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Ocular manifestation of HIV/AIDS infection among patients receiving highly active Anti retro viral therapy (HAART) in a tertiary eye care centre

Azonobi Richard Ifeanyi[1]*, Udoye Ezenwa[2], Tebepah Tarilah[1] and Opubiri Ibeinmo R.[1]

[1]Department of Ophthalmology, Niger Delta University, Amassoma, Nigeria.
[2]Department of Anatomical Pathology, Niger Delta University, Amassoma, Nigeria.

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The pattern of ocular manifestation of human immune deficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) infection in Bayelsa state, Nigeria is presently unknown. In order to effectively control HIV/AIDS infection in the state, it is important to know the ocular manifestation of HIV/AIDS infection in this locality. The purpose of this study was to ascertain the eye manifestation of HIV infection in patients receiving highly active anti retroviral therapy (HAART). A descriptive study was carried out on all consecutive HIV infected patients including those with the advanced stage of the disease. They were all receiving highly active anti retroviral therapy at the "Heart to Heart" clinic of the Niger Delta University Teaching Hospital (NDUTH). The study took place over a period of 16 months. A detailed medical history followed by a comprehensive ocular examination was carried out on each patient, and the findings were recorded. A total of 150 HIV positive patients were examined during the period of this study. They were 57 males and 93 females, with a male to female ratio of 1:1.6. Twenty one patients with ages ranging from 8 to 66 years old presented with ocular manifestation of HIV/AIDS infection. They had a mean age of 41.48 years old (standard deviation (SD) ± 13.98). The prevalence of ocular manifestation of HIV/AIDS infection was found to be 14% (95% confidence interval (CI), 8.4 to 19.6). HIV related microvasculopathy and uveitis (each 24%) were the commonest ocular manifestation in this population followed by retrobulbar optic neuritis (19.2%) and Herpes zoster ophthalmicus (9.6%). HIV related microvasculopathy, uveitis and retrobulbar optic neuritis were responsible for over 2/3 of ocular manifestation. Herpes zoster ophthalmicus, cytomegalovirus retinitis and conjunctiva microvasculopathy were rare findings.

Key words: human immune deficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), disease, ocular, highly active anti retroviral therapy (HAART), tertiary, eye centre.

INTRODUCTION

Human immunodeficiency virus infection (HIV) and the advanced form of the disease, acquired immune deficiency syndrome (AIDS) since its first report in the United States of America in 1981 has become a worldwide pandemic, with over 33.4 million persons globally living with the disease (MMWR, 1981; Martins and Peter, 2009). Over 90% of persons infected with the virus (HIV) live in developing countries, particularly those of Sub-saharan Africa and South-East Asia (UNAIDS, 2003). In Nigeria, HIV infection was first reported in 1986 (Mohammed et al., 1988). The epidemic has since then spread across the country like wild fire, with the national

*Corresponding author. E-mail: doctorazonobi2002@yahoo.com, richardify@ymail.com.

average prevalence currently at 3.6% (Fed Ministry of Health, 2010) despite all the concerted effort recruited to combat it. HIV is a multi-systemic disease affecting various systems and organs of the body including the eye. The ocular manifestation of HIV/AIDS was first reported by Holland et al. (1982) (Holland et al., 1982). Ocular manifestation may be the primary presentation of the disease (Sahu et al., 1999). Studies have shown that 70 to 80% of AIDS patients will experience an ocular manifestation at any point in time during the course of the disease (Saraf and Ernest, 1996). The frequency and form of ocular manifestation is variable, depending on the stage of HIV infection (Jabs, 1995).

In the early stage of the disease (CD4 count > 500 cells/µl), ocular manifestations are uncommon, usually in the range of 11.9%, while in advanced disease (CD4 < 50 cells/µl) it may approach 100% (Turner et al., 1994; Cunningham and Margolis, 1993). Ophthalmic manifestations are usually non-specific in the early stage of HIV infection but later gives way to specific ocular manifestations such as microvasculopathies (for example, cotton wool spots, haemorrhages and others), and external eye diseases (for example, molluscum contagiosum, keratoconjunctivitis sicca and herpes zoster ophthalmicus) as the disease progreses. As the immune system undergoes further suppression, opportunistic infections such as cytomegalovirus, cryptococus, and *Toxoplasma gondii* becomes obvious (Maclean et al., 1996; Ndoye et al., 1993).

The prevalence and the spectrum of ocular manifestation of HIV/AIDS differs from one environment to the other (Susan, 1995). In North West Ethiopia, Asefa et al. (2006) found that 60% of HIV/AIDS patients studied have ocular manifestations and retina microvasculopathy was the commonest ocular lesion seen (24%) (Asafe et al., 2006). Kehinde et al. (2005) in Northern Nigeria found the prevalence of ocular manifestation of HIV infection to be 12.3%, majority (69.6%) of the complications being due to Herpes zoster ophthalmicus (Kehinde et al., 2005). In Benin City, South-southern Nigeria, a prevalence of ocular manifestation of 4% was found among a group of HIV positive patients and herpes zoster ophthalmicus was the commonest, with a prevalence of 2.7% (Osahon and Onunu, 2007).

