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The burden of metabolic diseases amongst HIV positive patients on HAART attending the Johannesburg Hospital

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THE BURDEN OF METABOLIC DISEASES AMONGST HIV POSITIVE PATIENTS ON HAART ATTENDING THE JOHANNESBURG HOSPITAL

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Research report submitted to the Faculty of Health Science, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Masters of Public Health (Health Policy and Management)

Johannesburg 2009

DECLARATION

I, Henry Patrick Julius declare that this research report is my own work. It is being submitted for the degree of Masters in Public Health in the field of Health Policy and Management at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

.....

September 2009

DEDICATION

I dedicate this work to:-

My wife Karen and son Enrique for their kind understanding, patience, inspiration and motivation rendered throughout the period of my studies. I am eternally grateful for your support and encouragement as you stood by me throughout.

My family for their warm support and by making my studies easier by believing in me

God for sustaining me throughout

- “In His time He makes all things beautiful”

ABSTRACT

Background: The increase use of highly active antiretroviral therapy (HAART) among patients with HIV infection and AIDS has led to increasing reports of metabolic abnormalities such as diabetes mellitus, hypertension, dyslipidaemia and obesity. Therefore, it is important to explore the burden of these diseases among HIV infected patients.

Objectives: To determine the burden of metabolic diseases (hypertension, diabetes, obesity and dyslipidaemia) in patients attending HIV clinic at the Charlotte Maxeke Johannesburg Academic Hospital (JHBH).

Methodology: It was a cross-sectional study. The study population included patients attending JHBH HIV clinic and on HAART for more than one year. A sample size of 304 patients, including 237 females and 67 males partook in this study. Anthropometric measurements were taken from patients and blood samples of these patients were sent to laboratory for lipograms, HbA1c, random glucose, CD4 lymphocytes counts as well as HIV viral load testing. The data was analysed with standard statistical software Epi-info version 6.0. Both descriptive and analytical statistics was used.

Results: The prevalence of metabolic syndrome according to the IDF was 20.4 %; obesity (BMI≥ 30 kg/m^2) was 16.8% and patients that were overweight (BMI > 25 kg/m^2 and BMI < 29.9 kg/m^2) was 28.6%; hypercholesterolemia (TC ≥ 5.0 mmol/l) = 35.5%; HDL< 1.29 mmol\L in females was 58% and HDL <1.04 mmol/l in males was 36%; elevated triglycerides ≥ 1.7 mmol/l was 30% and only 16% was classified as being hypertensive (BP ≥ 140/90 mmHg and / or on Hypertensive medication). The majority of the patients (86.2%) had a CD4 lymphocyte count ≥ 200 X 10^6 cells/l and 84% of patients had less than detectable limits for viral loads (VL< 40 copies / µl), which has been reported as optimum levels for metabolic diseases in HAART recipients.

Conclusion: These results clearly indicate that there is a growing burden of metabolic diseases among HIV patients on HAART attending the Johannesburg hospital HIV clinic. The current study also indicates that the metabolic disturbances are more frequent in women than in men, except for hypertension.

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LIST OF ABBREVIATIONS

AIDS: Acquire Immune Deficiency Syndrome
ART: Antiretroviral Therapy
BMI: Body Mass Index
BP: Blood Pressure
HAART: Highly Active Antiretroviral Therapy
HDL: High Density lipoprotein
HIV: Human Immunodeficiency Virus
IDF: International Diabetes Foundation
JHBH: Charlotte Maxeke Johannesburg Academic Hospital
LDL: Low density lipoprotein
NCEP (ATP) III: National Cholesterol Education Programme
NHLS: National Health Laboratory Services
PI: Protease Inhibitor
SADHS: South African Demographic and Health Survey
TC: Total Cholesterol
VL: Viral load

GLOSSARY OF TERMS

Diabetes and abnormal glucose metabolism: Patients can be categorised as having glucose disorders if they have a fasting plasma glucose ≥ 110 mg/dl (6.1 mmol/l) or hyperglycemia defined as random glucose tolerance test ≥ 140 mg/dL (11.1 mmol/l) or HBA1c levels >7% (1). The World Health Organization (WHO) defines impaired glucose tolerance as fasting glucose > 110 mg/dL and diabetes as > 126 mg/dL (2).

Dyslipidaemia: These have been identified by increased total and low density lipoprotein (LDL) cholesterol, decreased high density lipoprotein (HDL) cholesterol and mixed forms (3). It can be defined by the occurrence of any one of the following: total cholesterol (TC) ≥ 240 mg/dl (>6.2 mmol/l), LDL cholesterol ≥ 160 mg/dl (4.1 mmol/l), or triglycerides ≥ 200 mg/L (>1.7 mmol/l) (1).

