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Full Length Research Paper

Evaluating the effect of highly active antiretroviral therapy on visual acuity and intraocular pressure among HIV/AIDS patients in Kano State, Nigeria

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Highly Active Anti-Retroviral Therapy (HAART) has been effective in reducing rapidly progressive retinopathies, there are other ocular manifestations of HIV and ocular side effects of HAART which are yet to be determined and evaluated. The aim of this study was to investigate and evaluate the effect of HAART on Visual Acuity (VA) and Intraocular Pressure (IOP) among HIV/AIDS patients in Kano State, Nigeria. This was a prospective hospital based cross-sectional study; consented patients that fulfilled the inclusion criteria were recruited and grouped into two groups A and B. Group A was those scheduled to commence HAART referred to as HAART naïve, while group B was subdivided into four groups, comprising B1, B2, B3, B4, termed as HAART experience. There were 400 participants aged 25 to 55 years with mean age of 37.86 ± 7.5 years. Their mean CD4+ T cell count was 476.94 ± 272.3 cells/mm^3. The mean IOP was 14.14 ± 2.65 mmHg and analysis of variance showed that there was no correlation of HAART on IOP. About 370 (92.5%) had the best corrected distance visual acuity (BCDVA) on OU of 6/6, while 30 (7.5%) had BCDVA of less than 6/6 or worse and there was a correlation between HAART and VA ($p < 0.01$), but statistically insignificant on CD4+ T-cells counts, HAART regimen and its durations. There was a correlation between VA and HAART among HIV/AIDS patients, but it showed no association with CD4+ T cell counts, HAART regimen and HAART duration. There was no correlation of HAART on IOP of the patients.

Key words: Highly active antiretroviral therapy (HAART), visual acuity, intraocular pressure (IOP), CD4+ T cell counts.

INTRODUCTION

Highly active antiretroviral therapy (HAART) or Antiretroviral therapy (ART) is the combination of several antiretroviral medicines used to slow the rate at which HIV makes copies of itself (replicates) in the body. A

combination of three or more antiretroviral medicines is more effective than using just one medicine (monotherapy) to treat HIV infection (UNAIDS/World Health Organization, 2013).

The goal of antiretroviral combined therapy is to reduce the viral load to a level that can no longer be detected. Evidence indicates that the optimal way to achieve this goal is by initiating combination therapy with two or more antiretroviral agents. HAART provides effective treatment options for treatment-naive and treatment-experienced patients. Six classes of antiretroviral agents currently exist, as follows: Nucleoside reverse transcriptase inhibitors (NRTIs), Non-nucleoside reverse transcriptase inhibitors (NNRTIs), Protease inhibitors (PIs), Integrase inhibitors (INSTIs), Fusion inhibitors (FIs) and Chemokine receptor antagonists (CCR5 antagonists)(Centers for Disease Control and Prevention, 2015). Each class targets a different step in the viral life cycle as the virus infects a $CD4^+$ T lymphocyte or other target cell. The use of these agents in clinical practice is largely dictated by their ease or complexity of use, side-effect profile, efficacy based on clinical evidence, practice guidelines, and clinician preference (Guideline Panel on Antiretroviral Guidelines for Adults and Adolescents, 2015). HIV is a retrovirus that primarily infects components of the human immune system such as $CD4^+$ T cells, macrophages and dendritic cells. It directly and indirectly destroys $CD4^+$ T cells (Evian, 2006).

Acquired immunodeficiency syndrome (AIDS) is defined in terms of either a $CD4^+$ T cell count below 200 cells per µl or the occurrence of specific diseases in association with an HIV infection. In the absence of specific treatment, around half of people infected with HIV develop AIDS within ten years (Chu and Selwyn, 2011). Salient ocular manifestations of HIV/AIDS, and the effect of HAART on the pattern of presentation of HIV/AIDS ocular disease based on the ocular visual functions, have also been reported (Rajesh et al., 2008).

