

Original Research Article

Prevalence and Determinants of HIV Related Eye Diseases in Patients on Highly Active Anti-Retroviral Therapy in Katsina State, Nigeria

Abstract

Background: HIV and its complication AIDS was a source of serious public health concern that greeted the end of the 20th century. Being a multi-systemic disease, it was also associated with different forms of ocular morbidities of interest.

Purpose: to determine the prevalence, patterns and determinants of HIV related eye diseases in patients attending anti-retroviral clinics in Katsina state, Nigeria.

Methods: Two hundred and twenty subjects met the inclusion criteria over a six month period. A questionnaire was administered for socio-demographic data, patients' history, record review and a detailed ophthalmic examination. Data was analysed using SPSS version 20. Parametric and non-parametric assessments were used to assess the relationship of various factors with manifestation of HIV associated eye diseases.

Results: Out of 220 respondents, 164 were females. The Male: Female was 1:2.9. The mean age was 28.5 years \pm 14.83 SD. About 65.5% of respondents had eye diseases while 46.4% had HIV associated eye diseases. Prevalence of HIV associated eye diseases was found to be 46.4%. The most common types of eye diseases found were Kerato-conjunctivitis Sicca (KCS) 25.5%, conjunctivitis 5.5%, herpes zoster ophthalmicus 3.2%, anterior uveitis 2.7% and molluscum

contagiosum 2.3%. Factors found to affect the manifestation of these eye diseases were CD4 cell count, WHO Clinical Stage of the disease and the Presence of eye symptoms.

Conclusion: The study showed a high prevalence of HIV associated eye disease. The Patient's clinical/WHO stage, CD4 cell count and presence of ocular symptoms were shown to have significant association with the ocular manifestation.

Keywords: *Prevalence, determinants, HIV related eye diseases, ocular manifestations, Katsina*

Introduction

Human immunodeficiency virus (HIV) appears to be one of the most devastating global public health challenges discovered towards the end of the 20th century. The challenge was more in developing countries which account for more than 95% of the global HIV infection.¹ Sub-Saharan Africa accounts for more than two third of global HIV infection and three quarters of all AIDS deaths in 2007. The latest data in Nigeria shows a HIV prevalence of 1.3% (1.2-1.5) in a country wide population based survey among people aged 15-49 years. A higher prevalence (1.8%) among women compared to men (0.9%).²

Ocular diseases can occur at all stages of HIV infection with some autopsy reports showing that up to 95% of AIDS patients have some form of ocular abnormalities.¹ Loss of sight is a feared complication of these ocular manifestations and some studies have estimated the prevalence of visual impairment amongst HIV positive patients to be up to 10.8%.³ Chime et al⁴ in Enugu in a

cross sectional study of patients on highly active antiretroviral therapy (HAART) reported that about 25% of the study participant who had HIV related ocular manifestation (HROM) had different levels of visual impairment (mild – 13.3%, moderate – 66.7%, blindness – 20%). However, about $\frac{3}{4}$ (75%) of patients with HROM in the study had normal Snellen's visual acuity. It has been estimated that there is a 52-100% lifetime cumulative risk of HIV patients developing eye problems.⁵ The prevalence of eye conditions among HIV positive patients has been as high as 18.4cc% in some Nigerian studies and as low as 4.0% in others.^{4,6,7}

The spectrum and prevalence of these eye diseases vary from region to region and between developed and developing countries.^{1,8,9} While diseases like cytomegalovirus retinitis are more common in the developed countries, herpes zoster ophthalmicus are more common in developing countries.¹⁰ The HROM way also be classified based on anatomical location or based on the underlying pathology.^{11,12} Anatomically, it may be orbital, adnexal, anterior segment, posterior segment and neuro-ophthalmic while pathologically, they may be opportunistic infections, non-infectious retinopathies, neoplasms and neuro-ophthalmic too. Also, there has been a difference in the pattern of HROM in the pre and post HAART era. While opportunistic infections held sway in the former era, the later era due the reactivation of the hitherto anergic immune system, ophthalmologists had the immune recovery uveitis (IRU) to contain.^{13,14} This report hopes to show the pattern of HIV related eye diseases with the view of comparing theme with patterns in existing literature.

