

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

Shakirat I. Bello^{1,*}, Winified A. Ojieabu²

¹Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, University of Ilorin, Ilorin, Nigeria

²Department of Clinical Pharmacy and Bio-pharmacy, Faculty of Pharmacy, Olabisi Onabanjo University, Shagamu, Nigeria

ABSTRACT

Keywords: Human immunodeficiency virus, blood pressure, body mass index, gender, women.

Author's Contribution

All the authors contributed significantly to the research that resulted in the submitted manuscript.

Article info.

Received: October 10, 2017

Accepted: December 14, 2017

Funding Source: Nil

Conflict of Interest: Nil

Cite this article: Bello SI, Ojieabu WA.

Hypertension and Related Risk Factors Among Clients on Combined Antiretroviral Therapy in Offa, Nigeria. *RADS J. Pharm. Pharm. Sci.* 2017;5(4):4-10.

*Address of Correspondence Author:
sibello10@yahoo.com

Justification: The hypertension pervasiveness is a major challenge in human immunodeficiency virus (HIV) afflicted people globally.

Aim: A prospective, cross-sectional research comprising two hundred and eighteen HIV afflicted patients was conducted in Antiretroviral Therapy Clinic of General Hospital, Offa, Nigeria between November 2015 and December 2016.

Methodology: Blood pressure of patients was evaluated with the use of Omron automated blood pressure monitor following standard procedures. Dual Weight and Height Balance device was utilized to measure the weights and heights of the subjects.

Results: Hypertension incidence among patients receiving combined antiretroviral therapy (cART) was 34%, while cART-naive was 9.6%. In women afflicted with HIV who were on cART, the hypertension occurrence was high (75.5%) compared to men (24.5%). 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; $p < 0.037$).

Conclusion: Patients on cART were found to have higher hypertension prevalence than cART-naive. On risk factors for hypertension, however, the cART was not inclusive.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

There is a great concern on the pervasiveness of hypertension in people afflicted with human immunodeficiency virus (HIV) globally. As from June 2016, 18.2 million individuals were gaining access to antiretroviral therapy [1]. Before the commencement of antiretroviral therapy, high blood pressure (BP) in HIV afflicted subjects were recurrently related with complications

including vasculopathy, renal failure, and stroke [2]. The individual cardiovascular threat, however, is influenced by myriads of risk factors like drug abuse, weight gain, elevated blood lipids, dyslipidaemia, age, diabetes, smoking and family history [3]. Cardiovascular diseases that accounted for 30% deaths worldwide are attributable to chronic and poorly controlled and uncontrolled hypertension [4]. Hypertension usually featured with a continual increase in arterial BP and is less prominent in developing

countries than the developed countries [5]. The zenith of HIV infection usually occurs from the age group of 25 to 49 years, whereas hypertension arises at more than 45 years age group [6,7] Sherer et al. [8] reported the hypertension manifestation risk factors of 18% in Uganda and 12% in Africa.

Combined antiretroviral therapy (cART), banishes mortality and morbidity amid HIV-afflicted clients over yesteryears. The cART has led to HIV replication suppression, opportunistic infections decline and nastiness related to AIDS, which enhanced life expectancy of the individuals and their quality of life. The upsurge of survival of people living with HIV brings about an advent of new chronic ailments that include hypertension, cardiovascular and renal diseases [4] 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 [9]. Research on BP among HIV afflicted individuals revealed contradictory reports concerning the occurrence of anti-retroviral drugs and the role of various courses of therapy [4,7,9]. Based on the foregoing, the significance of adopting sustained preventive measures in hypertension amidst HIV afflicted patients on cART is very necessary. This research evaluated the hypertension prevalence and conceivable risk factors amongst cART patients in the General Hospital, Offa, Kwara State, Nigeria.

METHODS

Setting

A prospective, cross-sectional research was performed from 26th November 2015 to 23rd December 2016 among HIV afflicted individuals on cART attending ART Clinic of the General Hospital Offa, Kwara State, Nigeria. Ethical Statement was collected from the Health Ethical Research Committee, Kwara State Ministry of Health with protocol number MOH/KS/EHC/777/99. Prior to the recruitment,

written and oral permission were received from the subjects.

