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Ophthalmic findings in HIV/AIDS patients in Calabar, Nigeria

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ABSTRACT

Objectives: Out of the 38.0 million (30.2–45.0 million) with HIV/AIDS globally, about 35.9 million (28.9–43.0) adults live in sub-Saharan Africa. Ocular findings in HIV/AIDS are a cause of morbidity, visual impairment, and blindness and differ in different environments. This study aimed to investigate the pattern and prevalence of ophthalmic manifestations of HIV/AIDS in Calabar, Nigeria.

Material and Methods: This study investigated ocular findings among patients attending the HIV/AIDS Special Treatment Clinic of the University of Calabar Teaching Hospital, Calabar, Nigeria. Using a descriptive cross-sectional study design, a total of 440 subjects met the inclusion criteria and were recruited into the study.

Results: There were 166 (37.73%) male and 274 (62.27%) female respondents, indicating a female preponderance with a male-to-female ratio of 1:1.6. The modal age group was 26–35 and formed 40.4% of study population while 415 (94.30%) of the study population were 55 years old or less. While 316 (72.00%) of the respondents had some ocular morbidity, 136 (30.91%) were HIV/AIDS related. A total of 155 respondents (35.20%) had ocular symptoms. No person was blind, while 154 respondents (35.00%) were visually impaired. HIV/AIDS-related findings were retinal microangiopathy in 60 respondents (13.60%), conjunctival microvasculopathy in 30 (6.80%) respondents, hypertrichosis in 22 (5.00%) respondents, dry eye syndrome in 17 (3.90%) respondents, anterior uveitis in 17 (3.90%) respondents, presumed squamous cell carcinoma of the conjunctiva in 7 (1.60%) respondents, facial nerve palsy in 5 (1.14%) respondents, and Kaposi sarcoma of the eyelids and conjunctiva was in 4 (0.91%) respondents. There was increased ocular involvement among those respondents with lower CD_4^+ counts ($P < 0.0001$).

Conclusion: Ocular manifestation of HIV/AIDS can occur in the presence of normal vision and are a cause of avoidable uniocular vision loss. Non-HIV/AIDS-related ophthalmic morbidity also occurs in patients with HIV/AIDS. These facts justify targeted scheduled ophthalmic screening. Ophthalmologists need to recognize and manage the varying patterns and sometimes location specific signs and symptoms.

Keywords: Ocular manifestations, HIV/AIDS, Calabar

INTRODUCTION

The impact of the HIV/AIDS has been significant. In 2020, about 38.0 million (30.2–45.1 million) globally were living with HIV/AIDS.[1] Sub-Saharan Africa with about 11% of the world's population bears a disproportionately greater global disease burden and about 35.9 million (28.9–43.0) adults living with HIV/AIDS.[1,2]

Ocular involvement including keratitis, uveitis, molluscum contagiosum, herpes zoster ophthalmicus (HZO), cytomegalovirus (CMV) retinitis, and Kaposi's sarcoma (KS) has been documented from studies done globally and in Nigeria.[3-8] They are reportedly seen in up to 80% of patients with HIV/AIDS at some time of the disease.[3] This and the added misfortune of socioeconomic consequences of this disease make a case for timely scheduled examination of all patients diagnosed with HIV/AIDS to reduce incidence of ocular involvement and ocular morbidity where present and prevent permanent visual disability.[3,9-11] Differences in spectrum of ocular disease appear to exist between patients in developed and developing countries.[12] Studies of region-specific pattern of ocular involvements in HIV/AIDS in Nigeria and other developing countries are needed to equip the eye care community to deal with this public health challenge. With availability of highly active anti-retroviral therapy (HAART) and other anti-retroviral therapies, and improvement in life expectancy, the African ophthalmologists need to be prepared to receive more cases of ocular involvements in HIV/AIDS.[13] There appears to be a dearth of information on this from the ancient port city of Calabar, Nigeria. This study investigated the prevalence and types of ocular findings among patients attending the Special Treatment Clinic (STC) of the University of Calabar Teaching Hospital, Calabar, Nigeria.

MATERIAL AND METHODS

This study was conducted in the UCTH, Calabar, HIV/AIDS STC which provides medical care to Cross River State and neighboring states as well as border towns in Cameroon Republic.