The purpose of this study is to determine the prevalence, patterns and determinants of HIV related eye diseases in patients attending anti-retroviral clinics in Katsina state, Nigeria.

Methods

This was a descriptive cross-sectional study conducted in selected antiretroviral (ART) clinics across the three senatorial zones in Katsina State between March and September 2015.

Inclusion Criteria: All consenting HIV positive patients attending the selected ART clinics who have agreed to participate in the study by self or legal representative.

Exclusion Criteria: Severely ill patients who are too sick to respond to the questionnaire or withstand an examination, patients that refuse to consent to the study, patients with incomplete records

Sample Size Determination: The sample size (n) was calculated using the Cochran formular.¹⁵

$$n = \frac{z^2 pq}{d^2}$$

n = minimum sample size

z = standard normal deviate at 95% confidence interval (1.96)

p = proportion of HIV positive patients with ocular manifestation of HIV in a previous study which is 14.3 % (0.143)³

q = complementary probability of p (1-0.143) = 0.857

d = degree of precision (0.05)

$$n = \frac{1.96^2 \times 0.143 \times 0.857}{0.05^2} = 188 + (10\% \text{ of } 188 \text{ for non-response}) = 206 \text{ patients}$$

In this study the sample size was rounded up to 220 to increase the power of the study.

Sampling Technique: There are 20 ART centres in Katsina State providing antiretroviral treatment and laboratory services. There are 79 prevention of mother to child transmission (PMTCT) centres.

A multi stage sampling technique was used to get the required sample size with probability proportional to size.

Stage one: Selection of LGA – From the list of all the 11 LGAs in each of the senatorial zones 2 LGAs per zone were randomly selected using simple random samplings by balloting giving a total of 6 LGAs. Consequently the following LGAs were selected – Katsina, Dutsinma, Malumfashi, Funtua, Daura and Kankia LGAs.

Stage Two: Selection of health facilities providing HIV services – From the list of health facilities providing HIV/AIDS services 1 health facility per LGA was randomly selected using simple random sampling by balloting. Consequently a total of 6 health facilities were selected. They included General Hospital Katsina, Dutsinma, Daura, Kanki, Funtua and Malumfashi

Stage Three: Selection of HIV Patients – The various ART centres that were selected had estimated patient load as follows as was obtained from the Katsina State Action Committee against AIDS (KATSACA)

General Hospital Katsina - 4860 patients

General Hospital Funtua - 4250 patients

General Hospital Daura - 930 patients

General Hospital Malumfashi - 450 patients

General Hospital Kankia - 660 patients

General Hospital Dutsinma - 550 patients

Total number of HIV patients in the selected centres was 11,700.

Proportionate allocation was used to assign a certain number of patients to be included in the study in each centre using the formula:

$$\frac{\text{Number of HIV patients in a centre}}{\text{Total number of HIV patients in all selected centres}} \times \text{sample size}$$

General hospital Katsina ART centre: $4860/11700 \times 220 = 91$ patients

General Hospital Funtua ART centre: $4250/11700 \times 220 = 80$ patients

General Hospital Daura ART centre: $930/11700 \times 220 = 18$ patients

General Hospita Malumfashi ART centre: $450/11700 \times 220 = 9$ patients

General Hospital Kankia ART centre: $660/11700 \times 220 = 12$ patients

General Hospital Dutsinma ART centre: $550/11700 \times 220 = 10$ patients

Each ART centre was visited on days in which clinics were run. On reaching the ART centre, folders of the patients were collected from the records of that ART centre and numbered. The numbers on the folders were randomly selected through balloting. The patient whose folder number corresponded to the selected number was then included in the study. Patients with incomplete records were not included in the study and another numbered folder was randomly selected Malumfashi

Ethical consideration: ethical approval was obtained from Health Research Ethics Committee (HREC) of the Ahmadu Bello University Teaching Hospital Zaria and Katsina State Ministry of Health Ethics and Research Committee. Also, permission, for the study, was obtained from the Katsina State Agency for Control of AIDS, before the commencement of the study..

Consent: written informed consent was obtained from included patients. Everyone was made to know they reserved the right to discontinue participation in the study any time they wished to.

