ORIGINAL RESEARCH REPORT

Vitreoretinal manifestations of human immunodeficiency virus infection and acquired immunodeficiency syndrome in patients attending an antiretroviral therapy clinic in Nigeria: A cross sectional study

Yewande O. Babalola, Tunji S. Oluleye, Adeyinka O. Ashaye

Department of Ophthalmology, University College Hospital, Ibadan, Nigeria

ABSTRACT

Background: The human immunodeficiency virus infection and acquired immunodeficiency syndrome (HIV/AIDS) is a multi-systemic disease with known manifestations involving all ocular structures from the orbit and ocular adnexa, anterior segment to the retina and vitreous. Some of these manifestations including cytomegalovirus (CMV) retinitis and HIV retinopathy are HIV/AIDS-defining illnesses. The aim of this study is to determine the vitreoretinal manifestations in patients with HIV/AIDS attending an antiretroviral therapy clinic in Nigeria. **Methods**: This was a prospective, cross-sectional study of consenting, confirmed HIV/AIDS patients attending an antiretroviral therapy clinic in Nigeria. All willing, consecutive patients who gave an informed consent were recruited. Sociodemographic data and clinical information were collected with the use of a structured interviewer–administered questionnaire. Best-corrected visual acuity was recorded. Anterior segment and ocular adnexa examination was performed with a pen torch. Detailed anterior and posterior segment examination was performed with slit lamp biomicroscopy with Volks +78 diopter lens and binocular indirect ophthalmoscopy. The data were analyzed with SPSS (statistical package for social sciences) version 16. Ethical approval was obtained from the institutional ethics committee. **Results**: Three hundred and eighteen patients were studied of which 85 (26.7%) had disorders affecting the retina and vitreous. The female-to-male ratio was 2:1. More than a third of patients (38.7%) were in the 40–49 years of age group and the mean age was 47.2 years. The most common vitreoretinal lesion was presumed ocular toxoplasmosis present in 9.7% of all respondents. This was closely followed by HIV retinopathy in 3.5%, ocular tuberculosis in 1.8%, and CMV retinitis in 1.6% respondents. Two hundred and seventy-seven (87.1%) respondents were on highly active antiretroviral therapy and 41 (12.9%) were not on treatment. **Conclusion:** A high prevalence of ocular conditions especially those affecting the retina and vitreous exists in patients with HIV/AIDS attending the antiretroviral therapy clinic in a tertiary hospital in Nigeria. Regular eye examinations are recommended for these patients to prevent potentially visual debilitating disorders.

Key words: Cytomegalovirus retinitis, highly active antiretroviral therapy, human immunodeficiency virus infection and acquired immunodeficiency syndrome, human immunodeficiency virus retinopathy, ocular tuberculosis, presumed toxoplasmosis, vitreoretinal lesions

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Address for correspondence:
Dr. Yewande O. Babalola, Department of Ophthalmology, University College Hospital, Ibadan, Nigeria.
E-mail: yewandeb@gmail.com

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INTRODUCTION

Human immunodeficiency virus (HIV) and the acquired immunodeficiency syndrome (AIDS) affect 38 million people worldwide with 36.2 million of these population living in Africa.[1] With a prevalence of 1.3%, about 1.8 million people in Nigeria are living with the virus.[2] The HIV/AIDS infection is a multi-systemic disease in which the eye is often affected with ocular involvement being one of the most common manifestations of this syndrome. The incidence of ophthalmic manifestations in HIV/AIDS may range from 14.2% to 39%.[3,4,5] All ocular structures may be affected including the ocular adnexa, anterior segment, posterior segment, and the optic nerve head. The immune status measured by the CD4+ count and viral loads may be a determinant of the onset and progression of these varying ocular manifestations.[4]

The first documentation of ocular manifestations of HIV/AIDS in literature was in 1982 and was highlighted by the eye complications of HIV/AIDS especially cytomegalovirus (CMV) retinitis and the impact on vision in these patients in 1982.[5] With the advent and availability of highly active antiretroviral therapy (HAART), the incidence of opportunistic infections like CMV retinitis has been noticed to decrease significantly in comparison to the pre-HAART era.[6]