A descriptive cross-sectional study design was adopted. Data collection lasted for a 16-week study period from July 1, 2010, to October 21, 2010 (this included data from new and old patients). Data collection was performed using a pretested and standardized semi-structured questionnaire. Following this, the questionnaire was modified to make questions unambiguous and applicable to the study objectives. This was administered by a trained interviewer, to every fourth patient (based on their number in the Clinic Register) who met the inclusion criteria. Respondents were recruited on a daily basis and were evaluated for all the study parameters on the day of entry into the study. HIV screening was by ELISA method while confirmation was performed by Western blot test. All patients enrolled in the study had CD_4^+ count performed.

One ophthalmic nurse research assistant performed vital signs assessment, obtained the bio data and history, and filled out that section of the questionnaire. A second research/ophthalmic-assistant assessed visual acuity (VA) of respondents. Visual impairment and blindness were defined using the revised WHO guidelines, where visual impairment is defined as presenting VA of <6/18 (0.3 Log MAR), but equal to or better than 3/60 (0.05), and blindness as presenting VA of <3/60 or worse, in the better eye.[14] The second research assistant also conducted patients to be examined by the ophthalmologist (principal investigator) (EDN). EDN employed a semi-structured examination protocol separate from the interviewer-administered questionnaire, to obtain the required information from ophthalmic examination. All study participants who required further/comprehensive ophthalmic evaluation including those whose distance VA was 6/18 or less or whose near VA was N_6 or less, were referred to the eye clinic of the UCTH.

HIV-positive and AIDS patients aged 16 and above registered in the STC at UCTH were recruited into the study by a systematic sampling technique after an informed consent had been obtained.

Patients reviewed in the pre-test, those who declined consent to participate in the study and, individuals too ill (needing emergency medical attention or life support) to have detailed ophthalmic examinations were excluded from the study population.

The sample size was calculated using the Cochran formula for simple proportions.[15] Using the standard normal deviate, which at the 95% confidence level of significance is set at 1.96, patients with expected ocular manifestations were assumed to be 50%. This gave a sample size of 384. Allowing for 10% attrition, it became 425.

This study was conducted according to the principles expressed in the Declaration of Helsinki. Ethical approval for its conduct was obtained from the UCTH Health Research and Ethics Committee.

All data obtained were methodically cross-checked, cleaned, and entered into Microsoft Excel 2007. All statistical data analysis was then performed using STATA IC version 10.

RESULTS

A total of 440 subjects who met the inclusion criteria participated in the study. The demographic characteristics of the 440 subjects who met the inclusion criteria are presented as [Table 1]. Females formed the larger part of the respondents 62.27%. The mean age of females 34.4 years, was lower than that of males 40.1 years, T-test = −6.017, $P \leq 0.0001$. The median age group was the 26–35 years age group who numbered 178 (40.45%) followed by those in the 36–45 years age bracket who numbered 137 (31.12%), both groups representing individuals in the most socioeconomically active age group. The median age was 25.55 years. The smallest group of respondents was in the >55 age bracket who numbered 25 (5.70%). Age group distribution in the group with ocular findings was similar to

Table 1: Demographic characteristics of study subjects (*n*=440).

Variable	Normal vision (6/6–6/18)	Mild visual impairment (<6/18–6/60)	Moderate visual impairment (<6/60–3/60)	Percentage
Sex				
Male	162	3	1	166 (37.73)
Female	271	3	-	274 (62.27)
Total	433	6	1	440
Age				
16–25	50	-	-	50 (11.36)
26–35	178	-	-	178 (40.45)
36–45	135	2	-	137 (31.14)
46–55	50	0	-	50 (11.36)
>55	20	4	1	25 (5.69)
Total	433	6	1	440
Education				
Tertiary	186	2	1	189 (42.95)
Secondary	159	0	0	159 (36.14)
Primary	65	2	0	67 (15.22)
None+	23	2	0	25 (5.69)
Total	433	6	1	440
Occupation				
Trading	124	1	-	125 (28.41)
Civil service	119	2	1	122 (27.73)
Artisan[£]	113	2	-	115 (26.14)
Applicant/retiree	31	-	-	31 (7.04)
(Para) military personnel	25	1	-	26 (5.91)
Student	21	-	-	21 (4.77)
Total	433	6		440

[£]Included professional drivers, farmers, hairdressers, and house-keepers

that of the rest of the study population. Trading was the most frequently seen occupation with 125 (28.41%) respondents, 74.5% of the respondents were gainfully employed, while students formed the smallest group; 21 (4.77%).

