Hypertension in HAART-Naïve HIV Subjects in Southeast Nigeria: A Single-Center Study

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Abstract

Background: Hypertension is a major healthcare problem in Nigeria with a probable prevalence of 36.6%. Human immunodeficiency virus (HIV) infection is a global healthcare problem. The factors which influence hypertension in HIV subjects have not been completely identified. The study aimed to determine the prevalence of hypertension and the factors which might influence hypertension in HAART-naïve HIV subjects.

Methodology: This was a cross-sectional study involving 393 treatment-naïve HIV subjects and 136 age and sex-matched HIV seronegative controls. Anthropometric and demographic data were obtained, blood pressure measurements and other relevant investigations were performed. Hypertension was defined here as systolic blood pressure (SBP) 140mmHg and diastolic blood pressure (DBP) 90mmHg. Hypertension was compared between the HIV subjects and the non-HIV control. The association of the variables with hypertension in HIV subjects were determined.

Results: The mean age of the HIV subjects was 39 ± 11 years. Females were 282(72.0%) and males 110(28.0%). The prevalence of hypertension was 23.7% in HIV subjects and 31.6% in the non-HIV control. The prevalence of hypertension was 17.2% in HIV subjects with high density lipoprotein cholesterol (HDL) <1.0mg/dl and this was significantly lower than the prevalence of hypertension of 27.1% in those whose serum HDL was 1.0mg/dl. There was no significant association between hypertension and 24-hour urine osmolality (24HUOsm) (p=0.094), body mass index (BMI) (p=0.572), 24-hour urine protein (24HUP) (p=0.606), serum total cholesterol (p=0.628), serum low density lipoprotein cholesterol (LDL) (p=0.116), triglyceride (TG) (p=0.925), Systolic blood pressure had a significant correlation with serum HDL, (r=0.114, p=0.024). Similarly, CD4 cell count correlated significantly with DBP (r=0.123, p=0.012. Serum HDL (p=0.0.024) and CD4 cell count (p=0.012) predicted hypertension in HIV subjects.

Conclusion: The prevalence of hypertension of 23.7% in HIV subjects was high in this study. Low CD4 cell count and low serum HDL were predictors of hypertension in HIV subjects.

Keywords: HIV; Hypertension; CD4 cell count; Serum HDL.

What is already known about this topic?

- Hypertension is a global healthcare problem in the general population and in some known sub-populations.
- The factors which influence hypertension in HIV patients are not completely defined.
- What this study contributes to knowledge
- The prevalence of hypertension of 23.7% was high in this study.
- Low CD4 cell count and low serum HDL were predictors of hypertension in HIV subjects.

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How to cite this article: Anyabolu EN, Okoye IC, Ufoaroh CU, Chukwuonye II, Echendu ST, Umeadi EN, Anyabolu AE. Hypertension in HAART-naïve HIV subjects in Southeast Nigeria: A single-centerstudy. Niger J Med 2022;63(5):425-431

Introduction

Hypertension is a major health issue globally especially in sub-Saharan Africa and has become a major public health challenge. Its age-standardized prevalence in Nigeria is 38.1%^[1] while globally 26% of the world's population has hypertension which is estimated to increase by 2025^[2]. The Human immunodeficiency virus (HIV) is a global health problem, with an estimated 37.7 million people living with HIV^[3]. HIV has been associated with several systemic illnesses including systemic hypertension and other cardiovascular illnesses. Systemic hypertension was said to be heightened in HIV patients through several mechanisms aside the traditional risk factors for hypertension namely vascular inflammation, intestinal problems, high cholesterol, HIV-related kidney disease.^[4] HIV leads to a chronic inflammatory process which also involves the blood vessels leading to thickening of the arteries with consequent elevation in blood pressure.^[4] Other risk factors found from previous studies include older age, male sex, family history, education status, ethnicity, longer duration of HIV infection, high viral load, smoking, alcohol use, comorbid state, low CD4 count, were attributed to the high burden of HTN in subjects living with HIV.^[5] Hypertension was found more in those living with HIV that are taken some specific anti-retroviral agents especially the protease inhibitors which are associated with disorders of lipid metabolism and abnormal lipid deposition.^[6] There is a paucity of data on Hypertension in HIV HAART- naïve HIV patients in this part of the world: hence this study.