Studies by Plummer et al. (1996) and Mueller et al. (1997) reported oculo-visual dysfunctions in a significant number of HIV positive patients without retinitis. Plummer et al. patients were assessed for visual field defects, whilst Mueller et al. (1997) participants were assessed for colour vision, contrast sensitivity and visual fields. A normal visual acuity does not preclude the possibility of visual function deficits as some sero-positive patients have been found to have deficits in visual function whilst visual acuity remains normal and CD4 counts relatively high (Plummer et al., 1996; Mueller et al., 1997). The long-term effects of HIV/AIDS, HAART and associated opportunistic infections on oculo-visual functions such as visual acuity and intraocular pressure have not been fully investigated. The type and association between CD4 count, HAART regimen and its duration on oculo-visual functions (Visual acuity and Intraocular Pressure) has not also been fully characterized or determined. The aim of this study was to investigate and characterized the effect of HAART on Visual Acuity (VA) and Intraocular Pressure (IOP) among HIV/AIDS patients in Kano State, Nigeria.

MATERIALS AND METHODS

This prospective hospital based cross-sectional study was carried out from April 2018 to November 2019. Consented patients that fulfilled the inclusion criteria were recruited. Criteria for inclusions are consent to participate, age between 25- 55years, tested HIV positive on ELISA test, recent CD4+ T cell count result (at least within 6 months), HAART naïve and had no ocular, medical (hypertension and diabetes etc., were screened and ruled out) or therapeutic histories known to affect any of the selected oculo-visual functions (such as visual acuity and intraocular pressure). Participates who refused to give consent, tested HIV sero-negative, below age 25 or above 55 years, without recent or more than 6 months CD4+ T cell count result, on HAART for more than 10 years and have major systemic (hypertension, diabetes etc.), medication or vision threatening ocular complication that may affect or preclude testing for the selected oculo-visual functions were excluded from the study.

Information obtained from the patients include: demographic profile, visual acuity, intraocular pressure, CD4+ T cell count, HAART regimen and HAART duration. Patients had unaided and pinhole visual acuity tested at a distance of 6m using Snellen's or tumbling "E" charts, intraocular pressure was measured with the air puff non-contact tonometer. Anterior and posterior segments examination was done using direct Ophthalmoscopy and slit lamp biomicroscope. All the patients that met the inclusion criteria were grouped into two groups A and B. Group A, consist of those that are about to commence HAART (HAART naïve patients), while group B were subdivided into four groups; comprising of B_1: those that have been on HAART from zero to two and half years (0 - 2½ years), group B_2 are those on HAART from two and half years to five years (2½ - 5 years), group B_3 are those on HAART from five years to seven and half years (5 - 7½ years), and group B_4 are those on HAART from seven and half years to ten years (7½ - 10 years), who are termed as HAART experience.

Data analysis

Data were entered into a Microsoft excel spreadsheet database before being exported, cleaned and analysed in SPSS 22.0 version. The patients' socio-demographic characteristics and measurement results were evaluated using descriptive statistics to show the frequency of occurrence and percentage of distribution age range. The analysis of variance, Fisher's exact test and Pearson's Chi-Square statistics was also used to analysed and compare the effect and association of HAART regimen and duration on VA, IOP and CD4+ count. All statistical significance was evaluated with 95% confidence level, where $p \leq 0.05$ was considered statistically significant.

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Table 1a. Socio-demographic characteristics of HAART naïve and experience Participants by gender and marital status.

Socio-demographic characteristics	HAART naïve	HAART experience				
	Group A (n=80)	Group B_1 (n=80)	Group B_2 (n=80)	Group B_3 (n=80)	Group B_4 (n=80)	Total (n=400)
Gender						
Male	36 (45.0%)	31 (38.8%)	36 (45.0%)	32(40.0%)	37(46.2%)	172(43.0%)
Female	44 (55.0%)	49 (61.2%)	44 (55.0%)	48(60.0%)	43(53.8%)	228(57.0%)
Marital status						
Single	12(15.0%)	19 (23.8%)	13 (16.2%)	12(15.0%)	5 (6.3%)	61 (15.3%)
Married	46 (57.5%)	52 (65.0%)	39 (48.8%)	38(47.4%)	49(61.1%)	224(56.0%)
Widow(er)	12(15.0%)	6 (7.5%)	12 (15.0%)	15(18.8%)	9(11.3%)	54 (13.4%)
Divorced	10(12.5%)	3 (3.8%)	16 (20.0%)	15(18.8%)	17(21.3%)	61 (15.3%)

