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Arterial Stiffness in HIV Patients in a Semi Urban Area of South Africa

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Abstract

Introduction: HIV infected patients are said to have increased cardiovascular risk which may result in large arterial wall stiffening. Aortic pulse wave velocity (PWV) provides a measure of this. This study investigated the relationship between aortic pulse wave velocity and the following variables: anthropometry, age, blood pressure and lipid profile.

Materials and methods: This was a cross-sectional study comprising 169 participants whose PWV was assessed using the Sphygmocor Vx.

Results: In total, 169 participants were examined. There were 63 HIV negatives, 54 HIV positives not on HAART and 52 HIV positives on HAART (62 males, and 107 females). In all the participants, HIV positives not on HAART, HIV positives on HAART, age ≥ 40 years, systolic blood pressure ≥ 130 mmHg, and hip circumference (HC) ≥ 97 cm were significantly and independently associated with elevated PWV ≥ 6.5 m/s (68.5%). In HIV positives not on HAART, only HC ≥ 97 cm was the most independent determinant of elevated PWV. In HIV positives on HAART, only age ≥ 40 years was the most independent determinant of elevated PWV. However, applying multiple linear regression analysis, and using continuous variables, and after adjusting for confounders (WC, TG, HC. and TC), increase in SBP (R^2=29.6%), age (R^2=9.2%), and decline of CD4 count (R^2=10.2 % predicted significantly and independently increasing values of PWV in HIV positives on HAART. PWV t was highest in the HIV positives not on HAART (Treatment naive).

Conclusion: Disproportionate rates of increased arterial stiffness, cardiometabolic risk, age, and low CD4 count are associated with HIV positives in these black South Africans.

Keywords: Arterial stiffness; Pulse wave velocity; HIV; Antiretroviral treatment

Introduction

South Africa had an estimated 6.3 million people living with human immuno deficiency virus (HIV) in the year 2013, the highest of any country in the world [1]. Highly active antiretroviral therapy (HAART) has however, greatly reduced early deaths and increased lifespan of people infected with HIV. Highly active antiretroviral therapy has significantly improved the prognosis for many individuals with HIV infection. Consequently, HIV infection has become a chronic and manageable disease. The focus on long-term management of patients with HIV infection has broadened to include comorbid conditions, most notably cardiovascular disease. Patients with HIV infection share many cardiovascular risk factors with the general population, and HIV infection itself may increase cardiovascular risk [2]. Changes in lipid profiles associated with increased cardiovascular risk that have been observed with some HAART regimens have been a cause for concern among clinicians who treat HIV-infected patients [3].

Lipid abnormalities are common in HIV-infected patients who are receiving HAART. Although the implications of dyslipidemia in this patient population are not fully understood. An increasing amount of data suggests that lipid abnormalities are associated with cardiovascular morbidity and mortality [4]. These epidemiologic observations have prompted increased awareness of the need for risk assessment and modification for cardiovascular disease as an integral part of routine HIV care.

There is very limited published data on the cardiovascular consequences of the HIV epidemic in the African but some researchers have found HIV itself increasing cardiovascular risks [5-8]. Potential contributory factors to cardiovascular complications in the HIV patient include, virus-induced endothelial injury and antiretroviral drug induced toxicity [2,9]. It is not clear if arterial stiffness is due to HIV, HAART or traditional risk factors like hypertension, lipidemia and smoking [9,10].

Traditional and nontraditional risk factors may contribute to atherosclerotic disease in HIV-infected patients [11-13]. Although the association of HIV infection and HAART with metabolic cardiovascular (CV) risk factors has been studied extensively, limited information is available on the association of this condition with central blood pressure (BP) alterations, which are more important than peripheral BP alterations [14].

Information is scant and contradictory on whether HIV infection and HAART are associated with a reduction in large artery distensibility [8-13]. HIV infected subjects present an unfavorable cardiovascular risk profile that is determined by the infection itself,

highly active anti-retroviral therapy (HAART) and other factors, such as chronic kidney disease (CKD) [9-12].

There is also contradiction on whether these factors are associated with arterial stiffness and blood pressure (BP) alteration [14-17].