Ocular manifestations associated with HIV/AIDS infection may be the initial presenting sign of this condition and may heighten suspicion for the presence of the disease with emphasis on lesions such as HIV retinopathy, CMV retinitis, squamous cell carcinoma and herpes zoster ophthalmicus to name a few. CMV retinitis, an intraocular infection and retinal microangiopathy are the most common ocular manifestations of HIV/AIDS and both commonly involve the posterior segment.[7] As many of these intraocular inflammations affect the retina and vitreous, it is important to know the incidence of these lesions as ocular manifestations of HIV/AIDS with preeminence on our peculiar environment of the developing world in Africa.

The occurrence of ocular manifestations of HIV/AIDS infection has been linked to CD4+ count with patients with lower the CD4+ counts having a higher risk of developing these ocular manifestations particularly lesions in the posterior segment.[8] Patients with CD4+ counts of <500 are at risk for developing Kaposi' sarcoma, intraocular lymphoma and ocular tuberculosis while a CD4+ count of <250 predisposes to opportunistic infections such as toxoplasmosis and pneumocystosis. CD4+ counts of <50–100 are associated with CMV retinitis, a leading cause of debilitating blindness, varicella-zoster retinitis, and retinal microangiopathy among others.

Various local studies have documented diverse retinal manifestations as the leading posterior segment finding in HIV/AIDS. A study in Port-Harcourt found that most patients with posterior segment lesions had CD4+ counts <200 mm^3 with retinal microvasculopathy being the commonest lesion; none of the study patients had CMV retinitis.[9] Presumed ocular toxoplasmosis was the commonest HIV/AIDS associated lesion in Lagos, Nigeria.[10] Worldwide, retinal microangiopathy otherwise known as HIV retinopathy is considered as the commonest ocular manifestation of HIV/AIDS.[11]

METHODS

A prospective study of HIV/AIDS-positive patients attending the antiretroviral clinic in a tertiary institution was carried out over a six month period. The clinic serves both people living with HIV/AIDS on antiretroviral therapy and those who are noneligible for therapy. Outpatient clinic are open all days of the week from 8.00 Am to 5.00 Pm except Friday when patients on admission on the wards are seen. Consultations for various complaints, monitoring of the CD4+ and viral load counts and response to therapy are carried out at the clinics. Antiretroviral therapy drugs and other required investigations and treatments are provided free for confirmed and registered HIV/AIDS patients attending the clinic. Antiretroviral therapy drugs are usually picked up once monthly by the patients. Patients attending the retroviral clinic who were willing to participate and gave informed consent were recruited into the study. Ethical approval was obtained from the ethics/ethical committee of the institution.

Data collection was through an interviewer-administered questionnaire. Detailed ophthalmic examination of all consenting patients and retrieval of CD4+ count, viral load values where available and staging of the HIV/AIDS disease from the patients' files at the antiretroviral therapy clinic were done.

Ophthalmic examination consisted of visual acuity measurement, anterior and posterior segment examination by the ophthalmologist. A detailed ocular examination which consisted of slit-lamp biomicroscopy, applanation tonometry, and dilated binocular indirect ophthalmoscopy was carried out on all patients.

The vitreoretinal manifestations were compared with the most recent viral load and CD4 count at the time of recruitment. To analyze the association, Chi-square test application was done to the data wherever possible and $P < 0.05$ was considered statistically significant. Data analysis was done with SPSS for Windows, Version 16.0. Chicago, SPSS Inc.

RESULTS

Three hundred and eighteen patients were recruited and this included 225 females and 93 males, respectively, with a

ratio of 2:1. The age range was 27–67 years with a mean age of 47.2 years. The 40–49 years of age group had the highest number of respondents with 123 patients (38.7%) [Table 1]. The females were younger than the males especially in the 20–29 and 30–39 years of age groups (26.9% vs. 47.1%). Forty-seven percent of the patients studied were traders or business people making this the commonest occupation or profession [Table 2]. One hundred and twenty-nine (40.6%) patients were educated up to secondary school level, 7.2% had no formal education, 28% were educated up to primary level while 24.2% had tertiary education.

