

Research Article

A Study of Risk Factors and Impact of HAART on Blood Pressure in North Indians Living With HIV/AIDS

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Abstract: This study was proposed to assess the risk factors and impact of HAART on blood pressure in HIV seropositive patients. Total 300 HIV sero-positive cases (150 treatment naïve and 150 cases taking HAART); above 18 years of age were recruited. Cases having ischaemic, rheumatic or congenital heart diseases prior to diagnosis of HIV infection, chronic renal failure, chronic lung disease, diabetes, thyroid dysfunction were excluded from the study. Out of 300 HIV sero-positives, 59/300 (19.67%) were found to be hypertensive. The hypertensives were significantly older in age than normotensives (38.89±7.95 years vs. 32.95±7.33 years, p<0.05). Systolic (SBP) as well as diastolic blood pressure (DBP), BMI and lipid parameters [triglycerides (TG), total cholesterol (TC) and low density lipoproteins (LDL)] were significantly higher in hypertensive group. HDL levels were also significantly lower in hypertensives. (p<0.05 for each). High BMI, high TG, high TC, high LDL and low HDL were significantly associated with HTN (p<0.05 for each). Both SBP and DBP had statistically significant correlation with the time since detection of HIV seropositive status and with the traditional risk factors of HTN (age, BMI, TG, HDL, LDL, and TC) (p<0.05 for each). Mean CD₄ count were found to be lower in hypertensives (377.27±189.12 cells/mm³ v/s 437.44±248.04 cells/mm³) (p>0.05). CD₄ count did not have a significant correlation with either SBP or DBP (p>0.05). Among 150 HIV cases taking HAART, thirty two were hypertensive and rest 118 cases were normotensive. HAART was not associated with hypertension. This study concluded that hypertension in HIV population is probably associated with the duration of HIV infection, aging, being overweight (BMI>25kg/m²) and abnormal lipid levels. Hypertension did not seem to be associated with use of any anti retro viral drug (HAART).

Keywords: Hypertension, risk factors, HAART , HIV infection

INTRODUCTION

Hypertension is a major risk factor for myocardial infarction, stroke, renal failure and atherosclerosis and contributes to significant cardiovascular and cerebrovascular morbidity and mortality [1]. Recent reports suggest increasing frequency of hypertension and other non-communicable diseases among HIV infected patients [2-3]. Whether these trends are due to the aging of the HIV population due to increased survival of these patients in the post highly active anti-retroviral therapy (HAART) era and therefore accumulation of the risk factors for the development of hypertension, or it being a direct effect of the HIV is still unclear. The association of specific HAART medications such as protease inhibitors (PIs) with hypertension has also been revealed in some studies [3,4].

Understanding the potential association between HIV and hypertension is crucial as there is paucity of data from Indian subcontinent regarding

occurrence and risk factors of hypertension in HIV patients. This cross-sectional study was undertaken to evaluate the presence of traditional risk factors associated with elevated blood pressure in these patients and to know whether blood pressure in these patients is affected by the use of HAART.

MATERIALS AND METHODS

This hospital-based observational study was done among 300 HIV seropositive cases (150 treatment naïve and 150 cases taking HAART); above 18 years of age; at Anti Retroviral Treatment (ART) centre in a tertiary care hospital in North India during the period of May 2012 to April 2013 after permission of institutional ethics committee. Informed consent was taken from all study participants. Cases having ischaemic, rheumatic or congenital heart diseases prior to diagnosis of HIV infection, chronic renal failure, chronic lung disease, diabetes, thyroid dysfunction were excluded from the study. Highly active antiretroviral therapy (HAART) was defined as the use of 3 or more

ARV medications as per the Department of Health and Human Services guidelines[5].

After taking detailed history and clinical examination, Anthropometric parameters (weight, height, body mass index [BMI]) were measured. Height was measured to the nearest 0.5 cm without shoes using a stadiometer. Each participant stood in such a way so that the Frankfort plane (a line connecting the superior border of the external auditory meatus with the infraorbital rim) was horizontal (i.e. parallel to the floor). Weight was measured using a standard physician's scale and was recorded to the nearest 0.1 kg. BMI was calculated as Weight (KG)/(Height in meters).² Normal BMI values were taken as 18.5-24.9 kg/m² and persons having BMI ≥ 25 kg/m² were termed as overweight. Blood pressure was measured using mercury sphygmomanometer with each participant over brachial artery in right arm in supine position. An average of three readings at least 10 minutes apart was taken as blood pressure level of the individual. Hypertension was defined as diastolic blood pressure (DBP) of ≥ 90 mm Hg or systolic blood pressure (SBP) of ≥ 140 mmHg at 2 or more clinic visit or patients on antihypertensive medication[6].