Observational studies of CVD outcomes and studies using carotid intima-media thickness suggest that there is a moderate increase in cardiovascular disease risk related to HIV sero-status [1]. Less can be said about the role of HAART and specific HAART therapies in CVD risk, mainly because imaging studies have had serious methodological limitations that diminish their general application [18]. In our setting, the first line HAART used in public hospitals comprises nucleosides and non-nucleoside analogues (Lamivudine, Efavirenz and Stavudine). In this communication, we assessed arterial wall stiffness measured as carotid pulse wave velocity and its associated factors in 3 groups of persons: HIV positive not on HAART, HIV positive on HAART and HIV negative.

Furthermore, the optimal cut off-points of PWV and its contributing cardiometabolic markers for treatment naïve HIV positives, and HIV positives on HAART in the general population are not known in South Africa. The present study will impact on clinical management and public health perspectives of subclinical atherosclerosis in South Africa. The initiation of this study, therefore, justifies further evidence-based knowledge on PWV and management of emerging atherosclerosis in South Africa with the highest prevalence of HIV infection [1]. We hypothesized that disadvantaged black Xhosa South Africans in general are more susceptible to the burden of cardiometabolic risk factors and complications. These complications ectopic fat deposition, high blood pressure, HIV per se and HIV related HAART that may exacerbate and accelerate independently early onset of elevated PWV (arterial stiffness: subclinical atherosclerosis). Paradoxes in terms of neutral, deleterious, and beneficial effects may be associated with HIV related HAART and the HI virus itself. Moreover, the novel vascular risk factors identified in HIV-related atherosclerosis, such as chronic inflammation, immune activation, and some antiretroviral agents, are not taken into account in the available risk scores, leading to underestimation of cardiovascular risk in the HIV population [16].

Thus, the aim of this study was to evaluate vascular effects of HIV disease and HIV treatment and to analyse contributing anthropometric, hemodynamic, immunity, and lipoid factors of elevated PWV in negatives, HIV positives, and HIV positives on ART.

Methods

Ethical approval

This was obtained from the Ethics Committee, Faculty of Health Sciences, Walter Sisulu University with ethical clearance certificate number 0043/009. Translated questionnaires were administered to the participants by someone who spoke fluent Xhosa. All participants granted consent.

Study design

This was a descriptive and analytical cross sectional study which was conducted from July 2012 to June 2013. A convenient sampling method was used was used to determine the sample size. There was insufficient information from literature for the sample size (Ni) calculation.

The dichotomous outcome with up to a frequency (p) of 0.05 (5%), is usually one of the best ways to increase power. The general formula for p (expected proportion), the desired total (W) of the confidence level and the confidence interval of (1-α), was as follows:

Zα=the standard normal deviate for a two sided α, where (1-α) is the confidence level of 95% since α=0.05, Zα=1.95;

Then the total number of participants was $Ni=4 \times (Z\alpha)^2 \times P \times (1-P)/W^2$;

$Ni=4 \times (1.96)^2 \times 0.50 \times 0.50/(0.15)^2$;

Ni=3.84/0.0225;

Ni=171 participants are therefore required for evaluation.

Study population

The HIV participants were recruited from the Infectious Disease, Stamford Terrace and Ngagalizwe clinics in Mthatha, Eastern Cape Province of South Africa. Inclusion criteria for subjects included antiretroviral therapy for ≥ 6 months or newly diagnosed HIV positive patients not on antiretroviral therapy. HIV infection was diagnosed using a licensed ELISA test kit and confirmed by a second method. Persons who were HIV negative that was attended to at Stamford terrace and Gateway clinics for various minor ailments were recruited as controls. Controls also included students and staff of Walter Sisulu University Campus in Mthatha.

Specific exclusion criteria in HIV positive subjects: These included not being on first line HAART, HAART for less than 6 months with detectable viraemia and recent life threatening opportunistic infections.

Non-specific exclusion criteria in HIV and non-HIV participants: use of slidenafil or other phosphodiesterase IV inhibitor within 12 hours of the vascular (Sphygmocor) studies, history of liver disease, inability to provide informed consent, pregnant and breastfeeding women, those not willing to fast overnight.

Grouping of participants: Participants were categorized as Groups A, B and C as follows: Group A, HIV Negative, Group B: HIV posititve not on treatment, Group C: HIV positive on treatment.

