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Hypertension and Related Risk Factors Among Clients on Combined Antiretroviral Therapy in Nigeria

Shakirat I. Bello[1] and Winified A. Ojieabu[2]

[1]Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences
University of Ilorin, Ilorin, Nigeria
[2]Department of Clinical Pharmacy and Biopharmacy, Faculty of Pharmacy
Olabisi Onabanjo University, Shagamu, Nigeria

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Abstract

Hypertension is a major challenge in human immunodeficiency virus (HIV) infected people globally. A prospective, cross-sectional study comprising two hundred and eighteen HIV-infected patients was conducted in Antiretroviral Therapy Clinic of General Hospital, Offa between November 2015 and December, 2016. Patients' blood pressure was evaluated using Omron automated blood pressure monitor following standard procedures. Dual weight and height balance was utilized to measure the weight and height of the subjects. Hypertension incidence among patients receiving combined antiretroviral therapy (cART) was 34%, while those that were yet to start cART was 9.6 %. In HIV-infected women on cART, occurrence of hypertension was high (75.5%) as compared to men (24.5%). The hypertension pervasiveness in HIV-infected patients on cART was 75.5% in women and 24.5% in men. Risk factors that were markedly linked with hypertension among patients on cART include body mass index (OR: 3.29,95% CI:1.21-2.27; $p< 0.050$), sedentary lifestyle (OR: 1.63, 95% CI:1.20-5.38; $p < 0.043$), age (OR: 2.17, 95% CI: 1.22-2.33; $p< 0.004$) and gender (OR: 1.63, 95% CI: 0.85-2.41; $p < 0.037$). Patients on cART were found to have higher hypertension prevalence than cART-naive. The cART, however, is not a risk factor for hypertension.

Key words: Combinedantiretroviral therapy, human immunodeficiency virus, hypertension, risk factors, Nigeria.

Introduction

There is a great concern on the prevalence of hypertension among people living with human immunodeficiency virus (HIV) globally; and as from June 2016, 18.2 million individuals were gaining access to antiretroviral therapy (UNAIDS 2016). Before the commencement of antiretroviral therapy, high blood pressures in HIV-infected subjects were frequently linked with complications including vasculopathy, renal failure and stroke (Ssinabulya *et al.* 2014). Individual cardiovascular threat, however, is influenced by myriads of risk factors such as weight gain, drug abuse, elevated blood lipids, dyslipidemia, age, diabetes, smoking and family history (Dimala *et al.* 2016). Cardiovascular diseases that accounted for 30% deaths worldwide are attributable to chronic and poorly controlled and uncontrolled hypertension (Arruda Junior *et al.* 2010). Hypertension usually featured with a continual increase in arterial blood pressure and is more prominent in developed countries than the developing countries (Bloomfield *et al.* 2014). The zenith of HIV infection that usually occurs from the age group of 25 to 49 years, whereas hypertension arises at more than 45 years age group (Friis-Møller *et al.* 2007, Baekken *et al.* 2008). Sherer *et al.* (2014) reported the hypertension incidence risk factors of 18% in Uganda and 12% in Africa.

Combined antiretroviral therapy (cART), banishes mortality and morbidity amid HIV-infected

Correspondence to: Shakirat I. Bello; Tel.+2348035675609; E-mail: sibello10@yahoo.com; bello.is@unilorin.edu.ng

clients over yesteryears. The cART has led to HIV replication suppression, opportunistic infections decline and nastiness related to AIDS which enhanced the quality of life and life expectancy of the patients. The upsurge of survival of people living with HIV brings about an advent of new chronic ailments that include hypertension, cardiovascular and renal diseases (Arruda Junior *et al.* 2010). Currently, many researchers have suggested the likelihood of anti-retroviral drugs inducing hypertension through the increasing rate of atherogenesis and hardening wall of the vessels (Dube *et al.* 2008). Research on blood pressure among HIV-infected individuals; revealed contradictory reports concerning the increased disease occurrence in clients on anti-retroviral drugs, and the role of various courses of therapy (Baekken *et al.* 2008, Dube *et al.* 2008, Arruda Junior *et al.* 2010). Based on the foregoing, the significance of adopting sustained preventive measures in hypertension amidst HIV-infected patients on cART is very necessary. This study was carried out to evaluate the occurrence of hypertension and conceivable risk factors amongst cART patients in the General Hospital, Offa, Kwara State, Nigeria.