Ocular adnexa findings were the most prevalent HIV/AIDS-related eye findings in the study population 95 (47%) while the least common findings were neuro-ophthalmic 5 (2%) [Figure 1]. Specific HIV/AIDS eye findings are described in [Table 2], while the most commonly occurring non-HIV/AIDS-specific ophthalmic finding [Table 3] was presbyopia 136 (30.9%).

Following analyses of the mean CD_4^+ count as it related with ophthalmic findings, HZO had the highest (622) while the lowest mean CD_4^+ count was seen in participants with chorioretinitis (159) [Figure 2]. CD_4^+ cell count groups by ophthalmic involvement analyses gave a statistically significant association, χ^2, df = 4, = 48.3031, $P < 0.0001$ [Table 4]. [Figure 3] presents the pattern of ophthalmic symptoms encountered. Most participants did not have ophthalmic symptoms 285 (64.77). In addition, majority 387 (88%) presented with normal vision and VA of 6/6 while about 4 (1%) had moderate visual impairment, as shown in [Figure 4].

DISCUSSION

There are reports of ocular findings in adult HIV/AIDS subjects in other parts of Nigeria.[4-7] While this list is not exhaustive, the index study is one of a group, performed on subjects in a STC, whose diagnosis had been clinically and serologically proven to be HIV/AIDS and related complex, many of which had no felt need to visit an eye care facility. The larger number of patients enrolled and the geographic location for the index study contributes to its uniqueness.

The modal age group (25–35 years) seen in this study was somewhat similar to what was obtained in some comparable studies.[4,6,7,16,17] This age group formed 40.4% of study population. A total of 94.3% of the study population were 55 years and below [Table 1]. This age group represents the most economically active segment of the population and highlights the serious socioeconomic consequence of the HIV/AIDS in Nigeria.[9,10]

With respect to sex, the male-to-female ratio of 1:1.6 found in the index study corroborates some other reports that show a female preponderance.[4,5,6,17]

Patients with HIV/AIDS had ocular morbidity in UCTH STC and some had ocular symptoms [Figure 3].

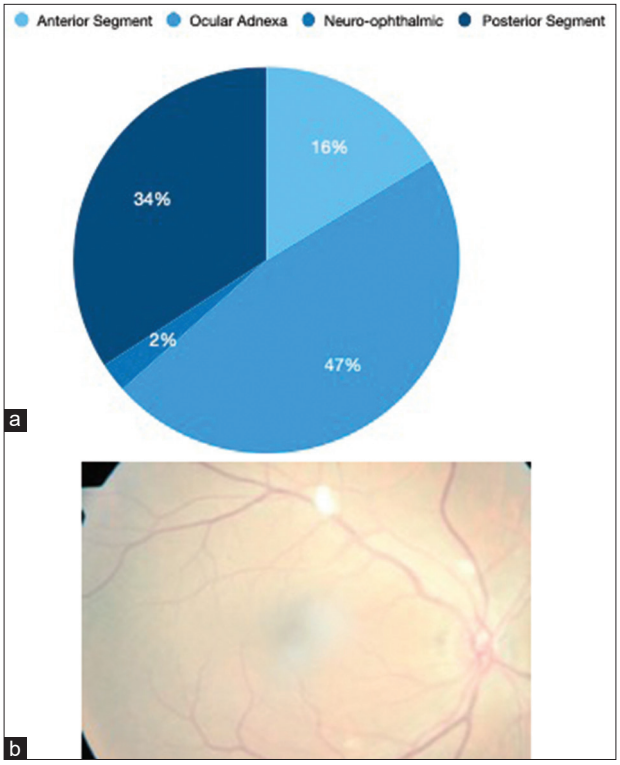

Figure 1: (a) HIV/AIDS-related ophthalmic findings by region of the eye involved. (b) Clinical photograph: Right retinal microangiopathy with cotton wool spots in HIV/AIDS.

Table 2: HIV/AIDS-associated ophthalmic findings in the study population.