Insulin Resistance: refers to the reduced action of circulating insulin to induce uptake of glucose into cells, where glucose serves as a major substrate for cellular function (4).

Metabolic syndrome: Metabolic syndrome (also called syndrome X), is phenotypically closely associated with visceral obesity, metabolic deregulation, and risk for diabetes mellitus and cardiovascular disease (4).
Metabolic syndrome according to the IDF and NCEP (ATPIII) criteria:
IDF criteria includes waist circumference >80 cm in women and >94 cm in men plus two of the following: triglycerides > 1.7 mmol/l, HDL <1.29 mmol/l, fasting glucose, ≥5.6 mmol/l, systolic blood pressure ≥130 mmHg, or diastolic blood pressure≥ 85 mmHg (5;6).
NCEP (ATPIII) criteria requires three or more of the following: waist circumference >88 cm in women and> 102 cm in men, triglycerides > 1.7 mmol/l, HDL <1.20 mmol/l in women or <1.04 mmol/l in men, fasting glucose ≥ 6.1 mmol/l, or blood pressure >130/85 mmHg (6).

Obesity and overweight: BMI is defined as the weight in kilograms divided by the square of the height in meters (kg/m2). The WHO suggested following weight categories (7):

- Under weight ($\leq$ 18.5 kg/m^2)
- Normal weight (18.5 to 24.9 kg/m^2)
- Over weight (25 to 29.9 kg/m^2) and
- Obese (30 kg/m^2 or more).

Population: The complete collection of elements, groups, or individuals to be studied

Risk: The probability that an event will occur, e.g. that an individual will become ill or die within a stated period of time or age.

Risk Factor: An aspect of personal behaviour or lifestyle, an environmental exposure, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition

Prevalence: The number or proportion of cases or events or conditions in a given population. Prevalence is a mathematical quantity that describes the presence of a disease Y in a population. It is the proportion of persons in the population with the disease Y:

Sample: A selected subset of a population. A sample may be random or non-random and it may be representative or non-representative

CHAPTER 1

INTRODUCTION

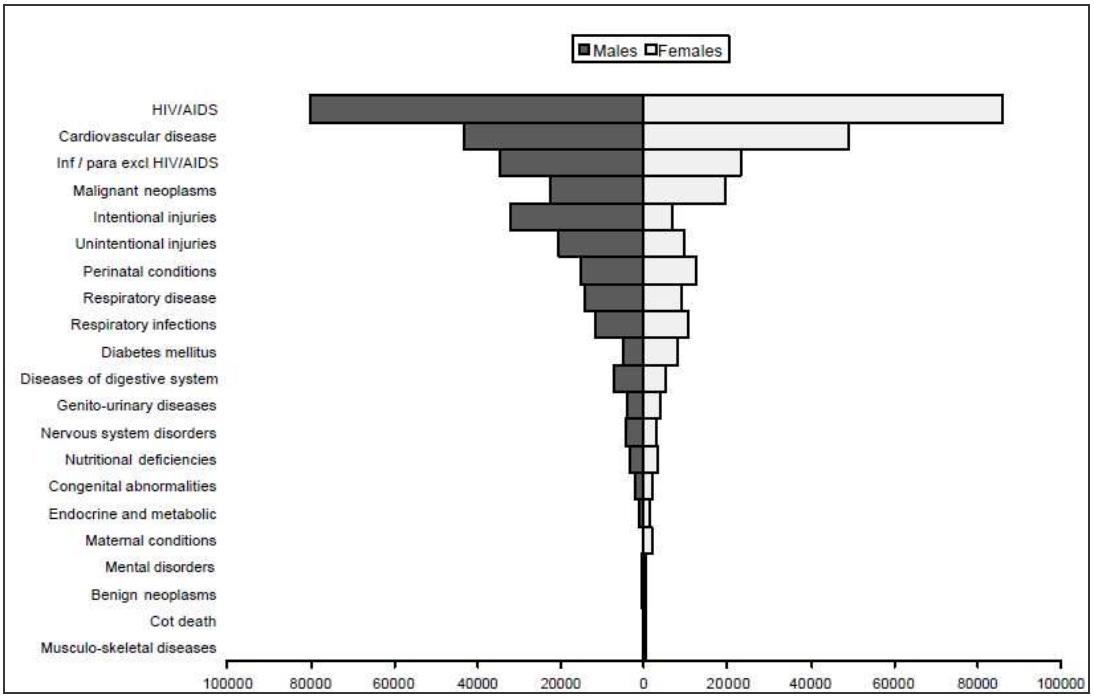
The purpose of this study was to determine the burden of metabolic diseases (hypertension, diabetes, obesity and dyslipidaemia) among HIV patients on HAART in patients attending HIV clinics at the Charlotte Maxeke Johannesburg Academic Hospital (JHBH).