Data presented as frequencies and percentages. Key Group A – HAART naïve, Group B – HAART experience (B_1 are those on HAART from 0 - 2½ years; B_2 on HAART from 2½ - 5 years; B_3 on HAART from 5 - 7½ years and group B_4 on HAART from 7½ - 10 years).

Table 1b. Socio-demographic characteristics of HAART naïve and experience Participants by age.

Age (years)	HAART naïve	HAART naïve				
	Group A (n=80)	Group B_1 (n=80)	Group B_2 (n=80)	Group B_3 (n=80)	Group B_4 (n=80)	Total (n=400)
Mean age ± SD	36.40 ± 7.4	35.11 ± 6.9	36.96 ± 7.5	39.19 ±7.6	41.65±6.3	37.86±7.5
25 - 34	38 (47.5%)	36 (45.0%)	33 (41.2%)	24(30.0%)	12(15.0%)	143(35.8%)
35 - 44	29 (36.2%)	36 (45.0%)	35 (43.8%)	33(41.3%)	40(50.0%)	173(43.2%)
45 - 54	11 (13.8%)	7 (8.8%)	10 (12.5%)	21(26.2%)	26(32.5%)	75(18.8%)
55 – 64	2 (2.5%)	1 (1.2%)	2 (2.5%)	2 (2.5%)	2 (2.5%)	9 (2.2%)

Data presented as frequencies and percentages. Key Group A – HAART naïve, Group B – HAART experience (B_1 are those on HAART from 0 - 2½ years; B_2 on HAART from 2½ - 5 years; B_3 on HAART from 5 - 7½ years and group B_4 on HAART from 7½ - 10 years).

RESULTS

A total of 400 participants were enrolled, using Dobson's formula for cross-sectional studies. Data for sample size calculation was taken from a 2001 study carried out in the department of Ophthalmology Chelsea and Westminster Hospital London, UK by Westcott et al. (2001) in which 30% of patients aged between 25 and 34 years had reduced amplitudes of accommodation and other oculo-visual functions below age-expected norms in HIV/AIDS patients on HAART population. From the calculation, the minimum sample size required was 323 patients and the sample sizes were increased to 400 patients to take care of attrition. Systematic sampling was used to recruit participants, taking one in every five patients that entered the consulting room to see a doctor. The participant's age ranged from 25 to 55 years with a mean age of 37.86 ±7.5years. There were 172 males (43.0%) and 228 females (57.0%). Most of the participants 224 (56.0%) were married, 61 (15.3%) were divorced, 54 (13.4%) were widow/widower and 61 (15.3%) were single. The socio-demographic characteristics of HAART naïve and HAART experience groups is presented in Table 1a and b.

The participants' mean CD4+ T cell count was 476.94± 272.3 cells/mm^3, ranging from 13 - 1848 cells/mm^3. Majority of them (152 participants; 38.0%) had CD4+ T cell levels above 500 cells/mm^3, followed by those (109 participants; 27.3%) with CD4+ T cell levels between 350 - <500 cells/mm^3 (Figure 1).The majority of the participants 146 (36.5%) had entry visual acuity (EVA) of 6/9 on the right eye (OD) and 129 (32.3%) had EVA of 6/9 on the left eye (OS). About 370 (92.5%) had a best corrected distance visual acuity (BCDVA) on both eyes (OU) of 6/6 or better while 30 (7.5%) had a best corrected distance visual acuity (BCDVA) of less than 6/6 or worse. Pearson's Chi-Square showed that there was a correlation or association between HAART and Visual Acuity with p-value of 0.01.