Ophthalmic manifestation	OD, *n* = 440 (%)	OS, *n* = 440 (%)
Ocular adnexa/orbit		
Trichomegaly	22 (5.0)	22 (5.0)
Kaposi sarcoma	4 (0.9)	2 (0.5)
HZO	1 (0.2)	2 (0.5)
Molluscum contagiosum	6 (1.4)	4 (0.9)
Presumed conj. SCCa	6 (1.4)	1 (0.2)
Conj. microvasculopathy	27 (6.1)	30 (6.8)
Dry eye syndrome	17 (3.9)	17 (3.9)
Total	83	78
Anterior segment		
Corneal ulcer	1 (0.2)	0 (0.0)
Anterior uveitis	17 (3.9)	15 (3.4)
Total	18	15
Posterior segment		
Chorioretinitis	1 (0.2)	0 (0.0)
Chorioretinal scar	3 (0.7)	4 (0.9)
Retinal microangiopathy	60 (13.6)	57 (12.9)
Maculopathy	1 (0.2)	0 (0.0)
Total	65	61
Neuro-ophthalmologic		
7th cranial nerve palsy	3 (0.7)	2 (0.5)

OD: Right eye, OS: Left eye, HZO: Herpes zoster ophthalmicus, Conj.: Conjunctival, SCCa: Squamous cell carcinoma. Some patients had multiple findings

Table 3: Non-HIV-related ophthalmic findings in study participants.

Variable	Number	Percentage
Pterygium	25	5.6
Pingueculum	31	7.0
Allergic conjunctivitis	33	7.5
Presbyopia	136	30.9
Cataract	59	13.3
Glaucoma suspect	21	4.7
POAG	2	0.4
Uncorrected refractive error	101	22.9
Retinal detachment	3	0.6
Others	32	7.2

Others: Chalazion, ARMD, blepharitis, albinism, non-proliferative diabetic retinopathy, alternating esotropia, corneal phlyctenulosis, cystoid macular edema, loasis, Nevus of Ota, right corneal scarring, traumatic optic neuropathy, complicated cataract, cyst of Moll, macula hole, optic disc hypoplasia, optic atrophy. Some respondents had multiple eye diseases

Respondents most frequently complained of impairment of vision 154 (35.00%) while redness of the eye, seen in 27 (6.14%), was statistically significantly related to ocular involvement, $P < 0.001$.

There was no case of bilateral blindness within the index study population and about 98% presented with good distance VA (VA 6/18 and above) as in some other studies [Figure 4].[4-6] However, 1.4% and 0.9% had uniocular blindness in the right and left eyes, respectively. In contrast, an eye clinic study in Lagos, Nigeria,[18] had 90.9% of study subjects with a VA of <6/18. This is not surprising as 10 of the 12 patients in their study had severe HZO with corneal involvement. Their finding also suggests a possible selection bias in an eye clinic study.

Incidentally, 170 (38.7%) had non-HIV/AIDS-related ophthalmic findings [Table 3] including uncorrected refractive errors, cataracts, and pterygium with the most common being presbyopia 136 (30.9%). Non- HIV/AIDS-related ophthalmic findings are not reported in some comparable studies.[4-7,17]

The mean CD4 cell count in the index study was 369.7. A total of 33 (67.34%) of the 49 respondents with CD_4^+ cell count of <100 cells/μl had ophthalmic involvement. Although the highest CD_4^+ cell count was encountered in patients with HZO, there was a strong relationship between CD_4^+ count and ocular involvement with increased ocular involvement for lower CD_4^+ counts ($P < 0.0001$). This pattern is similar to what obtained in some other comparable studies [Figure 2].[4,6,16,17]

A total of 136 (30.9%) of respondents had specific HIV/AIDS associated ophthalmic findings [Table 2].