Anthropometric measurements

Height was measured using the harpenden stadiometer (Holtain Ltd, Crymych, Dyfed, United Kingdom). The measurement was to the nearest 0.1 cm. Average of two readings were taken. Weight was measured by the participant standing bare feet on the center of the scale wearing only minimal clothing. Weight was read to the nearest 100 g (0.1 kg). The average of two weights was taken. Body mass index (BMI) was calculated using the following formula. Weight (in Kilograms) divided by height (in meters) squared $(Wt (kg)/(Ht (m)^2)$. Waist circumference was measured in cm at a level midway between the lower rib margin and iliac crest using a non-elastic tape around the body in horizontal position. Hip circumference was measured as the maximum circumference over the buttocks in cm.

Blood pressure measurements

Blood pressure was measured using the omron sphygmomanometer (Omron, Guangdong, China). Three supine blood pressure measurements were taken 1 min apart after 10 min rest, and the average of these readings was used in the analysis.

Measurement of carotid aterial pulse wave velocity

This was measured using the sphygmocor Vx system (SphygmoCor Vx version 7.01 software Atcor Medical, Sydney, Australia). The Sphygmocor Vx system provides the following quantitave aortic cardiovascular variables: systolic pressure, diastolic pressure, pulse pressure, augmentation pressure, pulse wave analysis and pulse wave velocity. The carotid femoral velocity was evaluated.

To perform a sphygmocor control measurement of the pulse wave velocity, the participants were placed supine with limbs cleaned using alcohol swab. Electrodes were placed on the participant's wrists and on the left leg. Carotid artery measurements were made with the participant's head tilted slightly to the back and to one side. The position of the strongest pulse was felt with the index finger and the tonometer placed directly on top of the skin at the base of neck. Femoral artery measurements involved the femoral pulse being felt and pressing directly using the probe backward at a point midway between the anterior superior iliac spine and the front of the pubic bone, with the thigh slightly flexed at the hip joint and slightly rotated laterally. The distance traveled by the pulse wave was measured over the surface of the body with a tape measure. PWV was calculated as the distance: transit time ratio and expressed as meters per second. This was also recorded automatically on the sphygmocor machine).

Laboratory investigations

After an overnight fast, 20 ml of blood was collected. This was divided into aliquots using plain tubes. These were centrifuged at 3000 rpm for five minutes. Serum was stored in aliquots at-80°C until analyzed.

Serum lipid profile assay

Total serum cholesterol was by the cholesterol oxidase phenol aminoantipyrine peroxidase method (CHOP-PAP) method (Enzymatic colorimetric determination of serum cholesterol). For the estimation of triglycerides peridochrom triglycerides GPO-PAP method was used. CHOD-PAP method (cat No. 543004, Boehringer Mannheim; Mannheim, Germany) was used to measure HDL. LDL was calculated from the values of Total cholesterol, Triglycerides and HDL. LDL cholesterol for each sample was calculated according to friedewalds formula: LDL cholesterol in mmol/l=total cholesterol-triglycerides-HDL cholesterol/5. Some specimens were also sent to the NLHS laboratoty for confirmation. The method used in the laboratory was the Cobas system by (Roche /Hitachi)

Statistical analysis and operational definitions

Quantitative variables in the text were expressed as means ± SD while categorical variables were expressed as proprtions. Means of quantitative variables were compared using ANOVA while categorical variables were assessed with Chi square test. Multiple comparisons of means were computed using post hoc bonferroni test. Mode of PWV ≥ 6.5 m/s was considered elevated arterial stiffness. Receiver operating curve method for both sexes, was used to define aging ≥ 40 yers, elevated WC (≥ 90 cm), low CD4 count<500 cells/mm3, elevated TC ≥ 4.3 mmol/L, wide HC ≥ 97 cm). IDF criteria 7 were used to define high SBP ≥ 130 mmHg, high DBP ≥ 85 mmHg, and elevated TG ≥ 1.7 mmol. Overweight-obesity was defined by BMI ≥ 25 kg/m² according to WHO criteria. Multiple linear regression analysis served to predict variability (adjusted R2) of continuous PWV (dependent variable) with its independent contributing continuous variables in all and in each group. Multivariate logistic regression models were used to determine the independent determinants of elevated arterial pulse wave velocity in HIV negative, HAART naïve HIV positive patients and HIV positive patients on treatment. P values<0.05 defined statistical significance. All analyses were performed using the statistical package SPSS version 19, Chicago, Illinois. P values<0.05 defined statistical significance.