The mean intraocular pressure (IOP) of the all the participants was 14.14± 2.65 mmHg, ranging from 8- 26 mmHg. About 69 (17.3%) of the participants had IOP of 14mmHg, followed by 64(16.0%) with IOP of 12 mmHg respectively. Group B_3 showed the highest mean

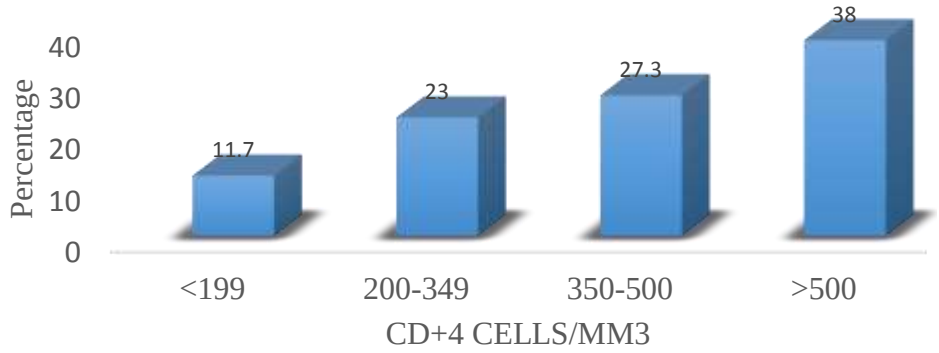

Figure 1. CD4+ T cell count levels among participants.

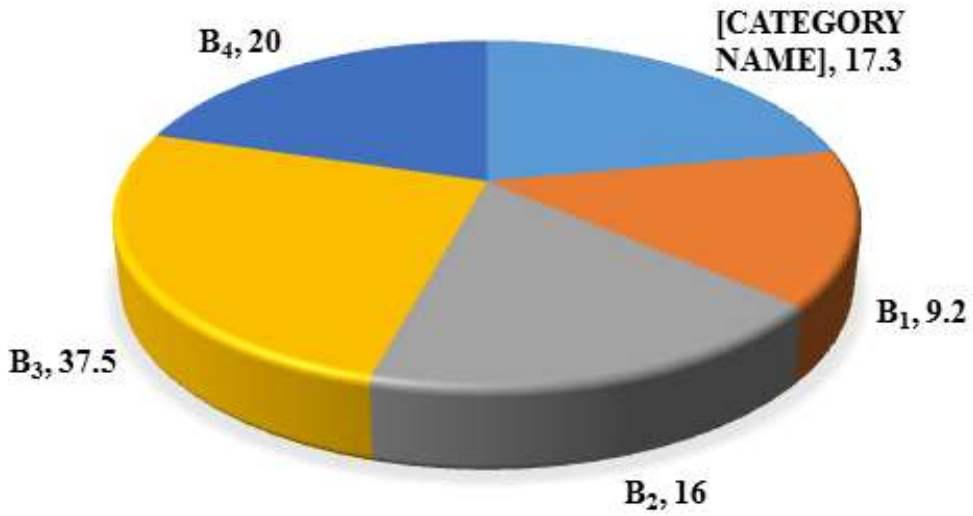

Figure 2. Percentage distribution of the highest mean of Intraocular Pressure among HAART naïve and HAART experience participants. Group A – HAART naïve, Group B – HAART experience (B_1 are those on HAART from 0 - 2½ years; B_2 on HAART from 2½ - 5 years; B_3 on HAART from 5 - 7½ years and group B_4 on HAART from 7½ - 10 years).

(14.49±3.3) and percentage (37.5%) of intraocular pressure among all the participants (Figures 2 and 3). Analysis of Variance showed that there was no correlation or association of HAART on Intraocular Pressure with p value of 1.00. There was no statistically significant relationship between visual acuity and CD4+ T-cells, P values obtained was 0.649 (Table 3). Test statistics using Fisher's exact test showed no relationship between the visual acuities, HAART regimen and duration (Tables 4 and 5).