Materials and Methods

Setting: This cross-sectional study was conducted between 26th November, 2015 and 23rd December, 2016 among HIV infected patients on Combined Antiretroviral Therapy (cART) attending ART Clinic of the General Hospital Offa, Kwara State. Ethical statement for the study was sought from the Health Ethical Research Committee, Kwara State Ministry of Health with protocol number MOH/KS/EHC/777/99. Prior to recruitment of the subjects, oral and written informed consents were obtained from the subjects.

Sampling technique: The sample size was determined using the Fisher's statistical formula by Araoye *et al.* (2004), $N = Z^2pq/D^2$, where N = minimum sample size, Z = standard deviation set at 1.96, p = Pre-study estimate of the hypertension occurrence in patients on cART (10.3%) and cART-naïve (4.9%) in Nigeria (Muhammad *et al.* 2013), q = 1 - p, D = measure of precision (0.05). The calculated sample size for patients on cART was 144, and 74 for cART-naïve patients (about to start cART). The 74 cART-naïve patients serve as positive controls for the study. The study inclueded patients on cART between 2 and 5 years or about to start cART, outpatients diagnosed to be HIV positive, patients aged 20 and 65 years, patients with normal blood pressure prior to cART and those consented to participate in the study. Those excluded from the study were patients less than 20 years old, pregnant women, patients with history of hypertension, diabetes mellitus and dyslipidaemia before commencing cART, patients on drugs that could affect blood pressure, and patients who declined consent.

Patient selection: Subjects who met the inclusion criteria were enrolled sequentially. Those on cART were recruited during prescription refills, while cART-naive patients were enrolled during their initial visit to the hospital.

Study procedures: Information on patients' medication history, past medical illnesses, history of HIV infection and socio-demographic characteristics were obtained through one-on-one interview with the patients and the patients' medical folders.

Blood pressure, weight and height measurements: The blood pressure (BP) of the patients were evaluated by established method with Omron automated blood pressure monitor (Omron M2, PK-HEM-7121-E-01). Patients found to be hypertensive were identified from the mean of four blood pressure values taken at two weeks interval. Identification of hypertension among the patients was attained with World Health Organization standard as systolic blood pressure greater than or equal to one hundred and forty millimeter of mercury and/or diastolic blood pressure greater than or equal to ninety millimeter of mercury (Chen *et al.* 2015). Patients' weights and heights were determined with using dual weight and height balance. Body Mass Index (BMI in kg/m^2) of the patients was estimated mathematically by weight divided by height square.

The CD_4 cells count of the patients were measured with automated flow cytometer. Overweight and obesity were defined as body mass index (BMI) between 25.0 - 29.9 kg/m^2 and ≥30 kg/m^2 (Ganz *et al.* 2014).

Data analysis: Analyses of the raw data were performed with the Statistical Application Software program version 9.2 (SAS 2012). Demographic and clinical profiles of the study population were described using mean with standard deviation and percentages. Student's t-test was used to compare means and regression analysis for determination of risk factors linked to hypertension.

Results and Discussion

Socio-demographic and clinical characteristics of the study population: The socio-demographic and clinical characteristics of the patients are shown in table 1. Of the 218 patients studied, 144 were on cART and 74 were yet to commence cART. There were statistically significant differences between the patients on cART and cART-naïve group, regarding the mean duration of HIV infection (57.91 ± 44.67 versus 3.28±9.14 months; $p < 0.001$), BMI (28.59 ± 3.71 versus 21.75 ± 4.38, $p < 0.020$) and mean CD_4 cells count (352.45 ± 89.04 versus 121.53 ± 44.18, $p < 0.034$). Also, patients on cART were significantly older (42.96 ± 8.61 years, $p < 0.05$) and heavier (64.44 ± 5.61 kg, $P < 0.027$) than the cART-naïve patients (37.11 ± 11.31 years; 51.73 ± 2.24 kg). There was no statistically significant differences in the cART group and cART-naïve arm with regard to gender, functional status and WHO clinical staging. The mean duration of patients on cART was 56.7 ± 20.51 months.

Table 1. Clinical and socio-demographic variables of HIV-infected patients.