Pre testing of questionnaire and training of personnel: Pre testing of the questionnaire was conducted in an ART centre not selected for our study. Ten percent of sample size of the study participants were selected for pre-testing of the questionnaire. The research assistant was trained by the researcher on the administration of consent form to patients, conducting and interpretation

of visual acuity (VA) results and dilatation of patients. The pre testing enabled the personnel to be trained and the team have a practical experience on how the research will be carried out and the challenges that might occur.

Study Instruments: HIV patients Questionnaire – The questionnaire was a structured; interviewer administered questionnaire which was adapted from the international council of ophthalmology, international clinical guidelines on Ocular HIV/AIDS Related Diseases (Initial and Follow- up Evaluation).¹⁶ The questionnaire has 4 sections (A to D) covering respectively: (A) Socio-demographic characteristics of respondents, (B) Patient history, (C) Record review and (D) Examination and diagnosis.

Data Collection procedures

Data collection was conducted by the principal investigator (PI, an ophthalmologist) and trained research assistants (an ophthalmic nurse and a technician) under the PI's close supervision. The slit lamp was set in each ART centre visited by a technician. The research was explained in detail to the selected patients by the PI. The research assistant then administered the consent form to the patient or care giver for signing/thumb printing. Patient's socio-demographic data was obtained and filled into the questionnaire by the research assistant. The research assistant then conducted the distance visual acuity for all patients above 5 years of age using the Snellen's distance visual acuity chart and near visual acuity using the near vision chart while the technician sets up the slit lamp. The tumbling E chart was used for children and selected patients who are not literate. Visual acuity of children less than 5 years old was assessed by the principal researcher. To assess the visual acuity of children between 0-<1 year age group, the central steady and maintained (CSM) method was used using a pen torch, 1-< 2 years of age, the

hundred and thousand sweet test was used, for children 2-<5years, preferential looking with graded acuity cards was used while the Snellen's acuity chart and the tumbling E chart was used for those above 5 years of age. Patients with visual acuity less than 6/18 were dilated by the research assistant using tropicamide and phenylephrine ophthalmic solution eye drops. Also, all children less than 5 years of age were dilated as well by the Research Assistant after their visual acuity was assessed by the researcher. All patients eventually came to the PI for history taking, record review and detailed eye examination. The anterior segment was examined using a pen torch and a slit lamp, the posterior segment was examined using a direct ophthalmoscope, a binocular indirect ophthalmoscope and a pan optic ophthalmoscope. Fundal photographs were taken using the pan optic ophthalmoscope in conjunction with an iPhone4s. Children were blanketed for eye examination where necessary for indirect ophthalmoscopy to be carried out. Schirmers' strips were used to test for dry eye among the patient. With the patient seated, the patient is asked to look up while the lower eye lid is pulled down gently temporally, the schirmer's strip is then gently inserted into the lateral 1/3rd of the lower lid margin avoiding the cornea, it's kept in that position for 5 minutes, the strip is then removed and length of moistened area read off the graduated Schirmer's strip. More than 15mm wetting in all age groups is considered normal, less than 10mm is suggestive of moderate dry eye while less than 5mm is diagnostic of severe dry eye.¹⁷

The PI was in charge of overall monitoring and coordination of the data collection and ensuring that the research protocol was strictly adhered to. Patients with eye diseases were either treated by the researcher or referred appropriately. Specific diagnosis were made based on certain specific defined criteria.^{11,16}

Statistical Analyses

The questionnaires were checked for accuracy and completeness. The data was analysed using IBM SPSS statistics 20. Descriptive summary statistics such as mean and standard deviation were computed for continuous variables (age of patients, duration disease, CD4⁺ T cell count, and duration of treatment) and proportions for categorical variables (sex, occupation, and presence of co morbidities) of the respondents. Data was presented in tables and figures. Chi-square test was used to assess statistical associations between categorical variable and p – value < 0.05 was considered significant.

Results

Out of 220 patients who participated in the study, 164 (74.5%) were females. The male to female ratio was 1: 2.9. Participants were aged between 22 and 81years with a mean of 43.6 ± 9.9 years. A total of 61 participants (18.4%) had ocular manifestation. The modal age group was those aged 30–39 years and the mean age of participants was $28.5 \text{ years} \pm 14.83 \text{ SD}$. A majority, 48.6% were married.