Results

In total, 169 participants (63 HIV negatives, 54 HIV positives not on ART, 52 HIV positives on ART, 62 males and 107 females with sex ratio of 1.1 Woman:1 Nan) were examined. Figure 1 presents significant and inequal variations of mean values of PWV across different study groups: highest PWV=7.2 ± 2.2 m/s was in HIV positives not on HAART in the study (ANOVA, P=0.037), HIV positives on treatment (PWV=6.8 ± 1.2 m/s) and HIV negatives (PWV=6.4 ± 1.7 m/s). (Post hoc bonferroni test<0.05 two by two).
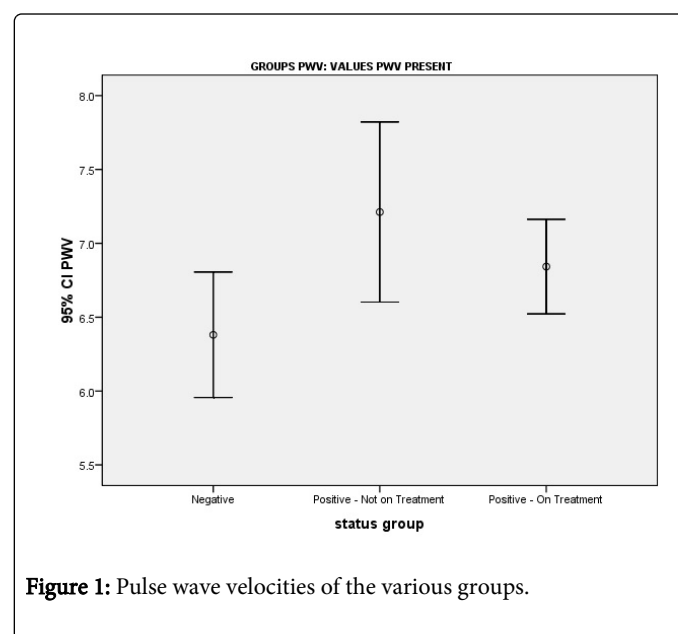

Figure 1: Pulse wave velocities of the various groups.

Out of all participants, 68.5%, 42.7%, 50.6%, 41.6%, 39.3%, 53.9%, 72.5%, 32.6%, 59.6%, and 44.4% were defined by elevated PWV, aging, wide WC, , high SBP, high DBP, elevated TG, wide HC, elevated TC, low CD4 count, and overweight-obesity, respectvely.

In all the participants, there was a significant univariate association between HIV status (82.1% n=46 HIV positives not on ART, 72.2% HIV positives on ART, and 54.4%; P=0.003), aging (82.9% aged ≥ 40 years vs. 57.8% n=59 aged<40 years, OR=3.5; 95% CI 1.7-7.2; P<0.0001), high SBP(79.7% SBP ≥ 130 mmHg vs. 60.6% , OR=2.6; 95% CI 1.3-5.1; P=0.007), elevated TG(87.5% n=84 TG>1.7 mmol/l vs. 46.3% , OR=8.1; 95% CI 3.9-17.1; P<0.0001), wide HC(76.7% vs. 46.9% , OR=3.7; 95% 1.9-7.5; P<0.0001), wide WC(76.7% WC ≥ 90cm vs. 60.2% WC<90 am, OR=2.2; 95% CI 1.1-4.2; P=0.018), and elevated PWV.

From multivariate logistic regression in all the participants, elevated PWV was significantly and independently predicted by age (adjusted OR=6.8; 95% CI 2.8-16.6; P<0.0001), high SBP (adjusted OR=2.4; 95% CI 1.1-5.3; P=0.035), and wide HC (adjusted OR=5.7; 95% CI 2.4-13.4; P<0.0001) after adjusting for high TG and wide WC.

In HIV positives not on HAART

After adjusting for sex, aging, WC, SBP, TG, and low CD4 count using multivariate logistic regression, only HC (adjusted OR=8.5; 95% CI 1.6-46; P=0.013) was significantly and independently associated with elevated PWV.

In HIV positives on HAART using multiple logistic regression analysis and after adjusting for WC, SBP, TG, HC, TC, sex, and CD4 only aging (adjusted OR=25.8; 95% CI 2.6-26; P=0.006) was significantly and independently associated with elevated PWV.