To ensure the optimal care of HIV/AIDS patients, it is important to know the ocular manifestation of HIV/AIDS infection in that particular environment. Presently, information is not available on the ocular manifestation of HIV/AIDS infection in Yenagoa, Bayelsa State, Nigeria. This study was therefore conducted to fill this gap in knowledge.

MATERIALS AND METHODS

Duration/place of study

This study took place over a period of 16 months (September, 2010 to January, 2012) at the Eye Clinic of the Niger Delta University Teaching Hospital, Okolobiri.

A descriptive study was carried out on every consecutive HIV positive patients receiving treatment (highly active anti-retroviral therapy - HAART) at the Heart-to-Heart Clinic of the above mentioned insttution. HIV positive patients referred from other units of the Hospital to the Eye Clinic were also included in this study. Their baseline data such as age, sex, and recent CD4 count were recorded in a proforma designed for the study. They were then classified according to the World health Organization (WHO) clinical staging criteria for AIDS definition. Patients that have been previously classified by the managing physician were not re-classified as the information was obtained from the patient's record. A brief ocular history was also obtained followed by visual acuity assessment and a detailed anterior and posterior segment examination. Visual acuity assessment was done by an ophthalmic nurse at a distance of 6 m using a snellen acuity chart. Those whose visual acuity showed an improvement with pin hole were referred to the optometrist for refraction. The anterior segment examination was done using a pen torch and a slit lamp biomicroscope (Haag-Strait). The posterior segment examination was done using direct and indirect ophthalmoscope (Keler) as necessary. Tropicamide (1%) dilatation was done in those whose pupil were too small for detail fundoscopy. Those that presented with tumour formation had excisional biopsy and the histology report was documented.

Consent/ethical approval

As at the time of this research, an ethical committee has not been set up for this institution. However, the recommendation of the International Committee on Ethics on Researches involving Human Subjects were strictly adhered to. Consent was obtained from the subjects by the referring physcian at the time of consultation at the "Heart to Heart" clinic.

Statistical analysis

Data was presented as frequencies, mean, standard deviation and percentages. They were analysed using the statistical package for social scientists (SPSS) version 16 and a scientific calculator.

RESULTS

A total of one hundred and fifty (150) HIV positive patients were examined during this period. They were 57 males and 93 females. Their ages ranged from 8 to 66 years, with a mean of 36.88 years ± 10.36 SD. Of this number, twenty one presented with ocular features of HIV/AIDS infection giving a prevalence of 14.0% (95% CI, 8.4 to 19.6). They were 9 males and 12 females (Table 1). Their ages ranged from 8 to 66 years, with a mean of 41.48 years ± 13.98 SD. The clinical staging of the HIV positive patients with ocular manifestation is shown in Table 2. Majority (85.7%) were in stage 3 of the disease while a minority (4.8%) each were in stage 2, 4 and 5 of the disease, respectively.

The ocular manifestation of HIV/AIDS in the study population is shown in Table 3. HIV microvasculopathy and uveitis were the commonest ocular manifestation, with each constituting 24% of cases seen. This is followed by retrobulbar optic neuritis and herpes zoster

Table 1. Age and sex distribution of patients in the study population**.**

Age (years)	Sex (n%)		Total
	Male	Female	
0 - < 10	1(4.8)	-	1(4.8)
10 - < 20	-	-	-
20 - < 30	-	-	-
30 - < 40	3(14.3)	7(33.6)	10(48)
40 - < 50	2(9.6)	1(4.8)	3(14.3)
50 - < 60	1(4.8)	4(19.2)	5(24)
60 - < 70	2(9.6)	-	2(9.6)
> 70	-	-	-
Total	9(43.2)	12(57.6)	21(100)

Table 2. Clinical staging of patients

Stage	Number	Percent
2	1	4.8
3	18	85.7
4	1	4.8
5	1	4.8
Total	21	100.0

ophthalmicus (19.2 and 9.6%, respectively). Cytomegalovirus retinitis, squamous cell papilloma, infective conjunctivitis, episcleritis and conjunctiva microvasculopathy each constituted 4.8% of cases seen. The CD4 count of patients with ocular features of HIV/AIDS infection is shown in Table 4. More than half (52.8%) of the patients have CD4 counts of less than 150 cells/µl, while 42.4% have CD4 counts of between 150 to less than 350 cells/µl.