Table 1: Socio demographic characteristic of HIV positive patients attending ART clinics in Katsina State (n=220)

Socio Demographic Characteristics	Frequency	Percent (%)
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Socio Demographic Characteristics	Frequency	Percent (%)
Age range		
0-9	37	16.9
10-19	10	4.5
20-29	54	24.6
30-39	63	28.6
40-49	36	16.4
50+	20	9.1
Sex		
Male	56	25.5
Female	164	74.5
Marital status		
Married	107	48.6
Single	47	21.4
Divorced	35	15.9
Widowed	31	14.1
Religion		
Islam	205	93.2
Christianity	15	6.8
Tribe		
Hausa	205	93.2
Yoruba	3	1.4

Socio Demographic Characteristics	Frequency	Percent (%)
Igbo	7	3.2
Others	5	2.3
Occupation		
Farming	5	2.3
Civil servant	19	8.6
Business	42	19.1
Not employed	104	47.3
Others	6	2.7
Child	44	20.0

Table 2 clinical profile of the respondents (n=220)

Variable	Frequency	Percentage (%)
Duration of disease		
<5years	147	66.8
>- 5years	73	33.2
Patients on HAART		
Yes	204	92.7
No	16	7.3
Duration on HAART		
< 5years	161	73.2
>- 5years	59	26.8

CD4⁺ cell count		
<- 200	15	6.8
201-499	99	45.0
>-500	106	48.2
WHO stage of HIV		
Stage 1	148	67.3
Stag 2	37	16.8
Stage 3	33	15.0
Stage 4	2	0.9
Comorbidities		
Yes	3	1.4
No	217	98.6

Variable	Frequency	Percentage (%)
Type of comorbidity		
TB	2	0.9
DM	1	0.5
Not applicable	217	98.6
Eye Symptoms		
Yes	75	34.1
No	145	65.9

Types of eye Symptoms

Foreign body sensation	28	12.7
Swelling	3	1.4
Discharge	10	5.0
Redness	1	0.5
Decrease/Loss of vision	22	10.0
Abnormal growth	4	1.8
Rashes	7	3.2

A large number of the respondents (66.8%) have been living with HIV for less than five years and majority (92.7%) are on HAART with up to 73.2% being on HAART for less than 5 years.

Only 6.8% of respondents had a Cd4 count below 200cell/mm³ and up to 63.7% of respondents were clinically in stage 1 of the disease (WHO staging). Only 1.4% of respondents had comorbidities as shown in table 2 above. Also, most of the respondents that had eye symptoms.

