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Relationship between Vasoactive Agents and Body Composition in HIV patients, Mthatha, South Africa

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Abstract

Background: Obesity increase risk of cardiovascular diseases and renal function disorders. Few studies have examined the physiological effects of the endothelin and NO activity in association to blood pressure and body composition. Therefore the aim of the study was to evaluate the physiological effects of HIV infection, blood pressure and body composition on the changes of endothelin and nitric oxide and association between endothelin and nitric oxide.

Methods: This was a descriptive and comparative study. The study population consisted of 154 participants categorized into the following groups: 57 HIV (-) participants, 40 HIV (+) not on treatment participants and 57 HIV (+) on treatment participants. Enzyme immunoassay and Nitrate/nitrite colorimetric assay kit was used for the quantitative determination of ET-1 and NO. All anthropometric measurements were also taken into account.

Results: Endothelin and Nitric oxide both presented significant (P<0.005) values during the interaction between HIV status and BMI. Interaction of blood pressure and Body Mass Index across the HIV status groups, there was significant (P<0.005) variation of mean values for SBP, DBP, PP to both HIV status groups and BMI. There was also a significant association in all variables presented age, weight, BMI, SBP, DBP, PP and endothelin, respectively.

Conclusion: The study showed that there is an uneven relationship between endothelin, nitric oxide levels and also these two are associated with overweight/ obesity, blood pressure. The findings revile that the positive relationship was lost in both HIV positives groups, possibly due to changes in the endothelium, HIV itself and HIV treatment.

Keywords: HIV-infection, Highly active antiretroviral therapy, Body mass index (BMI), Endothelin-1 (ET-1), nitric oxide (NO), Blood pressures (BPs)

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Introduction

Body composition is divided into two separate types of mass: fatfree mass which is comprised of all of the body's non-fat tissues and body fat. Fat-free mass includes bone, water, muscle, and tissues. Body fat is literally fat located within the body. Certain percentage in overall lipid profile helps to protect internal organs, provides energy and regulates hormones that perform various functions in body regulation. However, when someone is overweight or obese, they have an excessive accumulation of body fat. Body fat includes essential fats, such as lipids, and nonessential body fats; these fats make up around five percent of total body weight for men, and up to 12 percent for women. Nonessential fat is found mainly within fat cells and adipose tissue, below the skin and surrounding major organs. The levels of excess fat stored in the body can be determined based on factors such as age, gender and diet. Excess nonessential fat can normally be attributed to consuming more food energy than what is burned through metabolic functions and activity. Body fat percentage is described as a percentage of total body weight that is comprised of fat. A higher percentage of body fat has a negative effect on the cardiovascular system. Excess fat has been linked to numerous health problems such as increased risk for diseases

such as cancer, diabetes and heart disease. Excess fat, specifically around the internal organs, reduces their function and contribute to serious medical conditions such as liver disease [1]. Assessing body mass index (BMI) is a commonly-used method of measuring body fat. While BMI does not measure body fat directly, it helps to assess health risks related to body mass. Ways to assess your body composition, and body fat percentage, more directly include measurement with callipers and tests such as underwater body fat test, the BodPod, DEXA Scan, and Bioletrical Impedence [1]. Excess weight is said to increase risk of high blood pressure, high triglyceride levels, or blood fats, and high cholesterol [2]. High visceral fat, which accumulates around waist, is a specific risk indicating possible inflammation through blood vessels. Obesity further contributes to risk of renal function disorders that alter how body registers blood pressure [3]. The capillaries in tissues may experience wall stress and become unable to release oxygen to cells in order to make energy and relinquish waste products [4]. A BMI that is significantly underweight has implications for risk of athero thrombotic cardiovascular disease. This includes carotid artery insufficiency, transient, ischemic attacks, which are like miniature strokes, and circulatory problems [4]. Currently, few studies exist that have examined the physiological effects of the endothelin and NO activity in association to blood pressure and body composition. However, as mentioned previously endothelin has been associated with hypertension and obesity because of its vasoconstrictor activities [5]. It has been demonstrated that overweight and obesity are associated with enhanced ET-1-mediated vasoconstriction that contributes to endothelial vasodilator dysfunction and may play a role in the increased prevalence of hypertension with increased adiposity [6]. Mather's results suggested that obesity per se is associated with enhanced ETA-mediated vasoconstrictor tone in the leg circulatory bed and that blockade of ETA receptors reverses endothelial dysfunction in these patients. Blood pressure values in their group of obese patients were significantly higher than those of control subjects, which clearly showed that ET-1 in obesity is independent of blood pressure levels [7]. In previous studies it was also mentioned that atherogenic properties of ET-1 [8] may play a role in the development of the atherosclerotic vascular disease in obese hypertensive subjects. Similarly, it was stated that ET-1 may be involved in other complications of hypertension in obesity, such as cardiac remodelling and heart failure [9] or renal damage [10]. Current research has mentioned that excess basal ET-1 constrictor tone in peripheral vessels has been described in obese and diabetic subjects compared with that seen in lean subjects [7,11]. The aim of the study was to evaluate the physiological effects of HIV infection, blood pressure and body composition on the changes of endothelin and nitric oxide (NO) and association between endothelin and nitric oxide.