DISCUSSION

The prevalence of ocular manifestation of HIV/AIDS infection in this study was found to be 14.1% (95% CI, 8.4 to 19.6). This is similar with the findings of Kehinde et al. (2005) in Northern Nigeria where a prevalence of 12.3%. was found (Kehinde et al., 2005). However, this is at variance with findings in Ethiopia (Asefa et al., 2006), Morocco (Lamzaf et al., 2011) and Brazil (Muccioli et al., 1994) where the prevalence of ocular manifestations was found to be 24.3, 60 and 52%, respectively. Studies have shown that the clinical presentation of HIV related diseases may be modified positively by HAART (Whit cup, et al., 1997). The patients involved in the above studies were not on HAART. Similarly, it has been found that the frequency and nature of ocular complications of HIV infection is related to the stage of the disease (Kestelyn et al., 1985; Biwas et al., 2000). Majority (85.7%) of the patients studied were in stage 3 of the disease. These observations may be responsible for the lower prevalence of ocular complication of HIV/AIDS observed in this population.

HIV related microvasculopathy and uveitis were the commonest manifestation of HIV/AIDS infection in this population accounting for 24% (95%CI, 19.7 to 29.7) each of ocular manifestations. This is consistent with the findings of Asefa et al. (2006) in Ethiopia, Sahoo (2010) in Tanzania and Ndoye et al. (1993) in Dakar, Senegal where HIV related microvasculopathy constituted 24, 25 and 22% of ocular complications, respectively. However, our findings are lower than 50% reported by Biwas et al. (2000) in India. Jabs (1995) in his study have found that the occurrence of HIV retinopathy is related to the stage of the disease. In the early asymptomatic stage of the disease, HIV retinopathy is a rare occurrence, occurring in 3% of patients. As the disease progress to the symptomatic stage (AIDS related complex), the frequency of occurrence of HIV retinopathy increases to 34%. In advanced infection (AIDS), 50% of the patients presented with HIV related retinopathy.

The majority of our patients (85.7%) were in the intermediate stage of the disease (stage 3). This may explain why the occurrence of HIV related retinopathy is lower than that reported by Jabs in more advanced stage of the disease. Uveitis is not uncommon in HIV infection (Pathanapitoon et al., 2008; Mwanza, (2001). It was responsible for 24% of ocular manifestations in this population. This is similar with 25% recorded by Nwosu et al. (1996) in Eastern Nigeria and at variance with 7.4 and 15.8%, respectively reported by Asefa et al. (2006) in Ethiopia and Ebano et al. (2007) in Cameroon, respectively. The causes of uveitis in this study were determined clinically. Majority (60%) of the uveitis were presumed to be due to toxoplasmosis while in the remaining (40%), the cause of uveitis was not determined because of absence of appropriate laboratory backup and poor patient compliance to follow up.

Retrobulbar optic neuritis is a common complication of HIV infection and can be a first sign of HIV infection (Alimanovic and Ibisevic, 2007; Liu et al., 2005). In our study, retrobulbar optic neuritis was responsible for 19.2% (95% CI, 2 to 36.2) of the ocular complications. Half (50%) of the patients were unilaterally blind while the remaining half (50%) were bilaterally blind. In Lagos, western Nigeria (Akinsola et al., 1997), retrobulbar optic neuritis was responsible for 9.0% of the cases studied. In this era of HIV/AIDS pandemic, ophthalmologists must have a high index of suspicion of HIV associated retrobulbar optic neuritis in order to ensure early diagnosis and treatment.

Herpes zoster ophthalmicus is a commonly encountered infection among HIV positive patients (Umeh, 1998; Owoeye and Ademola-Popoola, 2003). Herpes zoster ophthalmicus was found in 9.6% (95% CI, 3 to 22) of our patients with HIV/AIDS infection. This observation is similar with 8.5 and 12.3%, respectively recorded by Ndoye et al. (1993) in Senegal and Ebano et al. (2007) in

Table 3. Ocular manifestation of HIV/AIDS infection in the study population.

Ocular manifestations	Number	Percent
HIV related retinopathy	5	24
Uveitis	5	24
Retrobulbar optic nuritis	4	19.2
Herpes zoster ophthalmicus	2	9.6
Cytomagalovirus retinitis	1	4.8
Squamous papiloma of the conjunctiva	1	4.8
Infective conjunctivitis	1	4.8
Bilateral episcleritis	1	4.8
Conjunctiva microvasculopathy	1	4.8
Total	21	100.0

Table 4. CD4 count of the study population.