However applying multiple linear regression analysis, and using continuous variables, after adjusting for confounders (WC, TG, HC. And TC), increase in SBP (R2=29.6%) (Figure 2), aging (R2=9.2%) 3), and decline of CD4 count (R2=10.2% (Figures 2-4) predicted significantly and independently increasing Values of PWV in HIV positives on ART.
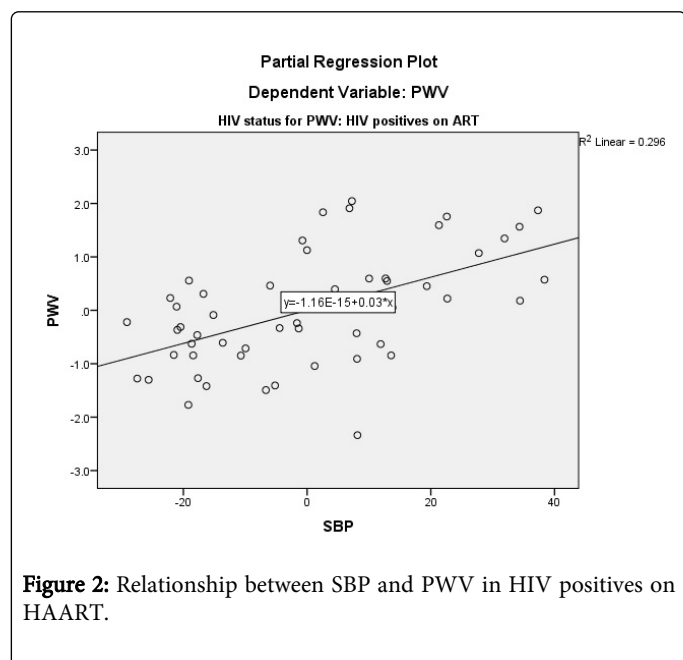

Figure 2: Relationship between SBP and PWV in HIV positives on HAART.

Lipid profiles

Table 1 shows increased levels of TC, and HDL cholesterol in HIV positive patients on treatment than the other groups. The levels of serum LDL cholesterol and triglycerides were similar across all groups.

Correlations of age, anthropometric parameters and smoking with pulse wave velocity.

Table 2 shows that HIV negative participants had a significant positive correlation between age, number of cigarettes, weight, waist circumference and PWV (P<0.05). In HIV positive not on HAART there was a significant positive correlation between weight, waist and PWV (P<0.05). HIV positive participants on HAART showed significant positive correlations between age, WHR and PWV, and a negative correlation between height and PWV.

Correlations between haemodynamic data and PWV. Table 2 also showed that there was a correlation between the haemodynamic data except for the heart rate. In all the three groups there was no positive correlation between the pulse wave velocity and diastolic blood pressure in the HIV patients.

Lipid correlates of PWV

Table 2 shows that only total cholesterol in HIV negative and triglycerides in HIV positive not on HAART were significantly and positively correlated with PWV (P<0.05), whereas the other lipid parameters were not significantly (P>0.05) correlated with PWV in each study group (Table 2).

Multivariate analysis (not shown)

Identifies Spa, age and triglycerides as the only independent and significant determinants of PWV among HIV negatives whilst MP as the only significant independent determinant of PWV in HIV positive participants not on treatment. Age, MP, HDL-C Age, MP, HDL-C, and triglycerides were identified as the significant independent determinants of the variations of PWV in HIV positive participants on HAART.

Variables	HIV negative (n=63)	HIV positive		P-value
		No treatment (n=54)	On treatment (n=52)	
PWV m/sec	6.38 ± 1.67	7.21 ± 2.17	6.84 ± 1.17	0.037
Age in years	35.9 ± 11.2	36.25 ± 10.785	40.21 ± 9.554	0.182
Weight (Kg)	71.35 ± 15.45	71.31 ± 19.64	68.50 ± 13.72	0.583
Height (cm)	164.77 ± 8.40	162.87 ± 7.61	162.72 ± 8.03	0.322
Waist (cm)	85.43 ± 15.32	85.84 ± 21.41	90.39 ± 10.58	0.209
Hip.circum (cm)	105.44 ± 14.02	102.12 ± 13.94	103.69 ± 10.30	0.439
BMI (Kg/m^2)	33.10 ± 38.57	26.38 ± 5.80	25.78 ± 4.79	0.17
Waist hip ratio (%)	0.83 ± 0.09	0.80 ± 0.19	0.88 ± 0.21	0.13
Spa (mmHg)	110.60 ± 14.90	115.41 ± 14.72	111.63 ± 18.06	0.257