Materials and Methods

This was a cross-sectional study of patients recruited consecutively from the HIV Unit and the general outpatient clinic in Federal Medical Centre (FMC), Owerri, South-East Nigeria. This study was conducted between April and August 2011. The hospital sub-serves the state and also receives referrals from the neighboring states. Owerri, where the hospital is situated, has a local municipal population of about 125,337, whereas the state population is conservatively put at 3,927,563.^[7] The study consisted of 393 newly diagnosed drug-naive, HIV-seropositive adult subjects (in the age range of 18–65 years) and 136 age-.and sex-matched HIV-seronegative subjects as control group.

The criteria for inclusion in this study were age range of 16-65 years and treatment-naïve HIVpositive status. Pregnancy, adrenal disease, renal or terminal illness and malignancy were the exclusion criteria. From each of the study subjects, informed written consent was obtained. The Ethics Committee of the hospital gave approval for the study.

Definition of Terms

Hypertension was taken as SBP 140 mmHg +DBP 90mmHg whereas non-hypertension was SBP < 140mmHg + DBP < 90mmHg. Under weight was taken as BMI $< 18.5 \text{ kg/m}^2$, normal weight BMI 18.5 - 24.9 kg/ m², overweight BMI 25.0 - 29.9 kg/m^2 , obesity class I BMI 30.0- 34.9 kg/m², obesity class II BMI 35.0 - 39.9kg/m², and obesity class III BMI 40.0kg/m².However, in this study, obesity was taken as class I, class II and class III obesity added together. Normal urine osmolality was taken as 24HUOsm 300- 750 mOsm/kgH₂O, dilute urine: 24HUOsm <300 mOsm/kgH₂O, and concentrated urine: 24HUOsm >750 mOsm/kgH₂O. Desirable serum LDL was taken as< 2.6 mmol/l, borderline serum LDL as 2.6 – 4.1mmol/l, and .high serum LDL: as >4.1mmol/l.Desirable serum cholesterol: was taken as<5.2mmol/l, borderline serum cholesterol: as 5.2 - 6.2 mmol/l., and high serum cholesterol: as >6.2mmol/l. Desirable serum triglyceride: taken as <1.7mmol/l., borderline serum triglyceride as 1.7 - 2.2mmol/l and .high serum triglyceride:as>2.2mmol/l. Low serum HDL: taken as <1.0mmol/l. and desirable serum HDL: as

1.0mmol.

From each of the subjects anthropometric and demographic data were obtained with the aid of a questionnaire administered by our laboratory technicians who explained to them the aim of the study. The place of domicile and origin, gender and age of the subjects were obtained. Weight and height were taken and BMI was rendered as weight/height2 (kg/m²). Blood pressure was measured.^[8] Blood pressure (mmHg) was recorded from the non-dominant hand in sitting position, after the subjects had rested for 10 minutes, using appropriate cuff size to cover about 80% of the arm, and Accoson mercury sphygmomanometer. Three blood pressure readings were taken 5 minutes apart, and the average

of each three readings was obtained.^[9]

Clear instructions were given to all the subjects on how to collect a 24-hour urine sample. For each subject, day-time blood samples and blood samples were collected at the end of the 24-hour urine sample collection.^[8,11]

From the 24-hour urine samples collected, 24-hour urine protein (24HUP), and 24-hour urine osmolality (24HUOsm) were performed. CD4 cells count was performed on the blood samples collected. Other tests done from the blood samples were HIV screening and confirmatory tests, fasting blood sugar and fasting serum lipid profile (FSLP) [total cholesterol, triglyceride, HDL, LDL]. Osmolality was determined by the freezing point depression method using Precision Osmette 5002 osmometer and protein by a photometric method.^[8,11] Hypertension was compared between the HIV subjects and the non-HIV control. The association of the variables with hypertension in HIV subjects was determined The potential risk factors for hypertension evaluated were age, BMI, serum total cholesterol (chol), serum LDL, serum HDL, serum TG, 24HUOsm and 24HUP.