Two hundred and twelve (66.7%) of the respondents were married, 36 (11.6%) were widowed, 10.4% were single, 9.4% separated, and 2.2% were divorced. The widowed respondents were mostly females. There was a statistically significant difference in marital status of HIV/AIDS patient ($P < 0.05$) with the largest frequency in the married females group [Table 3]. The major risk factor for HIV/AIDS infection was multiple sexual partners via the heterosexual route in 174 (54.7%) patients. Other routes of transmission include skin piercing, barbing, shaving and use of unsterilized objects in 36.2%, history of sexually transmitted diseases in 9.7%, and blood and blood product transfusion in 4.4% of respondents.

Two hundred and seventy-seven (87.1%) of the 318 patients recruited for the study, were on HAART of which 257 (80.8%) were on first-line HAART therapy and 20 (6.3%) on second-line therapy) while 41 (12.9%) were nontreatment eligible as at the time of the study. As at the time of the study, the decision on commencement of HAART at the antiretroviral clinic was based on the presenting values of the CD 4+ count, the viral load and presence of AIDS-defining illnesses.

According to the World Health Organization classification and staging of HIV/AIDS infection, more than half of the respondents were in stage 3 of the HIV/AIDS infection spectrum and accounted for 165 respondents (52%) of the total respondents, an equal number of patients, 57 (18%) were in stage 2 and 4, respectively, while only 38 (12%) were in stage 1 [Figure 1].

Majority of the patients, 313 (98%) had the HIV-1 strain and only three patients (1%) were positive for the HIV-2 variant. Two patients (1%) tested positive for both the HIV-1 and HIV-2 variants. Despite the fact that the HIV-2 strain is thought to be more common and peculiar in western Africa, the HIV-1 strain is still the predominant variant [Figure 2]. Eighty-five patients (26.7%) of the 318 studied had varying vitreoretinal lesions.

One hundred and nine (40.4%) respondents had CD4+ count >400 cells/mm^3 while 70 patients (25.2%) had CD4+ counts <200 cells/mm^3. The viral load values of 188 patients (71.3%) was <200 copies which is the expected normal range and signifies good response to HAART and thus fairly good immunity thereby limiting the probability of development of opportunistic infections. The CD4+ counts and viral load values were not available in the patient files of all the respondents recruited.

Among the patients with retinal lesions, 65 (76.5%) were on HAART while 20 patients were nontreatment

Table 1: Age and sex distribution of patients

Age-group	Male (%)	Female (%)	Total (%)
20-29	6 (6.5)	27 (12.0)	33 (10.4)
30-39	19 (20.4)	79 (35.1)	98 (30.8)
40-49	38 (40.9)	85 (37.8)	123 (38.7)
50-59	22 (23.6)	28 (12.4)	50 (15.7)
60-69	8 (8.6)	6 (2.7)	14 (4.4)

Table 2: Occupation of patients

Occupation	Male (%)	Female (%)	Total (%)
Trader	26 (28.0)	125 (55.6)	151 (47.5)
Artisans	20 (27.95)	54 (24.05)	75 (23.6)
Civil servant	14 (18.3)	29 (12.9)	43 (13.6)
Driver	18 (19.35)	1 (0.4)	18 (5.7)
Student	4 (4.3)	5 (2.2)	9 (2.8)
Unemployed	2 (2.2)	5 (2.2)	7 (2.2)
Military/paramilitary	4 (4.3)	2 (0.9)	6 (1.9)
Farmer	3 (3.2)	3 (1.3)	6 (1.9)
Clergy/imam	2 (2.2)	1 (0.4)	3 (0.9)

Table 3: Marital status of respondents

Marital status	Male (%)	Female (%)	Total (%)
Married	76 (81.7)	136 (60.4)	212 (66.7)
Single	8 (8.6)	25 (11.1)	33 (10.4)
Separated	6 (6.5)	24 (10.7)	30 (9.4)
Widowed	1 (1.1)	35 (15.6)	36 (11.3)
Divorced	2 (2.2)	5 (2.2)	7 (2.2)
Total	93 (100)	225 (100)	318 (100)