Dpa (mmHg)	80.21 ± 9.88	83.75 ± 9.90	84.80 ± 12.62	0.053
MP (mmHg)	92.76 ± 15.34	98.22 ± 11.25	97.33 ± 12.62	0.063
Ppa (mmHg)	30.39 ± 8.79	31.69 ± 10.06	28.09 ± 10.49	0.162
Sbp (mm/Hg)	121.25 ± 14.52	123.40 ± 21.99	126.44 ± 17.83	0.312
Dbp (mm/Hg)	79.72 ± 9.57	82.88 ± 12.05	84.63 ± 11.60	0.059
PBP (mmHg)	75.43 ± 11.88	77.29 ± 18.27	79.33 ± 18.69	0.458
HR (b/min)	67.58 ± 9.50	73.31 ± 11.54	72.83 ± 14.40	0.017
HDL-C (mmol/l)	1.39 ± 0.42	1.14 ± 0.34	1.56 ± 0.74	0.002
TC (mmol/l)	4.23 ± 1.09	3.64 ± 1.14	4.38 ± 0.96	0.005
TG (mmol/l)	0.97 ± 0.40	1.06 ± 0.46	1.19 ± 0.51	0.092
LDL-C (mmol/l)	2.40 ± 1.16	2.50 ± 2.76	2.34 ± 0.90	0.919
CD4	924.67 ± 316.6	307 ± 434	40.21 ± 95.54	<0.000

Spa: Aortic Systolic Pressure; Dpa: Aortic Diastolic Pressure; MP: Mean Aortic Pressure (aortic); Dpb: Brachial Pressure; PBP: Pulse Brachial Pressure; Sbp: Brachial Systolic Pressure; TC: Total Cholesterol; TG: Total Glycerides; HDL: High Density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; CD4: Cluster of Differentiation 4 Expressed on the Surface of T-Helper Cells

Table 1: Comparisons of mean levels of age, anthropometric and haemodynamic variables according to HIV status groups.

Variables	HIV negative		HIV positive			
			Not on treatment		On treatment	
	r	P-value	r	P-value	r	P-value
Age (years)	0.606	<0.000	0.269	0.057	0.641	<0.000
HC (cm)	0.086	0.512	0.012	0.389	0.033	0.816
BMI (Kg/m^2)	0.164	0.202	0.195	0.229	0.069	0.629
Weight (kg)	0.123	0.003	0.439	0.004	0.096	0.495
WHR (%)	0.479	0.585	0.211	0.345	0.319	0.037
Cigarettes (smk/day)	0.071	0.015	0.094	0.439	0.024	0.866
Waist (cm)	0.252	0.05	0.406	0.008	0.185	0.185
HR (b/min)	0.075	0.561	0.212	0.173	0.057	0.693
Ppa (mmHg)	0.472	<0.000	0.338	0.012	0.338	0.012
MP (mmHg)	0.446	<0.000	0.515	<0.000	0.4	0.003
Spa (mmHg)	0.635	<0.000	0.369	0.012	0.369	0.006
Dbp (mmHg)	0.436	<0.000	0.114	0.423	0.114	0.413
TC (mmol/l)	0.148	0.339	0.004	0.999	0.37	0.019
TG (mmol/l)	0.233	0.119	0.028	0.861	0.49	0.002
HDL-C (mol/l)	0.106	0.501	-0.124	0.143	0.239	0.143
LDL-C (mmol/l)	0.136	0.384	0.006	0.971	0.229	0.166

Table 2: Correlations of age, anthropometry, lipid profile, haemodynamic parameters and smoking with PWV in the study groups.

Discussion

In this study, participants who were HIV positive on treatment and HAART naive participants had significantly increased pulse wave velocity than those who were HIV seronegative (p=0.037) (Table1).

The results of this study are in accordance with a previous study that found increased arterial stiffness in patients with HIV infection compared with healthy controls [16]. Asymptomatic patients with human immunodeficiency virus (HIV) infection are at increased risk of vascular disease [16]. One postulated mechanism for increased pulse wave velocity in HIV is systemic chronic inflammation [19,20]. A recent study which assessed arterial stiffness using radial artery tonometry in 276 HIV-infected and 67 HIV-uninfected Rwandan women reported that HIV infection was associated with increased arterial wave reflection in females with limited exposure to HAART and without other CVD risk factors [21]. This is not very different from this study in which the PWV is highest in the HAART naïve participants. It shows increased arterial stiffness in the arteries of HAART naïve participants compared to those on treatment. Our study showed that PWV 6.5 m/sec is a cut off number for South Africans blacks. This means above this value the pulse wave velocity is on the high side of normal and physicians should be cautious. In all participants, HIV positives not on HAART, HIV positive on HAART, age ≥ 40 years, systolic blood pressure ≥ 130 mmHg, and hip circumference (HC) ≥ 97 cm were significantly and independently associated with elevated PWV ≥ 6.5 m/s (68.5%).