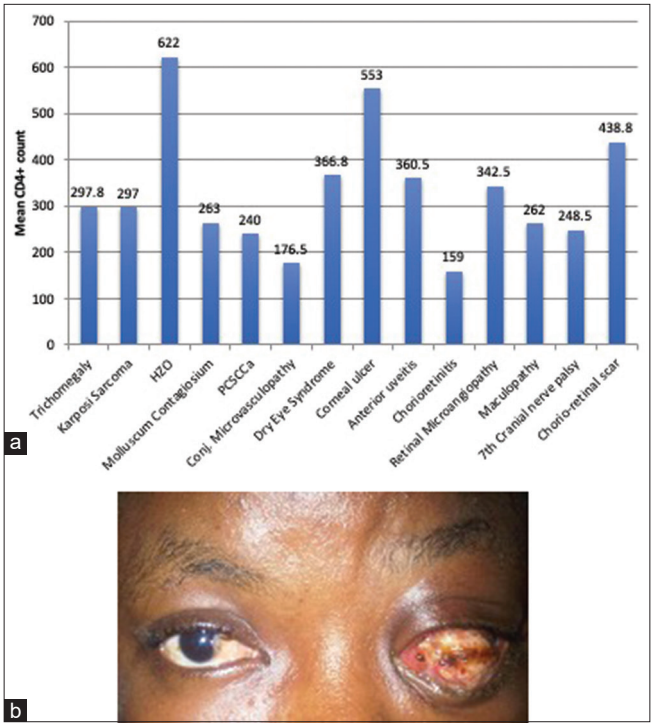

Figure 2: (a) Ophthalmic findings as they relate to CD4 count in the study population. (b) Clinical photograph: Left neglected conjunctival squamous cell carcinoma of the conjunctiva with destruction of the globe and orbital involvement in a 30-year-old HIV-positive female.

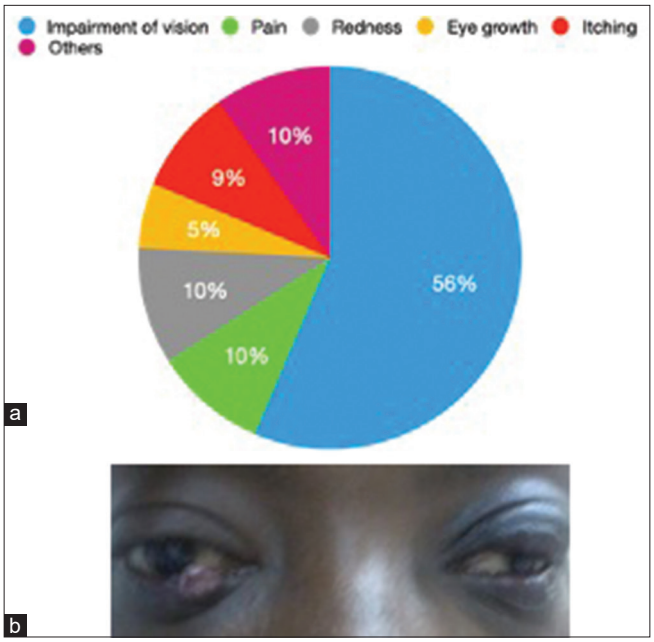

Figure 3: (a) Ocular symptoms among study participants. (b) Clinical photograph: Bilateral Kaposi sarcoma of the upper and lower eyelids and conjunctiva and left manifest exotropia in a 32-year-old HIV/AIDS-positive male.

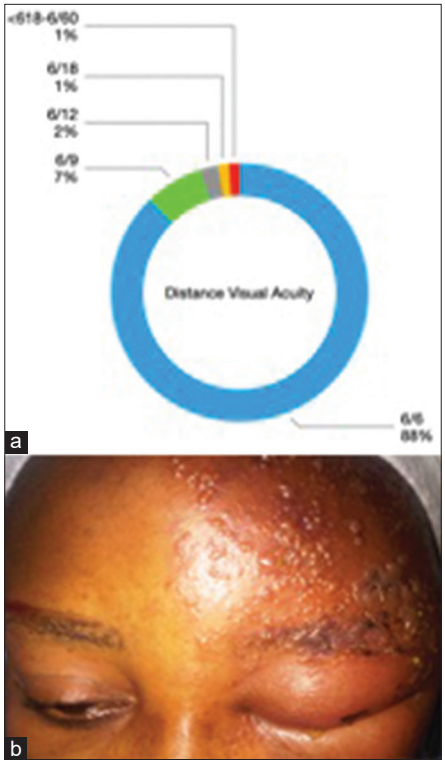

Figure 4: (a) Presenting visual acuity among the study participants. (b) Clinical photograph: Left herpes zoster ophthalmicus with active blistering rash and associated periorbital edema over the dermatome supplied by cranial nerve V1 in a 24-year-old female with HIV/AIDS.

Table 4: CD_4 + cell count groups by ophthalmic involvement.