DISCUSSION

This study reflects the distribution patterns of oculo-visual functions such as visual acuity and intraocular pressure status among HIV positive population on HAART therapy attending SS Wali ART clinic of Aminu Kano Teaching Hospital Kano, Nigeria. The pattern of the visual acuity obtained in this study indicated that majority, 146 (36.5%), of the participants had an entering visual acuity (EVA) of 6/9 on the right eye and 129 (32.3%) on the left eye, about 92.5% had best corrected distance visual acuity (BCDVA) of 6/6 after refraction, which indicate an improved vision especially those on HAART. This is in agreement with the study of Sharew and Azage, among HIV-positive patients in Ethiopia (Sharew and Azage, 2015). Mesaric et al. (2005) reported that the visual acuity in patients from the HAART era was significantly more frequently preserved than in patients from the pre-HAART era on follow-up examinations ($p<0.001$)(Mesarić et al., 2005).

Similar findings were recorded in this study, where the effect of HAART on visual acuity was found to be

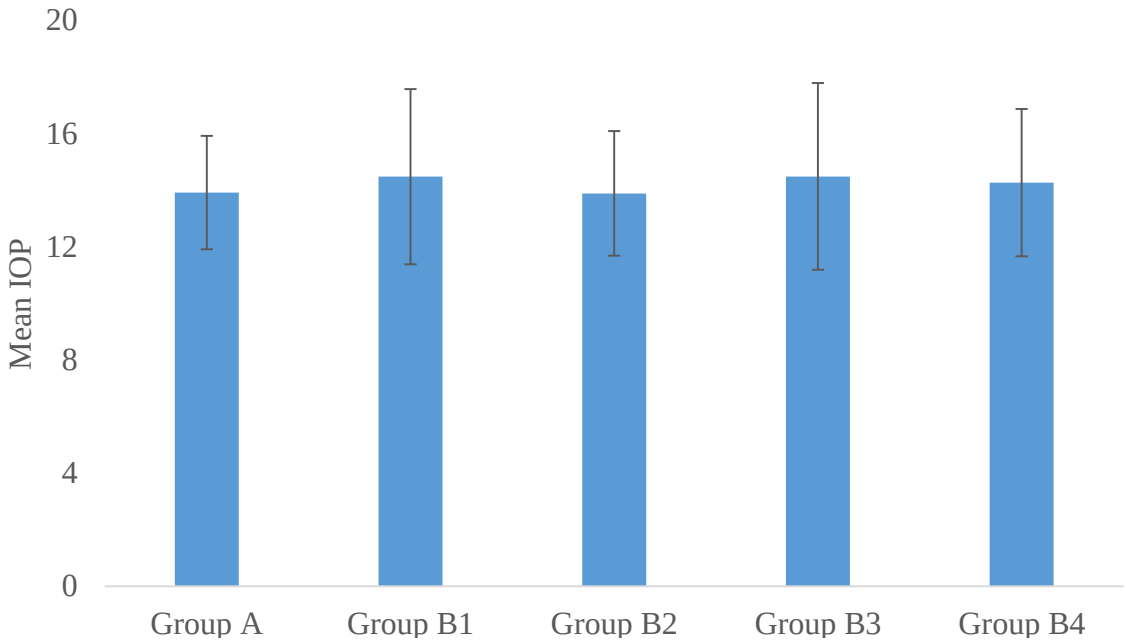

Figure 3. Intraocular Pressure of HAART naïve and HAART experience participants. Data presented as Mean and Standard error mean. Key Group A – HAART naïve, Group B – HAART experience (B_1 are those on HAART from 0 - 2½ years; B_2 on HAART from 2½ - 5 years; B_3 on HAART from 5 - 7½ years and group B_4 on HAART from 7½ - 10 years).

Table 2. Visual acuity of HAART naïve and HAART experience participants.