The stiffness of the vascular wall is dependent on the relative contribution of collagen and elastin [21]. An overproduction of abnormal collagen and diminished quantities of normal elastin may contribute to vascular stiffness [21]. We speculate that the HIV induced inflammation and increased production of collagen might have caused diminished quantities of normal elastin and not being treated may lead to arterial stiffness in the treatment naïve HIV participants, hence the increased PWV in our participants. This will be particularly evident in the aging population.

In general, the findings of studies using carotid ultrasound, coronary computed tomographic angiography, and aortic positron emission tomography agree with those from observational studies of cardiovascular disease (CVD) events and suggest that HIV infection is associated with an increased risk of CVD [22]. In a study, asymptomatic HIV patients present a similar burden of coronary stenosis and calcified coronary artery plaques but significantly higher rates of non-calcific coronary plaques at computed tomography [23]. With the highest level of PWV in the treatment naive HIV positives (Figure 2) it also explains that the HI virus itself contributes to arterial stiffening.

The elevated levels of aortic (central) pulse pressure (Ppa), aortic systolic pressure (Spa) and aortic mean pressure (MP) in the HAART naive HIV subjects may be related to HIV induced inflammation resulting in structural abnormalities to the elastin and collagen fibers of the blood vessels. While Spa, age, and triglycerides were significant independent determinants of PWV in HIV negatives persons, MP was also a significant independent determinant of PWV in HAART naïve and treated HIV positive participants in our study (Figures 3 and 4).

Elevated heart rate was observed in HIV positive participants compared to HIV negative participants. Chronically elevated heart rate may increase large artery stiffness by accelerating elastin breakdown in the arterial wall [24]. In paced animal models, increased heart rate was shown to increase stiffness of large elastic arteries while

having a variable effect on muscular arteries [24]. It could also be that the HIV participants had increased heart rate from sympathetic overdrive due to inflammation induced arterial stiffness [6].
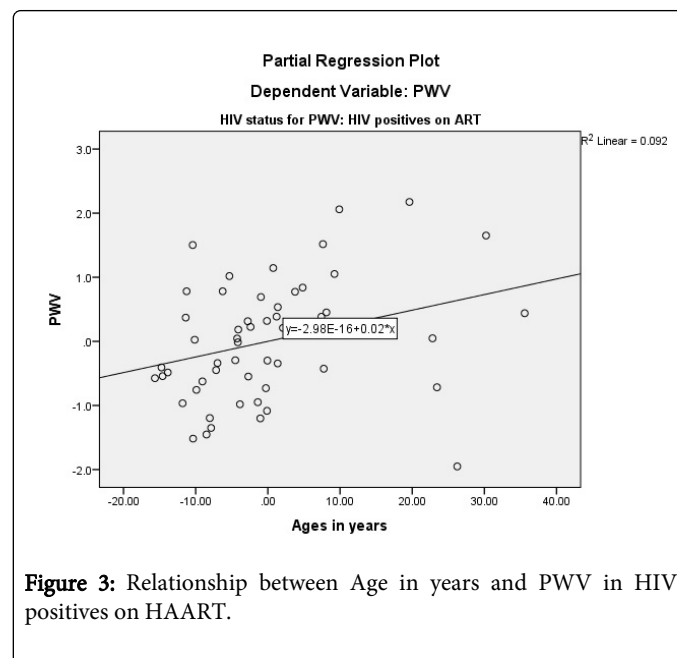