CD_4 + count groups	Ophthalmic involvement		Total
	No (%)	Yes (%)	
<100	16 (32.65)	33 (67.35)	49
100–199	38 (58.46)	27 (41.54)	65
200–299	59 (67.82)	28 (32.18)	87
300–399	61 (75.31)	20 (24.69)	81
>400	130 (82.28)	28 (17.72)	158
Total	304 (69.09)	136 (30.91)	440

χ^2, df = 4,=48.3031 $P < 0.0001$

Non-infectious HIV retinal microangiopathy is common and said to have a good correlation with viral load.[19] This manifestation was found in 58 (13.4%) and 57 (12.9%) of our subjects on the right and left eyes, respectively, and was the most frequently encountered finding. This is in contrast with the 5 (1.8%) of the 275 patients seen in a study in Abuja, Nigeria,[6] whereas a study done in Port Harcourt, Nigeria,[4] it was the second most frequently occurring finding. The study in Kenyan[17] reports retinal microangiopathy in 37.5% (n = 94) of respondents a larger proportion than seen in the

index study. Further studies may reveal reasons for these differences.

This is a non-specific condition that can also be found in diabetes mellitus, sickle cell hemoglobinopathies, nutritional deficiencies, and anemia but has been documented to occur as an adnexal manifestation of HIV/AIDS. The index study population was not screened to rule out the presence of other etiological factors, however, conjunctival microvasculopathy – the second most common finding in the index study, was seen to affect 27 (6.1%) of the subjects on the right eyes and 26 (5.9%) on the left eyes. In comparison, this is lower than the 109 (33.8%) seen in Makurdi,[6] and 64 (15.6%) seen in Port Harcourt,[4] where it was their most common finding. Some other studies did not report it.[6,7,17]

Acquired trichomegaly (hypertrichosis of the eyelashes) has been reported in HIV-infected individuals.[20] Trichomegaly has also been documented in patients with autoimmune disorders, malnutrition, allergic systemic diseases, and uveitis as well as in patients receiving specific medication such as streptomycin, cyclosporine, and zidovudine (where it is associated with poor tolerance to the drug).[20] Some respondents were on zidovudine as part of HAART. Acquired trichomegaly was seen in 22 (5%) of the study population. It has been suggested that cessation of eyelash growth may indicate effective antiretroviral therapy.[20] This finding was not reported in some comparable studies.[4,6,16]

Keratoconjunctivitis sicca is reported to appear to be more common among individuals with AIDS (21.4–38.8% of HIV-infected men 16.9% of HIV-infected women)[21] than in the general population (estimated to be 1%).[21] In this study, dry eye is seen in 17 (3.9%) of the subjects [Table 2]. This finding is not reported in similar studies in Nigeria.[4,6]

Anterior uveitis and vitreous inflammatory reactions have been described in association with rifabutin therapy for patients with AIDS, antifungal agents, and some protease inhibitors.[22,23] Immune recovery uveitis (IRU) as a component of ocular immune recovery inflammatory syndrome is also seen in association with HIV/AIDS. Anterior uveitis was seen in the index study affecting right eyes 17 (3.9%) and the left eyes 15 (3.4%), respectively [Table 2], similarly in Onitsha[7] and Kenya[17] where it was reported in 4% and 11 (5.5%) of their respondents, respectively. In Port Harcourt and Abuja, Nigeria, lower frequencies are reported,[4,6] while in Makurdi,[5] where it was the second most common finding, a much higher frequency than the index study 88 (27.1%) was reported. Reasons for these differences are unclear.

The previous studies support a strong association of squamous cell carcinoma of the conjunctiva (SCCa) with HIV infection in Sub-Saharan Africa.[4,8,16] In an Ibadan, Nigeria study of orbito-ocular diseases,[16] a frequency of 12.1% was reported and in Benin, Nigeria, it was 2(0.4%).[24] These study populations and study sites were, however, different from that of this study. SCCa was seen in 3 (1.1%) and 12 (2.9%) of the Abuja[6] and a Port Harcourt[4] studies, respectively, where the study populations were similar to that of the index study. In a study in Kenya[17] where almost 30% of participants had CD_4^+ cell counts of ≤200 cells/μl (a risk factor for the development of OSSN), it was seen in 13 (6.5%). The index study recorded presumed SCCa affecting 6 (1.4%) of the study population on the right eye and 1 (0.2%) on the left eye [Table 2]. This is somewhat comparable to what was seen in the Abuja[6] study but is lower than other work.[4,16,17]

In Blantyre Malawi,[8] 53 consecutive patients with conjunctiva SCCa and conjunctival intraepithelial neoplasia were studied and 79% (30 of 38) were HIV positive. None of the respondents with SCCa were aware of having symptoms of HIV.