Statistical Analysis

The data were analyzed using SPSS version 17.0 (SPSS Int. Chicago, II, USA). The distribution and characterization of the clinical and laboratory features among the subjects with different levels of hypertension were analyzed using cross-tabulation. For continuous variables, mean values and standard deviations were calculated and the means were compared using ANOVA or two-sample t-test. Categorical variables were compared using the nonparametric tests - Chi-squares. Multivariate linear regression analyses were used to determine the strength of variables to predict hypertension. All tests were two-tailed. P 0.05 was taken as statistically significant.^[8,11]

Results

This study recruited 393 HIV subjects. One subject was excluded on account of incomplete data and errors in sample collection. The mean age of the HIV-positive subjects was 39 ± 11 years; females were 282(72.0%) and males 110(28.0%). The non-HIV subjects were 136; females were 98(72.1%) and

males 38(27.9) and their mean age was 38.58±11.79 years. The female: male ratio was approximately 3:1 in both the HIV-seropositive subjects and the HIVseronegative control (Table 1A). BMI was 26.22 ± 5.40 kg/m² in HIV subjects and 25.51 ± 6.47 kg/m² in the control. However, this was not significant, p=0.211. 24HUP of 0.187±0.290g/l was significantly higher than the 0.095 ± 0.087 g/l in the control, p<0.001. 24HUOsm of 564±501mOsm/kgH₂O was significantly high in HIV subjects compared to 284±253 mOsm/kgH₂O in the control, p<0.001. LDL was significantly lower in HIV subjects $(2.05\pm0.58$ mg/dl) than in the control (2.87±1.07mg/dl), p<0.001. HDL was significantly high in HIV subjects (1.18±0.39mg/dl) compared to the control (0.97 ± 0.34 mg/dl), p<0.001. There was no significant difference in TG values between the HIV subjects (1.23±0.37mg/dl) and the control (1.27±0.40mg/dl), p=0.331 (Table 1B).CD4 count cells//ml (Median) was 391 in HIV subjects but was not evaluated in the control. The HIV subjects who had hypertension (SBP 140mmHg+DBP 90mmHg) were 93(23.7%) whereas those without hypertension (SBP<140mmHg+DBP<90mmHg) were 299(76.3%), indicating a prevalence of hypertension of 23.7% among the HIV subjects (Table 2). However, in the control subjects, the prevalence of Hypertension was 31.6%. There was no statistical difference in Hypertension values between the HIV subjects and the non-HIV control, p=0.525 (Table 1A).

One hundred and twenty-nine subjects had 24HUOsm <300mOsm/kg H₂O in HIV subjects. Out of this number, 24(18.6%) had hypertension whereas 105(81.4%) had not. The prevalence of hypertension of 29.1% was highest among the subjects with 24HUOsm 300-750mOsm/KgH₂O, but declined in those with 24HUOsm >750mOsm/KgH₂O <300mOsm/KgH₂O to 18.6% and in those with 24HUOsm >750mOsm/KgH₂O to 20.6%. However, this association of hypertension with 24HUOsm was not significant, p=0.094 (Table 3).

The prevalence of hypertension in HIV subjects was highest among those with normal BMI (18.5-24.9kg/m₂), 27.1%, but declined with overweight (21.3%) and obesity (24. 7%). Similarly, the

prevalence of hypertension declined in those with underweight to 16.7%. However, this association of hypertension with BMI was not significant, p=0.572(Table 3).

The prevalence of hypertension increased as 24HUP increased in HIV subjects. Hypertension was highest in the subjects who had 24HUP 300mg but declined in those with 24HUP 150.0-299.9mg to 23.5%. However, this association between hypertension and 24HUP was not significant, p=0.606 (Table 3).