CD4 count (cells/µl)	Number	Percent
0 - < 50	4	19.2
50 - < 100	3	14.4
100 - < 150	4	19.2
150 - < 200	2	9.6
200 - < 250	2	9.6
250 - < 300	4	19.2
300 - < 350	1	4.8
> 350	-	0
Not available	1	4.8
Total	21	100.0

Cameroon. However, our finding is higher than 6.2 and 5.0%, respectively recorded by Georgis et al. (2007) in Addis Ababa and Soumendra (2010) in Tanzania.In northern (Kehinde et al., 2005) and eastern (Nwosu et al., 1996). Nigeria, 69.6 and 75%, respectively of the patients with HIV/AIDS infection presented with herpes zoster ophthalmicus. In Lome, Ayena et al. (2010) reported that herpes zoster ophthalmicus was the second commonest ocular manifestation of HIV infection (19.6%). The disparities noted above may be due to individual patient's intrinsic factors and the fact that they were at different stages of immune supression in different population groups studied. The patients in our study and those in Lome were at different stages of treatment with highly active anti-retroviral therapy (HAART), while the ones in northern and eastern Nigeria as far as we know were not. The lower incidence of Herpes zoster ophthalmicus in our study compared to the ones in northern and eastern Nigeria may be due to the effect of HAART.

Even in the era of HAART, cytomegalovirus (CMV) retinitis has remained an important cause of ocular morbidity and a predictor of HIV mortality (Lai et al., 2011). However, CMV retinitis was a rare ocular complication of HIV/AIDS infection in this study and was responsible for 4.8% (95% CI, 1 to 9.4) of cases. This is similar with the findings of studies in Ethiopia (Georgis et al., 2010) and Tanzania (Soumendra, 2010) where CMV retinitis was responsible for 6.2 and 7.2%, respectively of ocular complications of HIV/AIDS infection. However, studies in Brazil (Muccioli et al., 1994) and Thailand (Ausayakhun et al., 2003) have reported a higher frequency of occurrence of CMV retinitis of 25 and 33%, respectively of ocular complications studied. Cytomegalovirus retinitis is known to occur in patients with profound immune-suppression, usually with CD4 count of < 50 cells/μ^3 (UNAIDS, 2003; Labetoulle et al., 1999; Jacobson et al., 1997). In our study, 80.8% of the patients have a CD4 count of greater than 50 cell/µ and were all on HAART regimen. Spontaneous resolutions of CMV retinitis have been reported in patients with increased CD4 count related to HAART therapy (Whitcup et al., 1997; Autran et al., 1997). These observations may be responsible for the lower incidence of CMV retinitis in our study population.

One of the patient (4.8% in our study of ocular complication) presented with bilateral squamous cell papiloma of the conjunctiva confirmed by excisional biopsy of that eye (OD). The CD4 count at presentation was 8 cells/mm^3. On follow up, the squamous cell papiloma on the unoperated left eye underwent gradual involution until it spontaneously resolved after several months on HAART therapy. On follow up, we discovered a recurrence of the squamous cell papiloma on the unoperated left eye. Investigation revealed stoppage of HAART regimen for a period of few months. Squamous papilomas are known to be caused by infection with the human papiloma virus (HPV) (Jack JK, 2007). This observation may suggest that squamous cell papiloma of the conjunctiva may be a manifestation of a non-opportunistic infection of the conjunctiva caused by HPV.

However, further studies are needed to confirm this observation.

Infective conjunctivitis, episcleritis and conjunctiva microvasculopathy are rare ocular manifestation of HIV/AIDS infection as recorded in this study (4.8% each of ocular complications). This is similar with findings of

studies in Nepal (Jabs, 1995) and Northern Nigeria (Kehinde et al., 2005) where conjunctivitis was responsible for 1.7% and conjunctivitis and episcleritis were responsible for 6.4% of cases seen. Patients with HIV/AIDS infection may present with asymptomatic conjunctiva microvasculopathy (Saraf and Ernest, 1996). This was recorded in 4.8% of our patients with ocular lesions of HIV/AIDS infection. In a study of ocular adnexa and anterior segment manifestation of HIV infection in Makurdi, North central Nigeria, conjunctiva microvasculopathy was the commonest finding (Bologi and Ojiabo, 2009). Conjunctiva microvasculopathy present as microaneurysms and segmental vascular dilatations and narrowing. The cause of these vascular changes is not clear but are thought to be due to deposition of immune complexes in blood vessels or the direct infection of conjunctiva vascular endothelium by the HIV virus (Engstrom et al., 1990).

CONCLUSSION

HIV related retina microvasculopathy, uveitis and retrobulbar optic neuritis are the commonly encountered ocular manifestation of HIV/AIDS infection (66.7%) in this population. As these diseases has potential to cause profound visual loss, control of HIV/AIDS infection in this population must pay priority attention to them. Squamous cell papilloma of the conjunctiva although not previously reported to our knowledge as one of the neoplasms associated with HIV/AIDS infection was found to be associated with HIV/AIDS infection in this population.

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