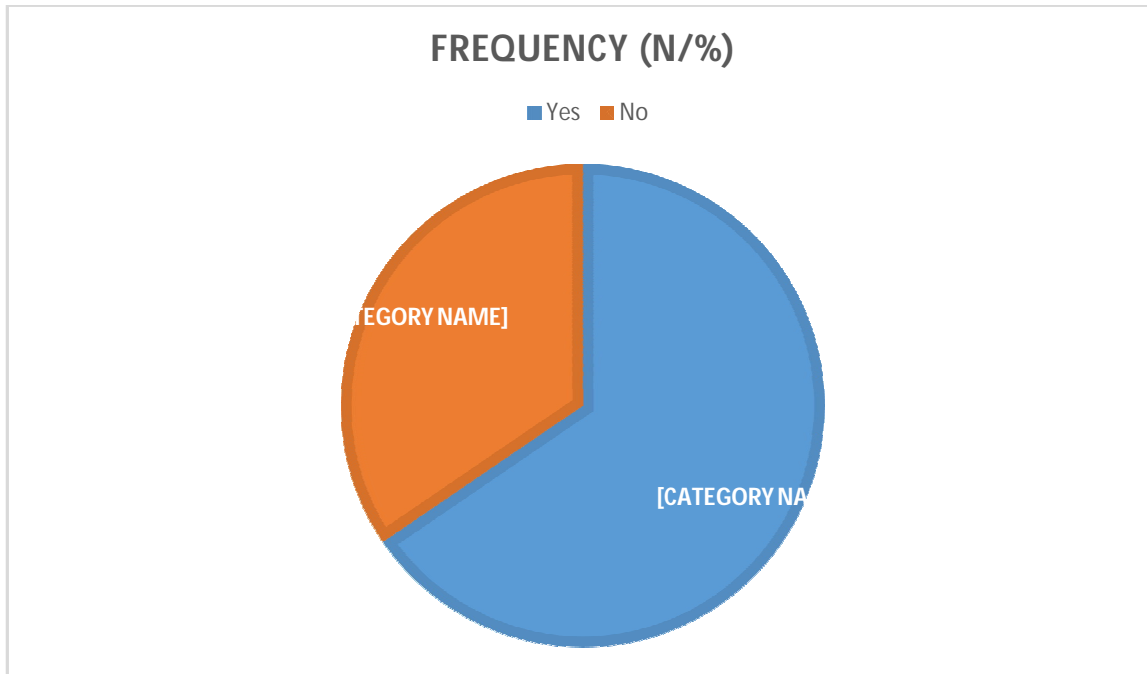


Figure 1: distribution of respondents with ocular conditions (n =22)

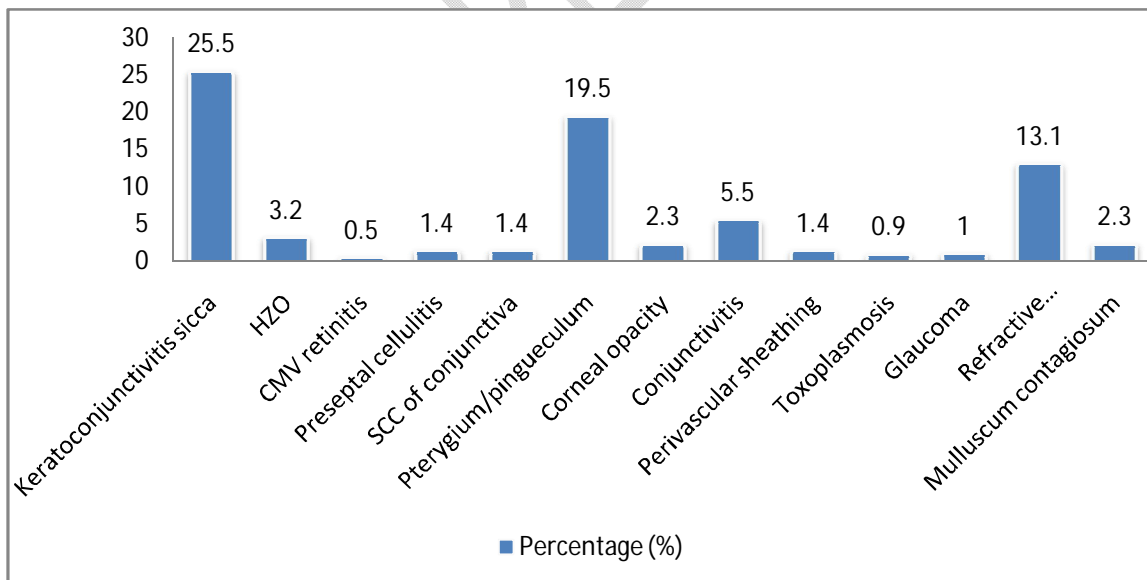


Figure 2 all types of eye diseases seen among HIV positive patients attending ART clinics in Katsina State