The prevalence of hypertension declined as CD4 declined in HIV subjects -24.0% in those with CD4

200 cell count/ml, but 22.4% in those who had CD4 <200 cell count/ml. However, there was no significant association between hypertension and CD4 cell count, p=0.814 (Table 3).

Out of 93 subjects who had hypertension in HIV subjects, the prevalence of hypertension declined as serum total cholesterol increased; 2.2% in those who had desirable serum total cholesterol, 7.5% in those with borderline total cholesterol and 2.2% in those who had high serum total cholesterol. Nonetheless, this association between serum total cholesterol and hypertension was not significant, p=0.628 (Table 3).

The prevalence of hypertension was 88.0% among those with desirable serum LDL levels in HIV subjects. This prevalence level declined to 12.0% in those with borderline serum LDL levels. However, this was not significant, p=0.116 (Table 3).

The prevalence of hypertension of 17.2% in hypertension subjects with HDL <1.0mg/dl was significantly lower than 27.1% found in those whose serum HDL was 1.0mg/dl (Table 3).

The prevalence of hypertension was highest in HIV subjects with serum TG borderline, 26.7%, but declined with increasing serum TG. However, this association between hypertension and serum TG was not significant, p=0.925 (Table 3).

Systolic blood pressure had a significant correlation with serum HDL in HIV subjects, (r=0.114, p=0.024). Similarly, CD4 cell count correlated

significantly with diastolic blood pressure (r=0.123, p=0.012 (Table 4). The association between hypertension and age (p=0.119), 24HUP (p=0.331), 24HOsm (p=0.589), serum total cholesterol (p=0.413), TG (p=0.981), serum LDL (p=0.172), BMI (p=0.203) were not significant (Table 4).

Serum HDL (p=0.024) and CD4 cell count (p=0.012) predicted hypertension in HIV subjects (Table 5).

Table 1A: Clinical characteristics of the studypopulation

Variable (mean)	All subjects (n=529)	HIV subjects (n=393)	Control	p value (n=136)
Age(yrs±SD)	38.77±10.94	38.84±10.65	38.58±11.79	0.814
Gender:				
Male (%)	148(28%)	110(28%)	38(27.9)	
Female(%)	381(72%)	283(72.0%)	98(72.1%)	
$BMI(kg/m^2 \pm SD)$	26.04±5.69	26.22±5.40	25.51±6.47	0.211
Male	2434±4.92	25.24±4.69	21.74±4.66	< 0.001
Female	26.70±5.84	26.61±5.61	26.98±6.50	0.588
SBP(mmHg±SD)	119.6±16.9	119.3±16.5	120.4±18.2	0.525
DBP(mmHg±SD)	75.9±10.6	75.6±10.6	76.9±10.7	0.201

BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, SD=standard deviation.

 Table 1B:
 Laboratory
 characteristics
 of
 the
 study
 population

Variable (mean)	All subjects (n=529)	HIV subjects (n=393)	Control (n=136)	p value
FSLP(mmol/l±SD)				
Total cholesterol	4.30±1.00	4.26±0.90	4.41±1.25	0.139
LDL cholesterol	2.26±0.82	2.05±0.58	2.87±1.07	< 0.001
HDL cholesterol	1.13±039	1.18±0.39	0.97±0.34	< 0.001
Triglyceride	1.24±0.37	1.23±0.37	1.27±0.40	0.331
24HUP(g±SD)	0.162±0.256	0.187±0.290	0.095±0.087	< 0.001
24HUOsm				
(mOsm±SD)	489±465	564±501	284±253	< 0.001

FSLP=fasting serum lipid profile, LDL=low density lipoprotein cholesterol, HDL=high density lipoprotein cholesterol, 24HUP=24-hour urine protein, 24HUOsm=24-hour urine osmolality

Table 2: Frequency of Hypertension in StudySubjects

	HIV Subject	\$	Control Subjects		
Variables	Frequency	Percentage	Frequency	Percentage	
	93	23.7	43	31.6%	
SBP<140+DBP<90mmHg	299	76.3	93	68.4%	
SBP=systolic blood pressure. D	BP=diastolic bl	ood pressure			