Visual acuity	HAART naïve	HAART experience				Total (n=400)
	Group A (n=80)	Group B_1 (n=80)	Group B_2 (n=80)	Group B_3 (n=80)	Group B_4 (n=80)	
BCDVA	OU = 6/9	OU = 6/5	OU = 6/9	OU = 6/9	OU = 6/9	OU = 6/9
Normal	61 (76.3%)	52 (65.0%)	53 (66.2%)	70 (87.5%)	57 (71.3%)	275 (68.8%)
Abnormal	19 (23.7%)	28 (35.0%)	27 (33.8%)	10 (12.5%)	23 (18.7%)	125 (31.2%)

Data presented as frequencies and percentages. Key Group A – HAART naïve, Group B – HAART experience (B_1 are those on HAART from 0 - 2½ years; B_2 on HAART from 2½ - 5 years; B_3 on ART from 5 - 7½ years and group B_4 on HAART from 7½ - 10 years), P value = 0.01 using Pearson's Chi Square when HAART experience were compared with HAART naïve.

statistically significant (p=0.01) as 87.8% of the HAART experience had a normal visual acuity as against 12.2% of HAART naïve. The result also showed that HAART experience for the period of two and half years had BCDVA of 6/5 on both eyes compared to HAART naïve (Table 2). However, Mueller et al. (1997) stated that normal visual acuity does not preclude the possibility of visual function deficits as some sero-positive patients have been found to have deficits in visual function whilst visual acuity remains normal and CD4+ counts relatively high (Mueller et al. 1997). This study also correlates with the report of Mueller et al., in that it showed some of the participants with normal CD4+ count (476.94± 272), yet had one or more abnormalities of the oculo-visual functions (Figure 1).

Comparing the CD4+ T cell levels among the five groups of the study, group B_4 had the highest mean of 529.82± 221, which indicated that long duration on HAART with good adherence to treatment may improve the CD4+ T cell level of a patient. This was agreed with works of Siegfried et al. (2010) and Onakoya et al. (2012).

On associating CD4+ T cell levels with the visual acuity, statistically insignificant relationship between the CD4+ T cell levels and visual acuity was observed (Table 3). This is also in agreement with the study of Westcott et al. (2001) and that of Neeta and Radhakrishnan (2017) that reported low amplitude of accommodation was not related to CD4+ T cells level, as also found in this study (Westcott et al., 2001; Neeta and Radhakrishnan, 2017).

This study also indicated that the abnormal oculo-visual

Table 3. Relationship between CD4+ T-cells count and visual acuity.

Oculo-visual functions	CD4+ <199 cells/mm^3 n (%)	CD4+ 200-349 cells/mm^3 n (%)	CD4+ 350-499 cells/mm^3 n (%)	CD4+4 >500 cells/mm^3 n (%)	Test Statistic (χ^2)	P- value
Visual acuity				Fisher exact test		0.649
Normal	8 (2.0)	19 (4.75)	27 (6.75)	29 (7.25)		
Abnormal	39 (9.75)	73 (18.25)	82 (20.5)	123 (30.75)		

Table 4. Relationship between HAART regimen and visual acuity.

Oculo-visual functions	1st Line regimen n (%)	2nd Line regimen n (%)	3rd Line regimen n (%)	Test statistic (χ^2)	P - value
Visual acuity			Fisher's Exact Test		0.70
Normal	225 (70.3)	15 (4.7)	5 (1.6)		
Abnormal	71 (22.2)	4 (1.2)	0 (0.0)		

Table 5. Relationship between HAART duration and visual acuity.

HAART duration	Group B_1 n (%)	Group B_2 n (%)	Group B_3 n (%)	Group B_4 n (%)	Test statistic (χ^2)	P - value
Visual acuity					3.867	0.28
Normal	66 (20.6)	71 (22.2)	45 (14.1)	63 (19.7)		
Abnormal	15 (4.7)	26 (8.1)	19 (5.9)	15 (4.7)		

functions such as visual acuity and intraocular pressure observed among HIV sero-positive participants on HAART was not related to their CD4+ T cell levels, and visual acuity had no relationship with HAART regimen and HAART durations.

Conclusion

There was a correlation between visual acuity (VA) as an oculo-visual function and highly active antiretroviral therapy (HAART) among HIV/AIDS patients, but showed no association with CD4+ T cell counts, HAART regimen and HAART duration. However, it also showed that there was no correlation or association of HAART on Intraocular Pressure (IOP) of the patients. The results of this study add to the growing body of literature on oculo-visual functions in HIV positive patients in this HAART era.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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