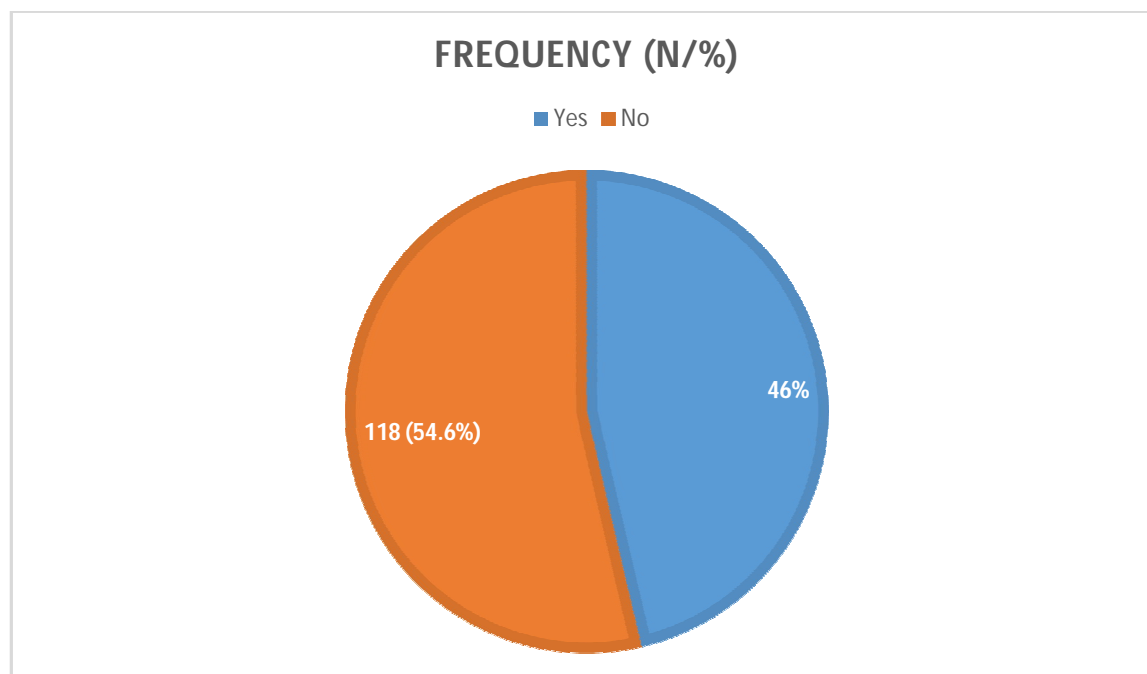


Figure 3 respondents with and without HIV associated eye diseases (n = 220)

From figure three above, the prevalence of HIV related eye disease in the different ART clinics was 46.4%.

Table 3: distribution of HIV associated eye diseases

HIV related Eye Disease	Frequency	Percentage (%)
Keratoconjunctivitis Sicca	56	25.5
Herpes Zoster ophthalmicus	7	3.2
Molluscum contagiosum	5	2.3
Conjunctivitis	12	5.5
Perivascular sheathing	3	1.4
Toxoplasmosis	2	0.9
CMV Retinitis	1	0.5

Squamous cell carcinoma of the conjunctiva	3	1.4
Preseptal cellulitis	3	1.4
Anterior uveitis	6	2.7
HIV retinopathy	3	1.4

From the table above keratoconjunctivitis sicca (25.5%), other conjunctivitis (5.5%), and herpes zoster ophthalmicus (3.2%) were the most common HIV related eye diseases in the study population.

Table 4 association between different variables and presence of HIV associated eye diseases (n=220)

Factors	HIV related eye diseases		Test statistics
	Yes	No	
Age (Years)			
0-14	21	23	$\chi^2 = 0.132$; df = 1; p = 0.736
≥15	81	96	
CD4+ Count			
<200	10	5	$\chi^2 = 7.171$; df = 2; p = 0.030*
201-499	52	47	
≥ 500	40	66	
Duration of disease			
<5 years	67	80	$\chi^2 = 0.110$; df = 1; p = 0.775
≥5 years	35	38	
Stage of disease (WHO)			
Stage 1	38	110	$\chi^2 = 83.949$; df = 3; p =

Stage2	31	6	0.000*
Stage3	31	2	
Stage4	2	0	
Patient on HAART			
Yes	95	109	$\chi^2 = 0.213; df = 1; p = 0.645$
No	7	9	
<hr/>			
Factors	HIV associated eye diseases		Test statistic
Comorbidities	Yes	No	
Yes	1	2	$\chi^2 = 1.000; df = 1; p = 0.05$
No	91	126	
Presence of eye symptoms			
Yes	56	46	$\chi^2 = 36.65; df = 1; p = 0.000*$
No	46	99	

* - Significant

There was a statistically significant relationship between CD4⁺ count (p = 0.030), clinical stage of HIV/WHO staging (p = 0.000), eye symptoms (p=0.000) and the manifestation of HIV associated eye diseases.