Table 3: Relationship between Hypertension andSelected Risk Factors in Study Population (n=529)

	HIV SUBJECTS n=393			CONTROL n=136				
VARIABLES	DBP (n/%)	SBP<140+ DBP <90mmHg (n/%)	$\int \frac{\Lambda^2}{d}$ f	LH R/p valu e	DBP (n/%)	SBP<140+ DBP <90mmHg (n/%)	λ ² / df	LH R/p valu e
BMI(kg/m ²) <18.5 18.5—24.9 25-29.9 ≫0	4(16.7%) 36(27.1%) 32(21.3%) 21(24.7%)	20(83.3%) 97(72.9%) 118(78.7%) 64(75.3%)	2.00 13	0.09 6 0.09 4	2(14.3%) 22(38.6%) 4(16.7%) 15(36.6%)	12(85.7%) 35(61.4%) 20(83.3%) 26(63.4%)	6.17 8 3	0.081 0.103
24HUOsm(mOsm /kgH ₂ O) <300 300-750 >750	24(18.6%) 43(29.1%) 20(20.6%)	105(81.4%) 105(70.9%) 77(79.4%)	4.72 9 2	0,096 0.094	27(29.0%) 9(31.0%) 7(50.0%)	66(71.0%) 20(69.0%) 7(50.0%)	2.48 0 2	0.312 0.281
24HUP (mg) 51-0-149.9 150.0-299.9	14(19.4%) 41(22.8%) 16(23.5%) 16(29.6%)	58(80.5%) 139(77.2%) 52(76.5%) 38(70.4%)	1.84 1 3	0.615 0.606	40(32.0%) 3(27.3%) 0(0.0%) 0(0.0%)	85(68.0%) 8(72.7%) 0(0.0%) 0(0.0%)	1.10 4 1	0.743 0.746
CD4(cells/ml) <200 ≷00	11(22.4%) 82(24.0%)	38(77.6%) 260(76.0%)	0.05 5 1	0.95 6 0.81 4	Xxxx Xxxx	Xxxx Xxxx	Xx xx xxx xxx x	Xxx x xxxx
FSLP (mmol/1) Cholesterol Desirable <5.2 Borderline 5.2- 6.2 High >6.2	84(90.3%) 7(7.5%) 2(2.2%)	264(88.3%) 31(10.4%) 4(1.3%)	0.93 0 2	0.62 5 0.62 8	32(29.6%) 7(46.7%) 4(30.8%)	76(70.4%) 8(53.3%) 9(69.2%)	1.7 73 2	0.43 2 0.41 2
LDL Desirable(<2.6) Borderline(2.6- 4.1) High(>4.1) HDL-Low (<1.0) High (≥ .0)	81(88.0%) 11(12.0%) XXX 23(17.2%) 70(27.1%)	242(80.9%) 57(19.1%) XXX 111(82.8%) 188(72.9%)	2.47 3 1 4.84 2 1	0.10 4 0.11 6 0.038 0.028	16(24.6%) 20(38.5%) 7(36.8%) 24(32.0%) 19(31.1%)	49(75.4%) 32(61.5%) 12(63.2%) 51(68.0%) 42(68.9%)	2.8 40 2 0.01 1 1	0.23 9 0.24 2 0.915 0.915
TriglycerideDesirable <1.7			0.47 0 3 molality				1.46 7 2 =fasting	

Table 4: Correlation of Hypertension with selected variables in HAART-naïve HIV-positive subjects (n=392)

Variables	Systolic blood p	ressure	Diastolic blood pressure		
	Correlation coefficient(r)	P value	Correlation coefficient(r)	P value	
Age	0.079	0.119	0.085	0.088	
Body mass index	-0.064	0.203	-0.043	0.393	
CD4 cells count	0.060	0.238	0.127	0.012	
24-hour urine osmolality	0.028	0.589	< 0.001	1.000	
24-hour urine protein	0.050	0.331	0.078	0.134	
Serum cholesterol total	-0.041	0.413	-0.041	0.414	
Serum LDL	0.069	0.172	0.068	0.178	
Serum HDL	0.114	0.024	0.009	0.869	
Serum Triglyceride	0.001	0.981	-0.068	0.181	
SBP=systolic blood pressu	re, LDL=low densi	y lipoprotein.	HDL=high density	lipoprotein	

