1%,²⁸ and Indonesia 63.3%.²⁰ This variation might be due to the difference in sampling technique and sample size. The study done in Gondar was on pre-HAART patients and also on patients who were in the advanced stage of the disease. So, this might overestimate the result of the study done in Gondar. The higher prevalence of ocular manifestation in Ghana might be due to the WHO clinical staging of the disease since 77% of the study patients were in WHO clinical stages III and IV. Also, in the study conducted in Kenya, 33.8% of the study participants were seeking eye ocular examination during the data collection time. This may overestimate the ocular manifestations of HIV/AIDS. About 30% of the study samples in the South-Korean study were patients referred to the eye clinic for medical treatment and the mean CD4 count was 266.7cells/ μ L. In the study done in Indonesia and Kenya, patients with other systemic diseases such as diabetes and hypertension were not excluded from the study. These differences might increase the prevalence ocular manifestations of HIV/AIDS.

On the other hand, the prevalence of ocular manifestations in our study was higher than the studies done at Hawassa (Ethiopia) 14.2%,²⁹ Burundi, 21%,³⁰ Taiwan 4.6%,²³ and India 8%.³¹ This discrepancy might be due to, different operational definitions and study designs. In Taiwan, a retrospective cohort study with a chart review of HIV patients for possible ocular problem records was conducted. This might underestimate the prevalence of ocular manifestation of HIV/AIDS. In the study conducted in Burundi and India, the sample size was 154 and 121 patients, respectively. So, this small sample size may underestimate the result of the study. Compared with the study done in India, the variation might be due to socioeconomic and sociodemographic differences.

Regarding the associated factors, age >35 years, WHO clinical stage II, CD4 count < 200 cells/ μ L, duration of HIV >5 years, and history of eye disease were statistically significant factors for ocular manifestations of HIV/AIDS.

In this study, patients in the age group older than 35 years had 2.5 times increased odds of having ocular manifestation compared with those younger than 35 years. A similar result was reported in Jimma, Ethiopia,¹⁷ and Ghana.²¹ The possible reason for this finding might be due to the effect of age on the patient's immune system. As the age of the patient increases the immune status of the body will deteriorate, which leads to low CD4 cells count in the blood.

According to this study, subjects who had a CD4 count <200 cells/ μ L had 4.7 times increased odds of having ocular manifestations compared with patients who had a CD4 count \leq 200cells/ μ L. This result was coherent with the studies conducted in Jimma,¹⁷ Bahirdar,¹² Gondar,²⁶ Ghana,²¹ and Indonesia.²⁰ CD4+ T cells count of less than 200 cells/ μ L is a well-established fact for higher ocular manifestations of HIV/AIDS. As the CD4 count cells deteriorate the patient's immune system also deteriorates, which increases the risk of immunocompromised disease including ocular manifestations.^{32,33}

In the present study, patients who had an eye disease history had three times more odds of having ocular manifestations. This finding was coherent with the study done in Bahirdar, Ethiopia.¹² The possible reason for this might be due to patients with the ocular disease have an increased risk of ocular coinfection. Also, some findings might be misdiagnosed as the ocular manifestation of HIV/AIDS.

According to this study, patients who were in WHO clinical stage II had 2.6 times more odds of having ocular manifestations of HIV/AIDS compared with patients who are in WHO stage I of the disease. This result was consistent with the studies done in Ghana²¹ and Indonesia.²⁰ The WHO clinical stage of HIV infection is based on the immune status of the patient. The immune status of patients who are in WHO clinical stages II, III, and IV are low. The risk of eye disease is increased with the advanced immune suppression stage of HIV infection.³³

In addition, patients with a longer duration of HIV/AIDS had 2.8 times more odds of having ocular manifestations. This finding was in line with the study done in Jakarta, Indonesia.²⁰ Nowadays, antiretroviral therapy contributes to the increasing life span of HIV-positive persons and they live longer. As the duration increases, the immune status of the patient decreases due to the long-term effect of the virus on white blood cells.

However, factors like sex, HAART, and eye checkup history were not associated with ocular manifestations of HIV/AIDS in this study, which were previously reported to have an association with the ocular manifestation of HIV/AIDS in other studies done before.^{12,17,21}

In this study, the commonest ocular manifestations of HIV/AIDS were adnexal of which seborrheic blepharitis is the commonest at 16.4% followed by squamoid conjunctival growth at 4.5% and molluscum contagiosum at 4.2%. This finding was similar to the result reported in Hawassa²⁹ Bahirdar,¹² Jimma,¹⁷ and the systematic review in England.¹⁰ However, this result is different from the study conducted in Gondar,²⁶ Taiwan,²³ and South Korea,²² where the commonest ocular manifestation was HIV retinopathy, CMV retinitis, and neurophthalmic disorders. This variation might be due to the studies in Gondar, Taiwan, and, South Korea being done on patients in an advanced stage of the disease (stage III and IV) where HIV retinopathy, CMV retinitis, and neurophthalmic disorders are common.

Limitation of the Study

In this study, the study design used was a cross-sectional study design, so it does not show the cause-and-effect relationship among variables. Also, as a result of time and resource constraints, pathology was not done to differentiate squamoid conjunctival growth from pterygium.

Recommendations

For the University of Gondar Comprehensive Specialized hospital

- It is better if the hospital gives regular follow-ups and manages HIV patients with low CD4 counts during follow-ups.
- It is also better if the hospital creates an integrated patient examination and link system in the ART clinic and eye clinic.

For the Ministry of Health

- It is better if the Ministry of Health also takes the responsibility to establish and expand integrated ocular screening, examination, and referral programs for HIV patients.

For future researchers

- I also encourage other researchers to focus on associated factors of ocular manifestations of HIV/AIDS with a comparative method.

Conclusion

The overall prevalence of ocular manifestations of HIV/AIDS among adult HIV patients was higher than some of the studies conducted in Ethiopia and Africa. The most common ocular manifestations of HIV/AIDS were seborrheic blepharitis and squamous conjunctival growth. The prevalence was higher among patients, age >35 years, CD4+ count <200 cells/ μ L, WHO clinical stage II, patients with history of eye disease, and duration of HIV >5 years.

Though ocular manifestations of HIV/AIDS were high, HIV/AIDS patients especially those with lower CD4+ cell count, patients with duration of HIV >5 years and patients with older age should have eye checkup and follow-up by an ophthalmologist and optometrists, and there should be concerted care with a multidisciplinary approach. Further prospective studies should be carried out to investigate why some ocular findings are rare in our setting so that the real clinical picture and possible reasons will be known. The association between age and ocular manifestation warrants further investigation.

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Disclosure

The authors report no conflicts of interest in this work.

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