- 1) To compare endothelin and nitric oxide between HIV groups using univariate and multivariate analysis;
- 2) To determine the association between gender, blood pressure, body composition and endothelin in each group (univariate and multivariate analysis);
- 3) To determine the association between gender blood pressure,

body composition and nitric oxide in each group (univariate and multivariate analysis);

The findings of the present study will assist health professionals to prevent early events on hypertension, the pathogenesis of atherosclerosis, endothelial dysfunction and arterial changes. They will also serve as an excellent marker for cardiovascular and inflammatory diseases in HIV patients, in Mthatha district.

Materials and Methods

This was a descriptive and comparative study. Participants were recruited from Clinics (Gateway and Infectious disease clinic), Nelson Mandela Academic Hospital (NMAH) in KSD Municipality, Eastern Cape Province, South Africa. This study was conducted in a random manner, planned to convenience population according to inclusion and exclusion criteria and the expected sample size was 180 participants of different sex groups and 154 participants completed the study. The purpose of the study was explained orally and in writing to obtain consent from recruited participants. HIV patients were considered eligible for inclusion in the study if at the time of data collection they accept to participate in the study by filling in questionnaire and signing consent form. They were informed that they may refuse to participate or withdraw from the study at any time without fear of victimization. Participants were assured of total confidentiality and that there will be no information that identified them in any manner. They were informed that the information will only be utilized for the purposes as stipulated and all possible steps will be taken to ensure that the information remained confidential. The age range of participants was between 20-50 years old, female and males of equal ratio. Excluded from participation were individuals who were under treatment for hypertension, had used ant diabetic agents, steroids, growth hormone, oral contraceptives pills, or any anabolic agent, substance abuse, appetite suppressor, pregnant, or had breast-fed in the past year, who have or who had an acute infection within 3 months of the study. The study population was consisting of 154 participants categorized into the following groups: 57 HIV positive participants (A), 40 HIV positive on HAART participants (B) and 57 HIV negative participants (C) (controls). Questionnaires and consent forms were issued to the participants. Body composition indices were measured using anthropometry, bioelectric impedance analysis (BIA) and also by the use of medical equations. The measurements of weight were performed before the use of bioelectric impedance analysis. Height was taken to the nearest 1 cm with the aid of Electronic body scale for weight and height (model: TCS-200-RT, China) with patients wearing light clothes without shoes. Weight (kg), body mass index (BMI in kg/m2), body fat (%), visceral fat levels (%), resting metabolism rate (calorie expenditure of resting body) all were automatically obtained using Omron body composition monitor BF 500 (Omron, Tokyo ,Japan). The body 4-sensor measurement technology uses both hands and feet, it requires age, gender, and height of the participant, the information was entered into the machine before it delivers the output. The machine was utilizes both upper body and lower body analysis and provided full Body Sensing in calculating Body Fat and body composition characteristics. 20 millilitres of venous blood was drawn at 08:00 am before breakfast after 8-12 h fast. Fasting blood serum was collected in tubes containing 50 mmol of EDTA as an anticoagulant. Blood serum was centrifuged for 15 min at 1000 x g within 30 min of collection. Samples were stored at -80°C refrigerator in the fridge at Walter Sisulu University department of physiology until the time for analysis. Data were analysed by using the Statistical Package for the Social Sciences (SPSS) Version 19.0 for Windows (SPSS, Chicago, USA). Multiday analysis of variance (MANOVA) and covariance (ANCOVA) were used to explore the association between blood pressure groups, body composition and age, and gender. In addition, these statistics were used to explore the effect of the study variables on the log-transformed hormone levels of ET-1, and NO. Turkey's multiple comparison post-hoc analysis was subsequently used. Descriptive statistics and Comparison study was used to calculate mean ± SD of all variables. Correlation analysis will also be used to look for the degree of correlation between ET-1, NO levels, body composition and arterial blood pressure. A P-value of <0.05 was considered significant. The Ethical approval was obtained from the Ethics Committee, Faculty of Health Science, Walter Sisulu University for ethical and bio-safety clearance, protocol number: 023/2012.