Variables	Patients on cART n=144 Mean (SD)	Patients not on cART n = 74 Mean (SD)	P-value
Body mass index (kg/m^2)	28.59 ± 3.71	21.75 ± 4.38	0.020*
Weight (Kg)	64.44 ± 25.61	51.73 ± 32.24	0.027*
Duration of HIV infection (months)	57.91 ± 44.67	3.28 ± 9.14	0.001*
Duration on cART(months)	56.7 ± 20.51	-	-
CD_4 (cells/microlitre)	352.45 ± 89.04	121.53 ± 44.18	0.034*
World Health Organization clinical stage 1 n (%)	137 (96.2%)	63 (87.3%)	0.223
Age (years)	42.96 ± 8.61	37.11±11.31	0.050*
Female n (%)	104 (72.2)	51 (69.9)	0.274
Functional status (Unemployed/sedentary life) n (%)	37 (25.9)	18 (24.5)	0.288

*Statistically significant at $p < 0.05$.

Table 2. Prevalence of hypertension among HIV infected patients.

Variables	Patients on cART N=144	Patients not on cART N=74	P-value
Hypertension n (%)	49 (34.0)	7 (9.6)	
Mean systolic blood pressure (mmhg)	127.20 ± 24.91	118.14 ± 26.41	0.416
Mean diastolic blood pressure (mmhg)	81.11 ± 10.67	74.86 ± 9.43	0.244

The mean systolic blood pressure, diastolic blood pressure and prevalence of hypertension of patients on cART and those that were off cART are presented in table 2. The prevalence of hypertension was greater in those patients on cART 49 (34.0%) as compared to cART-naïve patients (9.6%).

Table 3 indicates the distribution of the patients by gender. The prevalence of hypertension in HIV-infected patients on cART was 75.5% in women and 24.5% in men and 71.4% and 28.6%, respectively, in women and men of the cART-naïve group.

The various combinations of antiretroviral therapy and the number of patients on those regimens are described in figure 1. Most of the patients on cART were on first-line antiretroviral therapy containing classes of drugs with nucleotide/ nucleoside reverse transcriptase Inhibitors and Non-nucleotide reverse transcriptase inhibitors.

Table 3. Prevalence of hypertension among HIV infected patients by gender distribution.

Variables	Patients on cART with hypertension N=49	Patients not on cART With hypertension N=7
Hypertension n (%) male	12 (24.5)	2 (28.6)
Hypertension n (%) Female	37 (75.5)	5 (71.4)

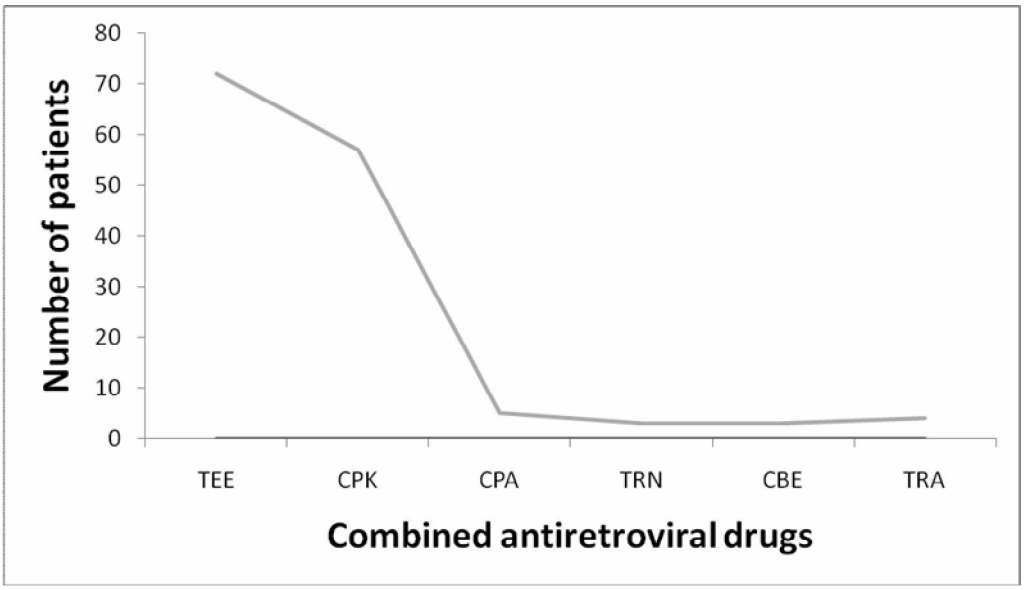

Figure 1. Combined antiretroviral drugs and HIV infected patients.

TEE - TenofovirEmtricitavineEfavirenz; CPK - Zidovudine Lamivudine Nevirapine; CPA -Zidovudine Lamivudine Ritonovirboosted Lopinavir; TRN - TenofovirEmtricitabineNevirapine; CBE- Zidovudine Lamivudine Efavirenz; TRA - TenofovirEmtricitavineRitonovirboosted Lopinavir.