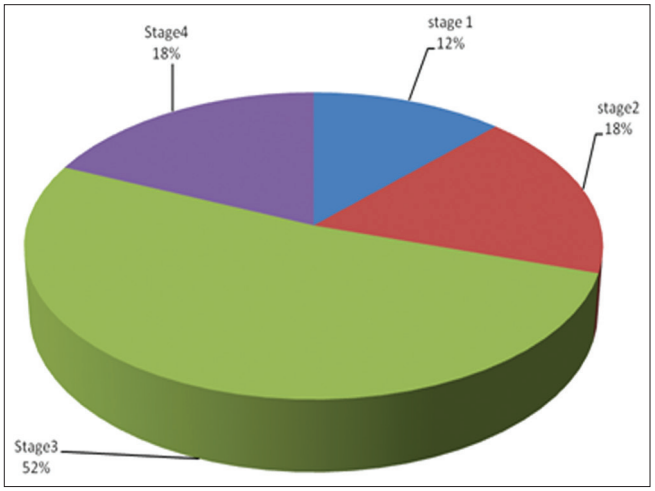

Figure 1: Distribution of 318 HIV/AIDS patients according to WHO clinical staging, HIV/AIDS = Human immunodeficiency virus infection and acquired immunodeficiency syndrome

eligible. The most common retinal finding which was also the most common HIV/AIDS-associated lesion presumed toxoplasmosis, was present in 31 (9.7%) patients followed by HIV retinopathy which was found in 11 (3.5%) patients [Figure 3]. The patients with presumed toxoplasmosis had high CD4+ counts >400 cmm^3.

CMV retinitis was present in only five of the patients (1.6%) studied. Two of the patients with CMV retinitis had bilateral disease while the other 3 were unilateral. The two bilateral cases of CMV retinitis had visual acuity of no light perception in both eyes and had both been commenced on HAART earlier but had defaulted from follow-up and treatment. CMV retinitis was more common in those not on HAART when compared to those on treatment (2.56% vs. 1.7%). The two patients who were bilaterally blind from CMV retinitis had CD4+ counts of 6 cells/mm^3 and 26 cells/mm^3 respectively **[**Figures 4 and 5].

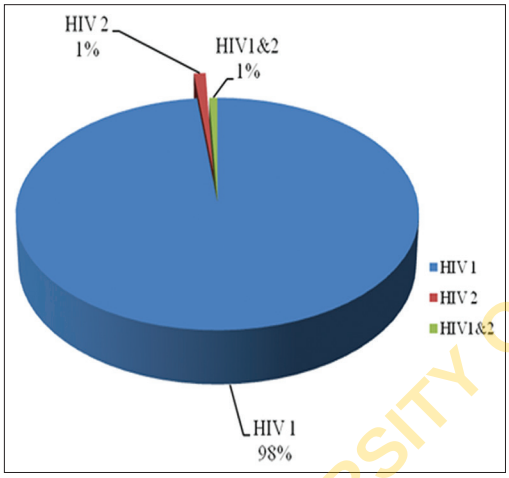

Figure 2: HIV serotypes of respondents, HIV = Human immunodeficiency virus

Figure 4: The fundus photo of a 37-year-old woman on second-line treatment for pulmonary tuberculosis showing tuberculous choroidal granulomas

Other HIV/AIDS-related retinal lesions diagnosed in the respondents include tuberculous choroiditis and granulomas which was present in 6 patients (1.6%). Fifty-eight (49.7%) of the total 318 patients studied had been diagnosed with pulmonary tuberculosis and were either on anti-Kochs' therapy at the time of the study or had been on treatment previously. Six patients had posterior segment features of ocular tuberculosis [Table 4].

Thirty-eight patients had concurrent systemic diseases in the study population while 280 did not. These comorbidities include hypertension in 32 (10%) patients and six patients (2%) with diabetes mellitus. Two patients had hypertensive retinopathy. Although none of the diabetic patients had features of diabetic retinopathy. A history of treatment for liver disease as a sequela of adverse effects of HAART was elicited in two patients.