Conjunctival and adnexal KS were among the first ocular lesions and can be the AIDS-defining illness.[4,25] Multifocal KS was seen in 4 patients (0.9%) of this study population [Table 2]. Multifocal, multiorgan KS constitutes part of the AIDS defining diagnosis and is documented to be seen in about 30% of cases ranking it second to *Pneumocystis jirovecii* infections.[26] In a Northeast Nigeria study, where respondents numbered 20, KS of the conjunctiva was seen in eight subjects and were the second most common manifestation of HIV/AIDS after KS on the lower limbs (44%).[26] The large percentage in the above study may be explained by the fact that this was one of the study objectives – to document AIDS-associated KS in the region. A Benin Nigeria study[24] reported 1 (0.5%) patient with KS and this agrees with the findings in the index study. A total of 10 (5%) participants had KS in Kenya.[17]

Facial nerve palsy (Bell's palsy): In this study, facial nerve palsy was seen in 3 (0.7%) and 2 (0.5%) of the participants right and left eyes, respectively [Table 2], with one participant presenting with multiple cranial nerve palsies. Facial paralysis is recognized as an external ocular manifestation of neuro-ophthalmic abnormalities associated with HIV/AIDS.[27]

HZO in young adults has been documented as a marker for HIV infection in Africa with a very high predictive value.[28] It has been said to be a significant cause of unilateral blindness in individuals with background HIV/AIDS following corneal involvement.[3,4,12,29] HZO was seen in a total of 3 (0.7%) subjects one of whom had the active disease and 2 (66.7%) of whom had best-corrected VA of PL in the affected eye. In Port Harcourt, Nigeria,[5] and Nairobi Kenya,[17] the frequency was higher at 5 (1.2%) and 12 (6.5%), respectively.

In Benin, Nigeria,[24] 3 (75%) of four patients seen in the University of Benin Teaching Hospital eye clinic, with HZO over a 5-month period were HIV positive. In a Lagos

eye clinic study,[18] of 12 HIV-positive patients, 10 (83.4%) had HZO. Another research done to evaluate the HIV seropositivity among 10 otherwise healthy looking patients with HZO in Ilorin, Nigeria reports that 50% of participants were HIV positive.[28] In contrast, respondents in the index study did not seek eye care at the point of their recruitment.

No case of CMV retinitis was seen in this study. This agrees with some related work done in Nigeria.[4-7] This finding supports the suggestion that this disease may be uncommon in sub-Saharan Africa or it may be missed because the study is not eye hospital based.[12,13] In addition, HAART has reduced the incidence of CMV retinitis[30] and may have contributed to its absence in the index study with 100 (73.5%) of respondents with ophthalmic features of HIV/AIDS (n = 136) already receiving HAART.

CONCLUSION

This study shows that HIV/AIDS patients accessing general care in the STC of the UCTH had ocular symptoms which were not always predictive of HIV/AIDS-associated ophthalmic findings. VA was also not predictive of HIV/AIDS-associated ophthalmic findings seen as some patients with these findings had normal VA and avoidable visual loss. Non-HIV/AIDS-related ophthalmic findings that potentially cause visual impairment and blindness were also encountered. Ophthalmic disease in these patients justifies the need for targeted scheduled eye examinations to prevent avoidable ocular morbidity, visual impairment, and blindness.

Limitations of the study

The study was conducted in a tertiary hospital setting and so findings may not be representative of the general population. Furthermore, the study excluded HIV/AIDS patients who were considered too ill to have detailed eye examinations in a general clinic setting. These patients may have had related eye disease.

Recommendations

Referral from STCs for screening in Nigeria is desirable:

- For ocular involvement or presence of ocular symptoms,
- At diagnosis of HIV/AIDS and or at CD_4^+ count of 500 cells/mm^3 or below,
- For patients who are on drugs known to induce uveitis, patients who already have IRU and patients on treatment for coinfection with tuberculosis with drugs that are known to induce optic neuropathy.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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