Results

The HIV positive participants on treatment and HIV negative are presented with the same percentile level, mean value is 37.01% on both. HIV negative participants had a small percentage value of 25.97%. This clearly illustrates the fact that this study had a large number of participants. Endothelin presented significant (P<0.005) values during the interaction between HIV status and BMI. In HIV positive participant on treatment with overweight (BMI), normal (BMI) and Obesity (BMI) showed high levels of mean values of endothelin compared to the rest of the groups. However, HIV positive not on HAART also illustrates high levels of endothelin but not excessive across the BMI groups (Table 1). Nitric oxide (NO) presented significant (P<0.005) values during the interaction between HIV status and BMI. In HIV positive participant on treatment and HIV positive participant not on treatment showed high levels on mean values of NO across BMI groups. However, HIV negative participants had low levels on mean values of NO across BMI groups (Table 2). Interaction of blood pressure and Body Mass Index across the HIV status groups, there was significant (P<0.005) variation of mean values for SBP, DBP, PP to both HIV status groups and BMI. SBP on HIV positive participants on treatment who are underweight seemed to be high. However, all other pressures are in normal range to HIV status and BMI (Table 3, Figure 1). Table 4 presents associated factors attributed by the presence of arterial hypertension in few participants (n=54). There was no significant variation of mean values of nitric oxide. However, there was significant association in all variables presented age, weight, BMI, SBP, DBP, PP and endothelin, respectively.

Discussion

In the present study, there was a large percentage of female participants emphasizing the fact that in South Africa, females

Table 1 Variations of mean levels on endothelin, across the groups of interaction of HIV status and BMI in all.

Variables of Interest	Underweight Mean ± SD	Normal Mean ± SD	Overweight Mean ± SD	Obesity Mean ± SD
HIV on HAART				
Endothelin	7.8 ± 2.0	10 ± 4.1	10 ± 4.1	8.8 ± 2.7
HIV not on HAART				
Endothelin	7.8 ± 2.8	7.2 ± 2.6	6.8 ± 2.2	8.2 ± 2.9
HIV negative				
Endothelin	5.9 ± 2.8	6.3 ± 2.2	6.3 ± 1.8	6.8 ± 2.0
P-value Anova	<0.0001	<0.0001	<0.0001	<0.0001

Table 2 Variations of mean levels on nitric oxide, across the groups of interaction of HIV status and BMI in all.

Variables of Interest	Underweight Mean ± SD	Normal Mean ± SD	Overweight Mean ± SD	Obesity Mean ± SD
HIV on HAART				
Nitric Oxide	5.1 ± 1.0	18.1 ± 6.6	18.5 ± 7.7	21 ± 7.0
HIV not on HAART				
Nitric Oxide	18.1 ± 3.3	19.4 ± 4.2	18.7 ± 4.8	20.5 ± 3.4
HIV negative				
Nitric Oxide	8.8 ± 0.5	13.5 ± 2.1	16.4 ± 2.2	15 ± 2.2
P-value Anova	<0.0001	<0.0001	<0.0001	<0.0001

Table 3 Variations of mean levels SBP, DBP, PP, across the groups of the interaction of HIV status and BMI in all.

Groups of Interaction	Groups of Mean ± SD	DBP Mean ± SD	PP Mean ± SD
HIV(+) on ART			
Obesity	129.1 ± 28.2	85.6 ± 18.2	87.0 ± 8.1
Overweight	129.2 ± 20.4	86.3 ± 15.1	86.1 ± 12.2
Normal	116.8 ± 15.0	79.1 ± 9.5	87.4 ± 14.1
Underweight	116.8 ± 15.0	67.3 ± 10.0	89.0 ± 23
HIV(+) not on ART			
Obesity	134 ± 17.4	95 ± 10.0	88.2 ± 9.7
Overweight	133.7 ± 25.4	86.3 ± 20.2	88.6 ± 12.8
Normal	122.6 ± 11.3	80.3 ± 9.7	86.4 ± 10.7
Underweight	178.4 ± 37.4	74.6 ± 32.6	108.8 ± 19.1
HIV (-)			
Obesity	130.0 ± 15.8	87.7 ± 11.3	84.3 ± 18.6
Overweight	138.7 ± 32.0	91.0 ± 12.2	82.1 ± 13.6
Normal	125.2 ± 9.8	83.4 ± 8.9	61.9 ± 25
Underweight	119.0 ± 17	77.5 ± 3.5	74.0 ± 4.2
ANOVA	0.018	<0.0001	<0.0001