Sampling Technique

A sample size of the research was determined utilizing a Fisher's statistical formula by [10] $N = Z^2pq/D^2$, where N = minimum sample size, Z = standard deviation set at 1.96, p = Pre-study estimate of the hypertension incidence in patients on cART $q = 1 - p$, D = measure of precision (0.05). The calculated sample size for patients on cART was 144, and 74 for cART-naïve patients (about to commence cART). The 74 cART-naïve patients served as positive controls. Included in the study were patients on cART between 2 and 5 years, cART-naïve, outpatients diagnosed to be HIV positive, patients aged between 20 and 65 years, and patients with normal BP prior to cART. Consent for involvement in the investigation was sought from the patients. The excepted criteria were the patients less than 20 years old, pregnant women and those with the history of hypertension. Others include patients with diabetes mellitus and dyslipidemia before commencing cART and those on drugs that could affect BP as well as 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-naïve 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 a one-on-one interview with the patients using the patients' medical folders.

Blood pressure, weight and height measurements

The BP of the patients were evaluated by the established method with Omron automated BP

monitor (Omron M2, PK-HEM-7121-E-01). Patients found to be hypertensive were identified from the mean of four BP values taken at two weeks interval. Identification of hypertension among the patients was attained with World Health Organization standard as diastolic BP over or up to 90mm of mercury and/or systolic BP over or up to 140mm of mercury [11]. Patients' weights and heights were ascertained using Height Balance and Dual Weight device. Body Mass Index (BMI) in kg/m^2 of the patients was estimated mathematically by weight divided by the square of the height. The CD_4 cells count of the patients was measured with an Automated Flow Cytometer. Obesity and overweight were described as BMI from 25.0–29.9 kg/m^2 to $\geq 30 \text{ kg/m}^2$ [12].

Data analysis

The raw data were analyzed with the Statistical Application Software program version 9.2 [13]. Demographic and clinical profiles of the studied population were described utilizing mean, percentages and standard deviation. Student's t-test was employed for the comparison of means

while regression analysis was exploited to verify the risk factors that linked to hypertension.

RESULTS AND DISCUSSION

Clinical attributes and socio-demographics of the subjects

The clinical attributed and socio-demographics of the subjects are depicted in Table 1. Of the 218 patients studied, 144 were on cART and 74 cART-naïve. There was markedly variation between the subjects on cART and cART-naïve for 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 ($64.44 \pm 5.61 \text{ kg}$, $P < 0.027$) than the cART-naïve (37.11 ± 11.31 years; $51.73 \pm 2.24 \text{ kg}$). There was no striking variation in the cART and cART-naïve patients 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-afflicted 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 of 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. Hypertension prevalence in HIV afflicted subjects.

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

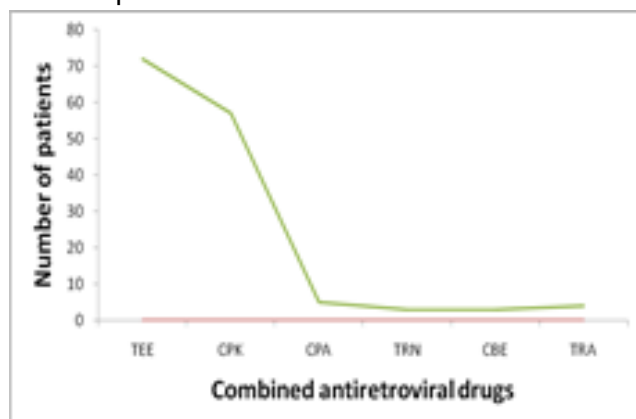
Table 3. Hypertension frequency in HIV afflicted subjects by gender distribution.

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)

The average diastolic BP, systolic BP and hypertension pervasiveness in the patients on cART and those that were off cART are presented in Table 2.

The hypertension incidence was greater in those patients on cART 49 (34.0%) as compared to cART-naïve (9.6%).

The various combinations of antiretroviral drugs 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.

**Figure 1.** Combined antiretroviral drugs and HIV afflicted patients.

TEE - Tenofovir Emtricitavine Efavirenz; CPK - Zidovudine Lamivudine Nevirapine; CPA - Zidovudine Lamivudine Ritonovir boosted Lopinavir; TRN - Tenofovir Emtricitabine Nevirapine; CBE - Zidovudine Lamivudine Efavirenz; TRA - Tenofovir Emtricitavine Ritonovir boosted Lopinavir.

Table 4 reveals the 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; $p < 0.043$) correlated with hypertension. Duration of HIV infection, CD₄ cells count and exposure to antiretroviral drug regimens were not connected with hypertension. In HIV afflicted clients and the general populace, hypertension is a principal risk factor for the deterrence cardiovascular disorders. This study indicates that substantial variation exists in hypertension pervasiveness in both cART-naïve and cART patients. The hypertension occurrence, however, was considerably greater in patients on cART as compared to cART-naïve patients. This observation corroborates with the previous studies that exhibited a greater hypertension incidence in the clients on cART. [14-18].