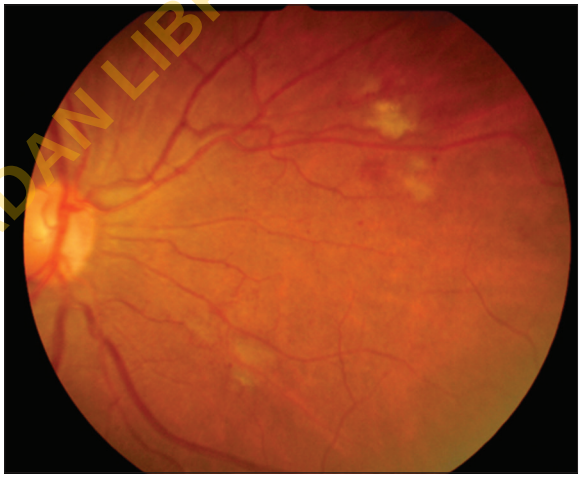

Figure 3: Fundus picture of the right eye of a 57 year old man with HIV retinopathy, HIV = Human immunodeficiency virus

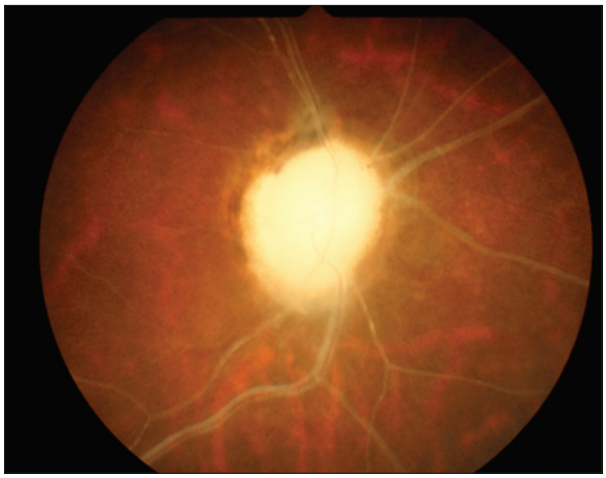

Figure 5: Fundus picture of a 38-year-old woman on HAART showing optic nerve atrophy with vascular sheathing secondary to presumed CMV retinitis, HAART = Highly active antiretroviral therapy, CMV = Cytomegalovirus

Best vitelliform macular dystrophy was a rare and unusual finding in one of the patients with the lesion being at the pseudohypopyon stage (stage 3) in the right eye and the vitello-disruptive stage (stage 4) in the left eye. Nonspecific sheathing of vessels in the absence of choroidal or retinal lesions was present in 6 patients and may be sequelae of previous pathology. The association between the presence of posterior segment lesions in those on HAART and the nontreatment eligible patients was not statistically significant.

Twelve out of 31 patients with presumed toxoplasmosis had CD4+ cell counts >400 cmm^3 and viral loads <200 copies, respectively, while the mean viral load was higher in patients with CMV retinitis. The CD4+ count of patients with CMV retinitis was <200 cmm^3 which corresponds with a low immune status which is a known risk factor for CMV infection.

Five of the patients with tuberculous choroiditis and granulomas all had viral loads <200 copies while the CD4+ count was >400 cmm^3 in four and only one had a CD4 count <200 cmm^3 which indicates a fairly good immune status in these patients. The sixth patient with ocular tuberculosis was on second-line anti-tuberculous therapy due to poor response to treatment with a viral load of 1,765,065 copies and a CD4+ count of 155,244 cmm^3 [Figure 6].

The most common neuro-ophthalmic manifestation was optic atrophy which was present in 12 of the respondents while features of glaucoma were seen in 20 of the respondents.

There was no statistical significance in the mean viral load and CD4+ count of patients with and without the known HIV-associated ocular lesions such as HIV retinopathy, presumed toxoplasma chorioretinitis, and CMV retinitis, respectively (P = 0.617).