Table 4 reveals risk factors associated with hypertension among patients on antiretroviral drugs. Age (OR: 2.17, 95% CI: 1.22-2.33, $p < 0.004$), gender (OR: 1.63, 95% CI: 0.85-2.41; $p < 0.037$), BMI (OR: 3.29, 95% CI: 1.21-2.27; $p < 0.050$) and sedentary lifestyle (OR: 1.63, 95% CI: 1.20-5.38; $p < 0.043$) were statistically associated with hypertension. Duration on HIV infection, CD_4 cells count and exposure to antiretroviral drug regimens are not implicated for hypertension.

In HIV-infected individuals and the general populace, blood pressure is regarded as a significant risk factor in the deterrence of cardiovascular disorders. This study indicates that substantial variation exists in hypertension pervasiveness in patients that were yet to receive cART and those on cART. The hypertension occurrence was considerably greater in patients on cART as compared to cART-naïve patients. This observation corroborates with previous studies of Lichtenstein *et al*. (2010), PefuraYone *et al.* (2011), Ekali *et al.* (2013), Muhammad *et al.* (2013) and Njelekela *et al.* (2016), which revealed a higher incidence of hypertension in patients on cART. Contrarily, the findings of other studies of Agrawal *et al.* (2015) indicated no disparity in the prevalence of hypertension between patients on cART and cART-naïve patients. Furthermore, lower hypertension prevalence was observed in patients receiving cART, as reported by Dimala *et al.* (2016). Also, 60 % prevalence rate in HIV patients on cART was documented by Kanegae *et al.* (2017). The prevalence rate of 34% in the patients on cART recorded in the present study was similar (34.9%) to the result of Mutede *et al.* (2015). The discrepancies of these findings could be linked to the parameters such as environmental variations, designs of the study, site of the study as well as mean duration on cART, demographic and clinical features of the study population.

Table 4. Logistic regression analysis of risk factors associated with hypertension in patients on cART.

Risk Factors	Adjusted odd ratio	95% confidence interval	P-value
Age	2.17	1.22-2.33	0.004*
Gender	1.63	0.85-2.41	0.037*
Body mass index (kg/m^2)	3.29	1.21-2.27	0.050*
Duration on HIV infection (months)	0.73	0.44-1.28	0.395
Duration on cART (months)	1.22	0.30-3.39	0.471
CD_4 (cells/microliter)	2.66	1.00-3.22	0.562
Sedentary lifestyle	1.63	1.20-5.38	0.043*
Exposure to first line cART regimen	1.66	0.89-8.06	0.201
Exposure to second line cART regimen	1.90	0.62-5.55	0.440

The patients on cART had significantly higher mean values of BMI, weight, age, CD_4 cells count and long duration of HIV infection than those that were yet to receive cART. This could probably be attributed to the fact that patients on cART are living longer and staying healthier due to the benefits of cART. These risk factors (age, BMI, gender and sedentary lifestyle) observed in this study could be responsible for the high hypertension pervasiveness among patients on cART. These results agreed with the earlier studies of Kaplan *et al.* (2007) and Deeks (2009) which identified older age, male gender, black race, smoking, overweight, diabetes mellitus, dyslipidemia, sedentary life style and a family history of hypertension as risk factors for high blood pressure among the patients.This study also revealed that exposure to cART is not a risk factor for hypertension. This is in line with the findings of Kowalska *et al.* (2012) and Agrawal *et al.* (2015) who reported that long duration of ART is not associated with hypertension. Contrariwise, the findings of Muhammad *et al.* (2013) signified that use of ART could be related to hypertension. Furthermore, duration of HIV infection was not markedly interrelated with hypertension in this study. This finding did not concurred with the previous studies of Harrison *et al.* (2011) whose results showed that alteration in immune system may be a reason and a consequence of hypertension. The female patients were at a greater risk of hypertension

than the male counterparts in patients on cART and cART-naive. This could be attributed to larger population of women involved in this study. Global Status Report (2010) indicated on the other hand, that incidence of hypertension is more incline in women than the men.

Conclusion

Patients on cART were found to have higher hypertension prevalence than cART-naive. The cART, however, is not a risk factor for hypertension. There is a need for continuous screening of hypertension in HIV infected individuals to prevent cardiovascular complications.

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Author Contributions

SIB: Conceived and designed the experiments. WAO and SIB: Performed the experiments and analyzed the data: SIB: Wrote the paper.

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