Table 4. Logistic regression analysis of risk factors related to hypertension among clients on cART.

Risk Factors	Adjusted Odds 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 of HIV infection (months)	0.73	0.44-1.28	0.395
Duration of 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

* Statistically significant at $p < 0.05$.

Contrarily, the previous report of Kanegae et al. indicated a non-disparity in the manifestation of hypertension between subjects on cART and cART-naïve [19]. The discrepancies of these findings could be associated with parameters such as environmental variations, study designs, site of the study as well as mean duration of cART, clinical and demographic features of the studied population. Furthermore, lower hypertension commonness was observed in cART patients. Also, 60% prevalence rate in HIV patients on cART was documented by [20]. The occurrence rate of 34% in the patients on cART recorded in the present study was similar (34.9%) to the result of [21]. The patients on cART had evidently greater average BMI, weight, age, CD₄ cells count and the long period of infection of HIV than those yet to receive cART. This could probably be attributed to better quality of life of those on cART. The patients on cART usually live longer and healthier. The risk factors for age, BMI, gender and sedentary lifestyle observed in this study could be responsible for high hypertension frequency among patients on cART (Table 3). These results agreed with the earlier studies that identified male gender, older age, black race, overweight, diabetes, smoking, dyslipidemia, sedentary lifestyle and a family history of hypertension as risk factors for high BP among

the patients [22,23]. This study also revealed that exposure to cART is not a risk factor for hypertension. This is in line with the findings of Harrison et al [24] and Kanegae et al [19] who reported that long period on ART was not interrelated with high BP in the patients. Contrariwise, the findings of Njelekela et al. [17] and Global status [25] signified that the use of ART could be related to hypertension.

CONCLUSION

Patients on cART were found to have higher hypertension prevalence than cART-naïve. On risk factors for hypertension, however, the cART was not inclusive. There is a need for continuous screening of hypertension in HIV afflicted individuals to prevent cardiovascular complications.

ACKNOWLEDGEMENT

The authors thank all the subjects involved in this study. Special thanks to Kwara State Ministry of Health for granting the approval for this study. Also, appreciation goes to the staff of ART Clinic, General Hospital, Offa for their unflinching support.