A venous blood sample, collected after overnight fasting, was sent for complete blood count (CBC), erythrocyte sedimentation rate (ESR), fasting blood sugar (FBS), renal function tests including complete urine examination, liver function tests, thyroid function test, lipid profile and CD4 count. The CD4 count was done on BD FACS Calibur™ system by BD Bioscience, US, at our institute.

Serum triglyceride level >150 mg/dl, serum total cholesterol level >200 mg/dl, serum HDL cholesterol 40mg/dl or lower in males and 50 mg/dl or lower in females, serum LDL level >100 mg/dl were considered as abnormal[7].

Statistical Analysis

Microsoft Excel and SPSS 17.0 for Windows were used for data storage and analysis. Continuous variables were expressed as mean \pm standard deviation. Chi square test and Student's t test were used to determine statistical difference between variables. Pearson's coefficient was used to investigate the correlation between the two variables. Statistical significance was set at P value ≤ 0.05 .

RESULTS

Demographic characters of the study population are given in table no.1. Total 300 HIV cases were taken in this study (157 male and 143 female) with mean age of 34.12 ± 7.81 years, mean systolic blood pressure 122.33 ± 17.34 mm Hg and mean diastolic blood pressure 81.32 ± 10.45 mm Hg. In this study 150 cases were taking HAART with mean duration of HAART 36.09 ± 21.43 months (range 2 months - 86 months)

Out of 300 HIV sero-positives, 59/300 (19.67%) were found to be hypertensive and rest (241/300; 80.33%) were normotensive. The hypertensives were significantly older in age than normotensives (38.89 ± 7.95 years vs. 32.95 ± 7.33 years, $p < 0.05$). Ethanol use was found in 23/59 (39%) of hypertensive v/s 58/241 (24.1%) of normotensives ($p > 0.05$). Similarly smoking was detected in 30/59 (50.8%) of hypertensive v/s v/s 93/241 (38.6%) of normotensives ($p > 0.05$). The difference for alcohol and smoking were not significant statistically among hypertensive and normotensive cases so these habits (alcohol and smoking) not confound our study.

Systolic as well as diastolic blood pressure, BMI and lipid parameters (triglycerides, total cholesterol and low density lipo proteins) were significantly higher in hypertensive group. HDL levels were also significantly lower in hypertensives. ($p < 0.05$ for each). [Table no.1]

High BMI, high triglycerides, high total cholesterol, high low density lipoproteins and low HDL were significantly associated with HTN ($p < 0.05$ for each). [Table no.1]

Both systolic and diastolic blood pressure had statistically significant correlation with the time since detection of HIV sero-positive status and with the traditional risk factors of hypertension (age, BMI, TG, HDL, LDL, and TC) ($0 < 0.05$ for each). [Table no.2]

Mean CD₄ count were found to be lower in hypertensives (377.27 ± 189.12 cells /mm³ v/s 437.44 ± 248.04 cells /mm³) but it failed to reach statistical significance ($p > 0.05$). [Table no.1] Also, CD₄ count did not have a significant correlation with either systolic or diastolic blood pressure ($p > 0.05$). [Table no.2]

Among 150 HIV cases taking HAART, thirty two were hypertensive and rest 118 cases were normotensive. HAART was not associated with hypertension in these cases. (Table no.1)

Table-1 : Distribution of HIV cases according to hypertension and study variables