Table 5: Multivariate linear regression of variables with SBP and DBP in HAART-naïve HIV-positive Subjects (n=392)

	Systolic blood pressure					
R2	Beta	Т	P value	95% CI		
0.013	0.114	2.264	0.024	0.016-		
				0.234		
	Diastolic blo	ood pressure				
0.016	0.127	2.526	0.012	0.001-		
				0.011		
	0.013	R2 Beta 0.013 0.114 Diastolic blo	R2 Beta T 0.013 0.114 2.264 Diastolic blood pressure	R2 Beta T P value 0.013 0.114 2.264 0.024 Diastolic blood pressure Personal pressure Personal pressure		

Discussion

In this study the prevalence of hypertension was 23.7% in HIV subjects and 31.6% in the non-HIV control. The prevalence of hypertension was 17.2% in HIV subjects with high density lipoprotein cholesterol (HDL) <1.0mg/dl and this was significantly lower than the prevalence of hypertension of 27.1% in those whose serum HDL was 1.0mg/dl. Systolic blood pressure had a significant correlation with serum HDL, (r=0.114, p=0.024). Similarly, CD4 cell count correlated significantly with DBP (r=0.123, p=0.012. Serum HDL (p=0.0.024) and CD4 cell count (p=0.012) predicted hypertension in HIV subjects.

This study showed a prevalence of hypertension to be 23.7%, in contrast with a similar study by Amusa et al^[6] done in north-central Nigeria which had a prevalence of 46% this difference may be due to the fact that those on HAART were also included in

their study, our study was on HAART naïve patients as anti-retroviral agents from previously documented studies increased the risk of developing hypertension. Hypertension was noted to be higher in those with lower urine osmolality. Urine osmolality is a measure of the concentrating ability of the kidney, the lower the osmolality the likely more kidney damage; kidney damage leads to elevated blood pressure.^[12] However, our study did not show any significant association of urine osmolality with hypertension; our study also did not evaluate renal function. Clients with greater proteinuria were at greater risk of having hypertension from our study. proteinuria is a marker of kidney damage, this agrees with the fact that in the pre HAART era, the major cause of hypertension in HIV patients was chronic kidney disease.^[13] Body mass index/Obesity was not an independent risk factor for hypertension in HIV HAART naïve patients, in contrast with the study by Okpah HO et al in Calabar^[14] where increased BMI and obesity were associated with hypertension, the study in Calabar included patients on HAART, in which their obesity and fat deposition may be linked to the HAART regimen. This further shows that there is always an interplay between several risk factors associated with an increase in blood pressure. Dyslipidemia from several studies has been seen in HIV patients especially with the decline in CD4 and an increase in viral load^[14,15], there is usually a decline in HDL levels and an increase in total cholesterol and both of them are associated with high cardiovascular risk. This is in contrast with the findings from our study where hypertension was observed from our study, Hypertension was observed to be more in HIV HAART naïve patients whose CD4 count were more than 200cc/ml with high HDL and increasing total cholesterol though not statistically for CD4 and total cholesterol, this may be due to the fact that most HIV patients with low CD4 count are likely to be on drugs because they are usually very symptomatic, while those with higher CD4 may be incidental findings on a presentation for other medical illness including hypertension.

Conclusion

The prevalence of hypertension of 23.7% in HIV subjects was high in this study. Low CD4 cell count and low serum HDL were predictors of

hypertension in HIV subjects. Abnormalities of CD4 cells count and low serum HDL were common in HAART-naïve HIV subjects with hypertension. Hypertensive HIV subjects should be evaluated in the early stages for immunosuppression and HDL dyslipidemia.

Limitations

The limitations of this study include the single study site and the non-assessment of confounding factors of hypertension in assessing other determinants of hypertension.

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