AUTHORS' CONTRIBUTIONS

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

REFERENCES

- UNAIDS, 2016. Fact sheet - Latest statistics on the status of the AIDS epidemic. Available at <http://www.unaids.org/en/resources/fact-sheet>. Retrieved on 7th June 2017.
- Ssinabulya I, Kayima J, Longenecker C, Luwedde M, Semitala F, Kambugu A, Ameda F, Bugeza S, McComsey G, Freers J, Nakanjako D. Subclinical atherosclerosis among HIV-infected adults attending HIV/AIDS care at two large ambulatory HIV clinics in Uganda. *PloS one*. 2014 Feb 28;9(2):e89537.
- Dimala CA, Atashili J, Mbuagbaw JC, Wilfred A, Monekosso GL. Prevalence of hypertension in HIV/AIDS patients on highly active antiretroviral therapy (HAART) compared with HAART-naïve patients at the Limbe Regional Hospital, Cameroon. *PLoS One*. 2016 Feb 10;11(2):e0148100.
- Arruda Junior ER, Lacerda HR, Moura LC, Albuquerque MD, Miranda Filho DD, Diniz GT, Albuquerque VM, Amaral JC, Ximenes RA, Monteiro VS. Risk factors related to hypertension among patients in a cohort living with HIV/AIDS. *Braz J Infect Dis*. 2010; 14(3):281-7.
- Bloomfield GS, Khazanie P, Morris A, Rabadán-Diehl C, Benjamin LA, Murdoch D, Radcliff VS, Velazquez EJ, Hicks C. HIV and non-communicable cardiovascular and pulmonary diseases in low-and middle-income countries in the ART era: what we know and best directions for future research. *J Acquir Immune Defic Syndr*. 2014 Sep 1;67(01): S40.
- DAD Study Group. Class of antiretroviral drugs and the risk of myocardial infarction. *N Engl J Med*. 2007; 356(17):1723-35.
- Baekken M, Os I, Sandvik L, Oektedalen O. Hypertension in an urban HIV-positive population compared with the general population: influence of combination antiretroviral therapy. *J Hypertens*. 2008; 26(11):2126-33.
- Sherer R, Solomon S, Schechter M, Nachega JB, Rockstroh J, Zuniga JM. HIV Provider–Patient Communication Regarding Cardiovascular Risk: Results from the 2010 AIDS Treatment for Life International Survey. *J Int Assoc Provid AIDS Care*. 2014; 13(4):342-5.
- Dubé MP, Lipshultz SE, Fichtenbaum CJ, Greenberg R, Schechter AD, Fisher SD, Working Group 3. Effects of HIV infection and antiretroviral therapy on the heart and vasculature. *Circulation*. 2008; 118(2): e36-40.
- Araoye MO. Research methodology with statistics for health and social sciences. Ilorin: Nathadex Publisher. 2003;115(9).
- Chen Y, Chen X, Dang G, Zhao Y, Ouyang F, Su Z, Zeng J. Hypertension criterion for stroke prevention—to strengthen the principle of individualization in guidelines. *The J Clin Hyperten*. 2015; 17(3):232-8.
- Ganz ML, Wintfeld N, Li Q, Alas V, Langer J, Hammer M. The association of body mass index with the risk of type 2 diabetes: a case–control study nested in an electronic health records system in the United States. *Diabetol. Metab Syndr*. 2014;6(1):50.
- SAS, 2012. The Statistical Application Software (SAS) Statistics System for Windows Release Version 9.2. SAS Institute, Inc. Cary, NC, USA.
- Lichtenstein KA, Armon C, Buchacz K, Chmiel JS, Buckner K, Tedaldi EM. et al. Holmberg SD, Brooks JT, HIV Outpatient Study (HOPS) Investigators. Low CD4+ T cell count is a risk factor for cardiovascular disease events in the HIV outpatient study. *Clin Infect Dis*. 2010;51(4):435-47.
- Yone EW, Betyoumin AF, Kengne AP, Folefack FJ, Ngogang J. First-line antiretroviral therapy and dyslipidemia in people living with HIV-1 in Cameroon: a cross-sectional study. *AIDS Res Ther*. 2011;8(1):33.
- Ekali LG, Johnstone LK, Echouffo-Tcheugui JB, Kouanfack C, Dehayem MY, Fezeu L, et al. Fasting blood glucose and insulin sensitivity are unaffected by HAART duration in Cameroonians receiving first-line antiretroviral treatment. *Diabetes Metab*. 2013;39(1):71-7.
- Njelekela M, Muhihi A, Aveika A, Spiegelman D, Hawkins C, Armstrong C, et al. Prevalence of hypertension and its associated risk factors among 34,111 HAART naïve HIV-infected adults

- in Dar es Salaam, Tanzania. *Int J Hypertens*. 2016;2016:5958382.
18. Agrawal A, Mital P, Goyal LK, Agarwal A, Nawal CL, Kumar V. Research Article A Study of Risk Factors and Impact of HAART on Blood Pressure in North Indians Living With HIV/AIDS. *Sch. Acad. J. Biosci*. 2015;3(1B):98-103.
 19. Kanegae H, Oikawa T, Okawara Y, Hoshida S, Kario K. Which blood pressure measurement, systolic or diastolic, better predicts future hypertension in normotensive young adults? *J Clin Hypertens*. 2017; 19(6):603-10.
 20. Mutede BR, Magure T, Gombe NT, Bangure D, Tshimanga M, Mungati M. Prevalence and factors associated with hypertension among anti-retroviral therapy patients aged 15 Years and above in Makonde District, Zimbabwe, 2012: an analytic cross-sectional study. *World J Cardiovasc*. 2015;5(09):266.
 21. Kaplan RC, Kingsley LA, Sharrett AR, Li X, Lazar J, Tien PC, Mack WJ, Cohen MH, Jacobson L, Gange SJ. Ten-year predicted coronary heart disease risk in HIV-infected men and women. *Clin Infect Dis*. 2007; 45(8):1074-81.
 22. Deeks SG, Phillips AN. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. *BMJ*. 2009;338: a3172.
 23. Kowalska JD, Reekie J, Mocroft A, Reiss P, Ledergerber B, Gatell J, Monforte AD, Phillips A, Lundgren JD, Kirk O, EuroSIDA study group. Long-term exposure to combination antiretroviral therapy and risk of death from specific causes: no evidence for any previously unidentified increased risk due to antiretroviral therapy. *Aids*. 2012;26(3):315-23.
 24. Harrison DG, Guzik TJ, Lob H. Inflammation, immunity, and hypertension. *Hypertension*, 2011; 57:132-40.
 25. Global Status Report on Non-Communicable Diseases, 2010. Available from http://www.who.int/nmh/publications/ncd_report_full_en.pdf.