Table 4: Distribution of vitreoretinal manifestations of human immunodeficiency virus infection and acquired immunodeficiency syndrome

Ocular diagnosis	HAART (%)	Non-HAART (%)	Total (%)
Presumed toxoplasmosis	27 (31.7)	4 (4.7)	31 (36.4)
HIV retinopathy	5 (5.9)	6 (7)	11 (12.9)
White without pressure	6 (6.8)	2 (2.6)	8 (9.4)
TB choroiditis	5 (5.9)	1 (1.2)	6 (7.1)
Nonspecific sheathing of vessels	4 (4.7)	2 (2.4)	6 (7.1)
CMV retinitis	2 (2.4)	3 (3.5)	5 (5.9)
Lattice degeneration	2 (2.3)	1 (1.1)	3 (3.4)
Hereditary familial drusen	3 (3.4)	0	3 (3.4)
Tilted disc	2 (2.4)	0	2 (2.4)
Hypertensive retinopathy	2 (2.4)	0	2 (2.4)
Atrophic maculopathy	1 (1.2)	1 (1.2)	2 (2.4)
Old central retina artery occlusion	1 (1.2)	0	1 (1.2)
Best disease	1 (1.2)	0	1 (1.2)
Choroidal rupture at macular	1 (1.2)	0	1 (1.2)
Cystoid macula oedema	1 (1.2)	0	1 (1.2)
Ocular albinism	1 (1.2)	0	1 (1.2)
Retinal detachment	1 (1.2)	0	1 (1.2)
Total	65 (76.4)	20 (23.6)	85 (100)

HIV=Human immunodeficiency virus, TB=Tuberculosis, CMV=Cytomegalovirus, HAART=Highly active antiretroviral therapy

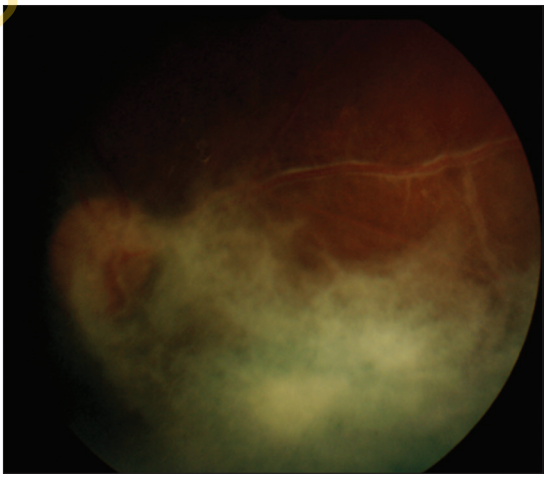

Figure 6: Fundus picture of a 25-year-old woman with cytomegalovirus retinitis on HAART, HAART = Highly active antiretroviral therapy

DISCUSSION

Over a quarter of the respondents in this study had vitreoretinal manifestations. Ocular manifestations of HIV/AIDS have been documented worldwide and even in Nigeria since the advent of the HIV/AIDS pandemic.[5] The prevalence of HIV/AIDS in Nigeria is about 1.4% with about 1.9 million people currently living with the virus with about 1.1 million of this population currently on HAART.[12] There was a female preponderance with many patients in the 40–49 year age group as noted in various local studies.[9,10,13] This may be due to higher risk of infections in females or the fact that a number are picked up during routine screening at the antenatal clinics. The mean age was 47.2 years which is similar to the study in Benin with a mean age of 46.5% but in contrast to the study in Port-Harcourt where the mean age was 36.5 and Lagos were the mean age was 40 years, respectively.[10,14,15] These may be attributable to the fact that Port Harcourt and Lagos are more urban and cosmopolitan cities. A little over half of the study respondents were in stage 3 of the HIV/AIDS spectrum using the WHO classification.[1] This late presentation may be attributed to poor health seeking attitudes and patterns of the patients which is common in our environment leading to diagnosis at the advanced stage of the disease.