are willing to participate in all kinds of research that can facilitate good health. For total body fat in our study we included skeletal muscle fat and whole body fat which both have shown to be significantly high in females compared to males. It is known that excess weight increases risk of high blood pressure, high triglyceride levels, or blood fats, and high cholesterol [2]. High visceral fat, which accumulates around waist, is a specific risk

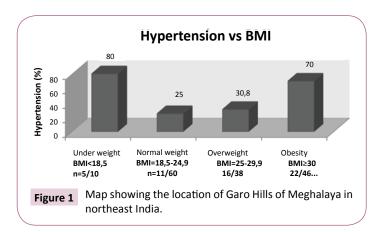


Table 4 Univariate associated factors with presence of arterial hypertension (n=54).

Variables of interest	Presence of hypertension Mean ± SD	Non hypertension Mean ± SD	ANOVA Mean ± SD
Age (years)	41.2 ± 11.5	35 ± 11.4	0.002
WEIGHT (kg)	74.3 ± 14.6	66.4 ± 15.5	0.003
BMI (kg/m²)	28.9 ± 7	25.4 ± 5.3	<0.001
SBP (mmhg)	148.9 ± 27.8	118.6 ± 13.1	<0.0001
DSP (mmhg)	98.4 ± 11.3	77.6 ± 7.2	<0.0001
PP (mmhg)	89.5 ± 17.5	81 ± 17.2	0.004
Endothelin (pg/mL)	5.6 ± 1.7	7.9 ± .3.9	0.002
Nitric Oxide (nmol)	17.9 ± 5.5	16.7 ± 5.6	0.211

indicating possible inflammation through blood vessels. Body mass index as expected was high in females with its mean value range being 28.4 ± 6.1 , which depict overweight and as a sign of early obesity stage. Obesity is one of earlier markers of renal function disorders that alter how body registers blood pressure [3], other complications of hypertension in obesity, such as cardiac remodelling and heart failure [9]. HIV positives on treatment and HIV positive not on treatment had levels of BMI, whole fat, SMF, resting metabolism, similar to those of HIV negatives, the levels indicate overweight of the participants. This suggests that all the groups are in risk of pre exposure to type II

diabetes, hypertension, urinary stress, sleep apnea etc because of elicited BMI. A high BMI is a risk factor for mortality from overall cardiovascular disease. Endothelin-1 (ET-1) and Nitric oxide (NO) are natural counterparts in vascular function, and it is becoming increasingly clear that an imbalance between these two mediators is a characteristic of endothelial dysfunction and is important in the progression of vascular disease [12]. Indeed, the present study showed that there is an uneven relationship between endothelin, nitric oxide levels and also these two are associated with overweight/obesity, blood pressure. The findings revile that the positive relationship was lost in both HIV positives not on treatment and HIV positives on HAART, possibly due to changes in the endothelium, HIV itself and HIV treatment. Further studies are needed on the relationship between endothelin, lipid profile, blood pressure and glucose levels in HIV positive patients.

Health professionals who are in charge of HIV infected patients have to monitor BMI, fat redistribution, blood pressure and drug toxicity regularly when these patients visit their clinics/Hospitals. Appropriate diet (5 different fruits intake/day), physical activity, and avoidance of known behavioural risk factors (smoking, excessive alcohol, fat and sugar intake) should be recommended to HIV infected patients. Community, policy makers, and researchers should be involved in health promotion in general and in curbing the HIV/AIDS pandemic and the emerging epidemic of obesity and cardiovascular diseases. The study was limited by age distribution and over representation of females that made it difficult to generalize the ability of the results, the strength of this study comes from strong and significant associations using statistical analysis as well as from valid and standardized measurements of anthropometric/body composition, blood pressure, nitric oxide and endothelin.

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