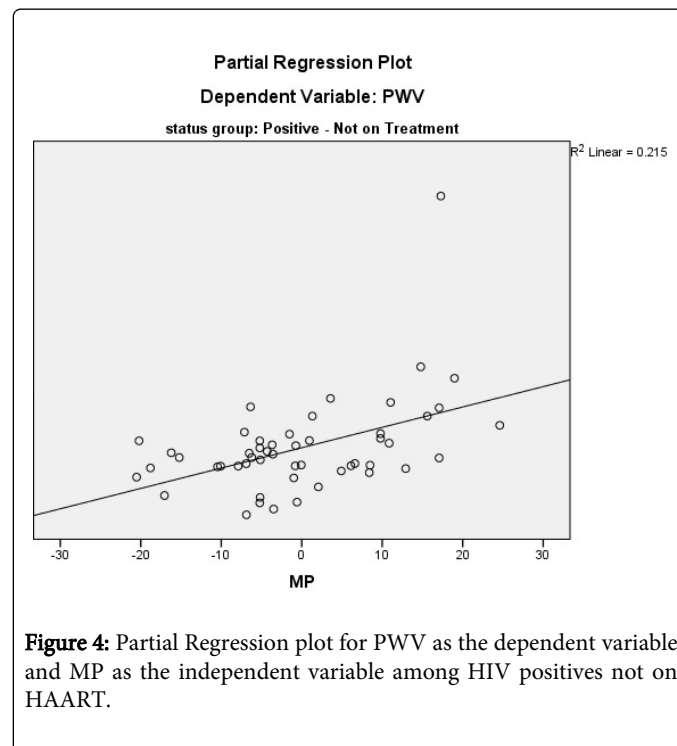**Figure 3:** Relationship between Age in years and PWV in HIV positives on HAART.

Figure 4: Partial Regression plot for PWV as the dependent variable and MP as the independent variable among HIV positives not on HAART.

Many infections are implicated in lipid metabolism abnormalities and increased risk of coronary heart disease [6]. Grunfeld [25] found that HIV infection was associated with elevated triglyceride levels that worsened with progression of HIV-related disease. HIV itself has been shown to increase lipogenesis in the liver and to alter lipid profile [25] HIV-1 infection causes a specific pattern of dyslipidemia, resulting from a combination of increased production and decreased clearance of lipoproteins. The virus may also directly impair HDL metabolism,

thus enhancing transfer of HDL to atherogenic apolipoprotein B lipoproteins [26].

This potential mechanism is consistent with findings in the SMART trial analysis indicating an association of total HDL particles with risk of CVD in patients in the drug-conservation group. In particular, risk was elevated in patients with declining HDL cholesterol levels after stopping non-nucleoside reverse transcriptase inhibitor (NNRTI) treatment. HDL-C can also be regarded as anti-inflammatory but further research needs to be done to confirm this. Many infectious agents including HIV-1 have profound impact on adipocytes which become dysfunctional and cannot store most lipids that is, triglycerides properly [27]. The above factors might also explain the elevated levels of triglycerides and cholesterol found in the HIV positive participants in this study. Multivariate analysis also shows HDL-C as a determinant of arterial stiffness.

One strength of this study is that arterial stiffness was assessed by carotid pulse wave velocity (PWV) which is recognized as the gold standard [28]. Carotid-femoral PWV has been used in epidemiological studies demonstrating the predictive value of aortic stiffness for CV event [28]. Pulse wave velocity (PWV) is considered a non-invasive diagnostic test for subclinical atherosclerosis (SA) or arterial stiffness. PWV is a predictor of cardiovascular risk and a surrogate marker of vascular disease [23]. Alterations in arterial stiffness are known to precede clinical hypertension by a substantial period of time and increased arterial stiffness has been linked to a higher rate of future cardiovascular complications and death [28-33].

Limitation

This is a cross sectional study and the values might change if they were followed up.

Females were more in the two HIV positive groups. This may be because most attendees in our public hospitals were females and therefore most willing participants were females. There was a high dropped out because of financial reasons, diet, and non-compliance and leaving their homes to search for jobs.

Perspectives

One should be able to evolve potential mechanism for evaluating the effects of antioxidants and anti-inflammatory agents in HIV and HAART-related endothelial dysfunction. It will be of value if a network of multidisciplinary, clinical research sites with the capability for detailed study of cardiovascular/metabolic complications of HIV disease and its treatments are established in sub Saharan Africa. The use of statins may be introduced after a PWV of 7 meters/sec. Aspirin may also be considered.

Conclusion

This study shows that HIV infection and HAART increase arterial stiffness. The use of NNRTI and NRTI to treat the HIV patients may increase the risk of cardiovascular disease as indicated by the increases in triglyceride levels and HDL. Raised MP is a good indicator of arterial stiffness.. Life style modification should be incorporated into the management of HIV patients so as the continuous monitoring of their haematological and lipid profile.

Conflict of Interest

There is no conflict of interest.

Acknowledgement

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