Risk factor		Total N 300(100%)	Hypertensive N 59(100%)	Normotensive N 241(100%)	P
Age (years)		34.12±7.81	38.89±7.95	32.95±7.33	<0.05
Sex M/F		157/143	39/20	118/123	<0.05
Duration of HIV (months)		34.28±25.62	47.88±24.68	30.95±24.78	<0.05
Alcoholic n (%)		81 (27%)	23 (39%)	58 (24.1%)	>0.05 [@]
Smoker n (%)		123 (41%)	30 (50.8%)	93 (38.6)	>0.05 [@]
SBP (mm Hg)	≥140	59 (19.67%)	59 (100%)	00 (00%)	NA
	<140	241 (79%)	00 (00.0%)	241(100%)	
DBP (mm Hg)	≥90	44(14.67%)	44 (74.6%)	00 (00%)	NA
	<90	256(85.33%)	15 (25.4%)	241(100%)	
BMI (kg/m ²)	<25	287(95.7%)	50 (84.7%)	237 (98.3%)	<0.05
	≥25	13 (4.3%)	9 (15.3%)	4 (1.7%)	
TG (mg/dl)	>150	89 (29.7%)	26 (44.1%)	63 (26.1%)	<0.05
	≤150	211 (70.3%)	33 (55.9%)	178 (73.9%)	
TC (mg/dl)	>200	32 (10.7%)	13 (22%)	19 (7.9%)	<0.05
	≤200	268(89.3%)	46 (78%)	222 (92.1%)	
HDL (mg/dl)	Low	70 (23.3%)	20 (33.9%)	50 (20.7%)	<0.05
	Normal	230(76.7%)	39 (66.1%)	191 (79.3%)	
LDL (mg/dl)	>100	46 (15.3%)	18 (30.5%)	28 (11.6%)	<0.05
	≤100	254(84.7%)	41 (69.5%)	213 (88.4%)	
CD4 count(cells/μl)	>200	246 (82%)	44 (74.6%)	202 (83.8%)	>0.05 [@]
	≤200	54 (18%)	15 (25.4%)	39 (16.2%)	
CD4 count(cells/μl)		425.61±238.53	377.27±189.12	437.44±248.04	>0.05 [@]
Duration on HAART (months)		36.09±21.43	38.63±22.24	34.86±21.02	<0.05
HAART	On HAART	150(100)	32(21.33)	118(78.66)	>0.05 [@]
	HAART naive	150(100)	27(18)	123(82)	
SBP(mm Hg)		122.33±17.34	150.47±10.25	115.44±10.35	<0.05
DBP(mm Hg)		81.32±10.45	96.91±6.62	77.50±7.14	<0.05
BMI (kg/m ²)		19.59±2.89	21.29±3.14	19.17±2.67	<0.05
TG(mg/dl)		137.60±78.87	165.41±93.65	130.79±73.44	<0.05
TC(mg/dl)		128.82±65.34	179.73±64.95	116.36±59.22	<0.05
HDL(mg/dl)		91.14±60.85	46.12±8.79	102.17±63.04	<0.05
LDL(mg/dl)		69.03±28.89	83.69±25.5	65.44±28.58	<0.05

@ = Non-significant

Table-2: Correlation of systolic and diastolic blood pressure with different variables

	SBP		DBP	
	R	P	R	P
Age	0.388	<0.05	0.291	<0.05
Time since detection of HIV status	0.207	<0.05	0.167	<0.05
BMI	0.309	<0.05	0.381	<0.05
TG	0.141	<0.05	0.147	<0.05
HDL	-0.238	<0.05	-0.244	<0.05
LDL	0.186	<0.05	0.145	<0.05
TC	0.209	<0.05	0.226	<0.05
CD4	-0.030	>0.05	-0.057	>0.05 [@]
ART duration	0.150	>0.05	0.095	>0.05 [@]

@ = Non-significant

Table-3: Association between hypertension and HAART

HAART Drugs	Subjects on HAART (150)	Hypertensive (32)	Normotensive (118)	P
AZT	116	23	93	>0.05 [@]
3TC	150	32	118	>0.05 [@]
d4T	49	11	38	>0.05 [@]
NVP	126	27	99	>0.05 [@]
EFV	37	11	26	>0.05 [@]
TDF	27	5	22	>0.05 [@]
Atv/	11	2	9	>0.05 [@]
R	11	2	9	>0.05 [@]
@ = Non-significant				

DISCUSSION

In this study, as seen in the general population, the development of hypertension is also seen with the increasing age in HIV population [8-10]. Aging population is a well known risk factor for hypertension. Aging causes a loss in vessel function by stiffening of the arterial vasculature[11]. The vascular changes include the advanced reduction in visco-elastic properties of vessels, progressive atherosclerotic arterial disease, and hypertrophy or sclerosis of muscular arteries and arterioles which narrow the vessels wall and make a resistance to blood pressure and flow. Furthermore, HIV infection has been linked to arterial stiffness and proinflammatory responses[12]. Hence the virus may lead to premature vascular dysfunction causing elevation in blood pressure.