Discussion

Prevalence: This study has reported a high prevalence of HIV related ocular diseases in almost half (46.4%) of the respondents. This is unlike 18.4% reported recently by Chime et al⁴ in

Enugu. Possible reasons for the difference include smaller sample size in this index study, inclusion of some respondents who were not on HAART (though few), majority in this study have been on HAART for less than 5 years, which was not the case in Enugu which had all respondents on HAART, most of whom were on it for over 5 years. The result however was similar to an earlier report in Makurdi, Nigeria, a study conducted between 2002-2006 published a prevalence of 45%.¹⁸ Studies in Ghana and India have also reported a similar prevalence of 48% and 46% respectively.^{19,20} On the other hand, there are studies in neighbouring Mali, Cameroon, and distant Indonesia which all reported higher prevalence rates of 61.9%, 63.2% and 63.7% respectively.²¹⁻²³ Unlike most other studies, the study in Jakarta, Indonesia tested for dry eyes in which may have accounted for high prevalence of HIV associated eye diseases reported.²³

Pattern of HIV associated eye disease: KCS was found to be the most common eye manifestation in our study (25.5%), followed by conjunctivitis (5.5%), herpes zoster ophthalmicus (3.2%), the least being presumed toxoplasmosis (0.9%) and CMVR (0.5%). This is comparable to a study in Jakarta,²³ Indonesia where they found KCS(54%) to have the highest prevalence among the ocular diseases, however presumed toxoplasmosis and CMVR which had the least prevalence in our study had a relatively higher prevalence (8.4% and 5.8% respectively) in that study. Optic neuropathy and cranial nerve palsies were eye diseases that were found in the Jakarta study but were not found in ours, the reason for this difference may be because they had a larger sample size than we had. Conjunctivitis, HZO, Mulluscum contagiosum, perivascular sheathing, SCC of the conjunctiva, anterior uveitis, HIV retinopathy and preseptal cellulitis were diseases found in our study which were not found in the Jakarta study. On the other hand, in Enugu Nigeria HIV microangiopathy (18.8%) conjunctival

microangiopathy (14.5%), and KCS (14.5%) were the most common eye manifestations.⁴ The Enugu also had a higher sample size of 331 unlike this study.

Determinants of HIV associated eye diseases: similar to our results, Shivayogi and Gururaj²⁰ in Davangere, India reported a significant association between CD4 count, WHO stage count and ocular manifestations of HIV. Also, Aboubacar et al²¹ in Mali, Divilisteri et al²³, in Indonesia reported a significant association between CD4⁺ count and the ocular manifestation of HIV. In contrast to our study however, Divilisteri et al²³ reported co infection with TB and hepatitis as statistically significant determinants in the ocular manifestation in HIV. Our study had relatively very few respondents with a co infection (only 3) i.e. TB and DM, could have been responsible for this.

Conversely, Pathai et al²⁴ in a similar study in India reported that eye symptoms were not independently predictive of ocular diseases, this is in contrast to our study where we found that there was a significant association between eye symptoms and having the HIV related eye disease. The reason may be that usually, there is no ophthalmologist associated with these hospitals where our study was carried out hence the presence of one (the PI) may have prompted the patients to complain of eye symptoms.

A prospective study in Cameroon reported that 91.7% of patients with ocular lesions had CD4⁺ cell counts less than 200/ μ l,²⁵ which is in keeping with the results of our study that which showed that CD4⁺ cell count is a significant factor that influences the manifestation of ocular diseases among HIV positive patients.

This study had a number of limitations which include a seemingly small sample size. However, this was scientifically calculated in the right proportion of the respective clinics. Also, the study

did not note the eye diseases in the few patient who were not on HAART. It would have being more interesting to specifically note the findings in this group and the result somewhat compared with that of those on HAART. This provide a possible are for future studies to explore. Despite these, the study was able to provide answers to the questions it set out to determine.

Conclusion

Eye diseases cause significant morbidity among HIV positive patients, with a prevalence of 46.4% among our respondents. CD4 cell count, WHO Clinical staging of the disease and the presence of eye symptoms were the only factors that were found to affect the manifestation of these eye diseases.

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UNDER PEER REVIEW