Eighty-five of the 318 patients studied (26.7%) had various manifestations of the retina and vitreous which was similar to different local studies which ranged from

14% to 60%.[4,14-19] Posterior segment manifestations of HIV/AIDS has been documented in literature and typically classified into four major groups namely vasculopathy, opportunistic infections, unusual malignancies, and neuro-ophthalmologic abnormalities.[11,20] Posterior segment lesions in our study were distributed into all the groups with the exception of unusual malignancies.

This wide range and variety of vitreoretinal diagnoses in our study may be attributed to the fact that all patients had both dilated binocular indirect ophthalmoscopy and slit lamp biomicroscopy with +78D Volks lens and not just the patients presenting with retinal symptoms. These other varied retinal pathology such as lattice degeneration, best disease, familial hereditary drusens to mention a few are likely incidental findings and not associated to the underlying HIV/AIDS infection.

The most common vitreoretinal lesion was presumed ocular toxoplasmosis which was present in 9.7% of patients and was higher in prevalence compared to the findings in Lagos and Benin.[10,14] This might be attributable to the fact that quiescent, presumed toxoplasmosis scars occur commonly in our population in general with our study patients being no exception as only three of the patients had active inflammation and borderline CD4+ counts of around 200 cmm^3. However, our findings are similar to that of a study from Brazil with an 11% prevalence of patients with features of ocular toxoplasmosis.[21] HIV retinopathy was seen in 3.5% of all respondents and was within the prevalence range of 0.3% and 4.6% in Lagos and PortHarcourt, respectively. It differed from two other similar studies in Benin and Owo in which no diagnosis of HIV retinopathy was documented.[10,13-15]

CMV retinitis was present in five patients (1.6%) which similar to 1.8% in Lagos though there was no report of CMV retinitis in Port Harcourt.[9,10] The frequency of CMV retinitis in African AIDS patients is generally said to be less than in developed countries.[22] Two of the severely immunocompromised patients with bilateral CMV retinitis had low CD4 counts of 6 and 26 mmm^3 respectively which is in keeping with literature that CMV retinitis occurs when CD4 count is <50 c/mm^3 which may be a sequelae of late diagnosis or failure of HAART.[23,24] Approximately 15% of patients with active CMV retinitis are asymptomatic. Therefore, routine screening with dilated indirect ophthalmoscopy has been recommended at 3-month intervals in patients with CD4+ counts <50 cells/µl.[25] HIV retinopathy was present in 11 patients (3.5%) and was more prevalent in those with CD4 count <200 mm^3 similar to the study in Ethiopia but differed from their lower prevalence of 0.6%.[26]

Choroidal tuberculosis was diagnosed in six of our study respondents (1.8%) and differed from other local studies in which no case of ocular tuberculosis was diagnosed. Ocular tuberculosis has been said to be relatively rare in AIDS and occurs at even CD4 counts > 200 cells/mm^3.[27,28] A similar study in India had 1.95% of patients having ocular tuberculosis and in Malawi, 2.8% of the patients had ophthalmic features of tuberculosis.[22,28] A recent study in Tunisia had a prevalence of 7.1% of patients with tuberculous choroiditis.[29]

A wide range of various retinal lesions nonspecific to HIV/AIDS ranging from lattice degeneration to best disease, hereditary familial drusens, and choroidal rupture among others were seen in this study compared to other similar studies. There was only a single case of retinal detachment with prevalence of 0.85% which is similar to the findings in Benin City in which two patients had retinal detachment (0.4%).[14]

CONCLUSION

The most common vitreoretinal manifestations of HIV/AIDS in this study were from the opportunistic infections group. Of these, presumed ocular toxoplasmosis, CMV retinitis and choroidal tuberculosis were the predominant lesions. HIV retinopathy occurred in both patients on HAART and the nontreatment eligible. Tuberculous choroidal granulomas though thought to be uncommon may occur in HIV/AIDS as seen in our patients in Ibadan. Other retinal lesions seen include white without pressure, lattice degeneration and hypertensive retinopathy among others. It is recommended that scheduled ocular examinations may be beneficial in these patients aiding in prompt diagnosis and prevention of visually debilitating sequelae.

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Conflicts of interest
There are no conflicts of interest.

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