This study also highlights the important association of hypertension with duration of HIV exposure in north Indian HIV infected population. Previous studies from other parts of the world have also similarly revealed significant association between duration of HIV infection and hypertension ($p < 0.001$)[8,13]. However, it is yet to determine that this association is merely a function of increasing age of the patients or in fact due to HIV disease duration per se.

Previous data shows that HIV duration reflects cumulative time spent with various harmful influences, i.e. viral replication, immune activation, low-grade inflammation, metabolic aberrations related to both HIV and ART, and mitochondrial dysfunction[14]. Consequently, these patients may have been exposed to multiple stimuli which may affect endothelial function and vascular structure. In the general population, raised BP had been related elevation of inflammatory biomarkers such as CRP, fibrinogen and IL-6[15-17]. These biomarkers are often elevated in individuals with HIV and had associations with increased cardiovascular morbidity[14, 18, 19].

Similar to the other studies, we also found significant association of occurrence of hypertension with the presence of traditional risk factors (age, obesity and dyslipidemia) in our study population.

The occurrence of higher frequency of hypertensive HIV patients with increased BMI (BMI $> 25 \text{ kg/m}^2$) and higher mean BMI level in hypertensives were in accordance with previous studies[8, 10, 20] reinforcing the previously known fact that obesity is a well known risk factor for hypertension in HIV population as well as in general population[21]. HIV patients should strive to maintain a healthy weight through a balanced diet and exercise.

Similar to this study, previous reports also revealed association of hypertriglyceridemia with hypertension in HIV population[22]. Some authors observed high prevalence of hypertriglyceridemia in hypertensive HIV cases compared to normotensive cases of HIV subjects but without significant association[8, 20].

The association of hypercholesterolemia in hypertensive HIV patients has also been reported in previous studies[8, 20]. Our finding of significant association between hypertension and low HDL levels is, however, in contrast to other studies[20, 22]. Occurrence of hypertension was significantly associated with raised LDL levels in the current study. Previous reports also observed raised LDL in hypertensive HIV patients but without it reaching statistical significance[20, 22].

CD₄ count were comparatively lower in hypertensive HIV patient as compared to non hypertensive HIV patients but this finding fails to gain statistically significance ($p > 0.05$) which is similar to other studies[8, 20, 23].

Hypertension and HAART :

A total of 150 patients were on any form of HAART for at least 2 months. We compared the number of hypertensive and normotensive patients among cases receiving different ARV drugs (zidovudine (AZT), lamivudine (3TC), stavudine (d4T), nevirapine (NVP), efavirenz (EFV), tenofovir(TDF), atazanavir (ATV) and ritonavir (R)) however, no statistically significant association was found between the occurrence of hypertension with intake of any

individual ARV drug ($p > 0.05$). This observation is in echo with other studies who also did not find any significant association between hypertension and intake of individual ARV drug (> 0.05) [8, 2, 24].

Study Limitations:

There are several limitations to the present study. Since this study investigated a cross-section of the study population, data can be specified only to the studied sample population. The results cannot be applied to all people living with HIV including those receiving treatment from other hospitals in the country. Since there is no follow-up about changes in hypertension status among studied population, we cannot predict the development of hypertension in the future. Furthermore, due to small sample size and duration of use, the effect of HAART (as a whole or individually) may not correctly reflect real scenario. Notwithstanding these limitations, the study provides a valuable data on the occurrence of hypertension and causative risk among high risk HIV adults from North India.

CONCLUSION

Hypertension in HIV population is probably associated with the duration of HIV infection, aging, being overweight ($BMI > 25 \text{ kg/m}^2$) and abnormal lipid levels. Hypertension did not seem to be associated with use of any anti retro viral drug (HAART). HIV patients should be advised to adopt a healthy lifestyle and regular monitoring of blood pressure.

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