1.1 BACKGROUND

South Africa has one of the highest prevalence of Human Immunodeficiency Virus (HIV) infection in the world (8), with over 5 million people infected with the virus, which accounts for more than 10% of the countries' total population (9). This has led to high morbidity and mortality rates. In 2004, the South African government has approved the roll out of antiretroviral therapy (ART) to all HIV infected people who fulfil certain criteria. Highly active antiretroviral therapy (HAART) has shown to increase the life expectancy of HIV infected patients and their overall health outcome (10). However, the use of protease inhibitor (PI), which is part of the HAART and ART regiment, has been associated with various chronic diseases like metabolic diseases (11). Therefore, it is important to explore the burden of these diseases among HIV infected patients.

1.2 JUSTIFICATION FOR THE STUDY

The quadruple burden of disease in South Africa (figure 1.1) indicates that HIV/ADS (29.8%), followed by cardiovascular disease (16.6%) was the two main causes of death in the year 2000, followed by infectious and parasitic diseases (10.3 %), and injuries, both intentional (7.0%) and unintentional (5.4%) (12). This data, on cardiovascular diseases, indicates that there is a high prevalence of metabolic diseases in South Africa.



(Bradshaw et al. 2003)

Figure 1.1: Cause of death by category, in South Africa 2000

However, the recent introduction of HAART for HIV positive patients exposes them to cardio-metabolic diseases. However, no study has explored this problem in South Africa.

1.3 PROBLEM STATEMENT

The burden of metabolic diseases among HIV positive patients in South Africa has not been fully explored.

1.4 STUDY OBJECTIVES

1.4.1 BROAD OBJECTIVE

To determine the health burden of metabolic diseases (hypertension, diabetes, obesity and dyslipidaemia) in patients attending HIV clinic at the

Charlotte Maxeke Academic Johannesburg Hospital (JHBH).

1.4.2 SPECIFIC OBJECTIVES

1) To determine the prevalence of metabolic diseases (hypertension, diabetes, obesity and dyslipidaemia) in patients attending the HIV clinics at JHBH

2) To determine the prevalence of metabolic syndrome among patients attending the HIV clinics at JHBH

3) To determine the association between specific risk factors (such as: age, gender, CD4 lymphocyte count, viral load) and metabolic syndrome in HIV infected patients

1.5 SUBSEQUENT CHAPTERS OF THE REPORT

The background to the research has been discussed and the objectives were defined up to this point. The subsequent chapters will focus on:

Chapter two: Literature review.
The purpose of the literature review is to elaborate on key concepts and to identify related prevalence and risk factors that has been documented in similar studies.

Chapter three: Methodology
This chapter describes the methodology that was used to conduct this study and elaborates on the sampling method, scope, data collection as well as the pilot study.

Chapter Four: Results
The findings of the results are contained in this chapter and are aligned with the objective of this study.

Chapter Five: Discussion

The results and the literature review are integrated in this chapter in order to address the problem statement and the objectives of the study.

Chapter six: Conclusion and recommendations

This chapter concludes the research report and draws conclusions from the research data and makes recommendations regarding the need to test HIV positive patients for metabolic related diseases.

CHAPTER 2

LITERATURE REVIEW

In this chapter, relevant literature related to metabolic diseases and associations with HIV and HAART are discussed.

2.1 INTRODUCTION

At the end of 2007 the United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) jointly estimated that 33.2 million people worldwide were infected with HIV. This data also confirmed the disproportionate impact of HIV/AIDS on sub-Saharan Africa, in that the sub-Saharan Africa accounts for 68% of the persons living with HIV/AIDS worldwide and accounts for 76% of deaths due to AIDS. (9)

Table 2.1: Global HIV statistic

	People living with HIV	New infections 2007	AIDS deaths 2007	Adult prevalence %
Sub-Saharan Africa	22 million [20.5 – 23.6 million]	1.9 million [1.6– 2.1 million]	1.5 million [1.3 – 1.7 million]	5% [4.6% – 5.4%]
South and South-East Asia	4.2 million [3.5 – 5.3 million]	330 000 [150 000 – 590 000]	340 000 [230 000 – 450 000]	0.30% [0.2% – 0.4%]
East Asia	740 000 [480 000 – 1.1 million]	52 000 [29 000 – 84 000]	40 000 [24 000 – 63 000]	0.10% [<0.1% – 0.2%]
Latin America	1.7 million [1.5 – 2.1 million]	140 000 [88 000 – 190 000]	63 000 [49 000 – 98 000]	0.50% [0.4% – 0.6%]
North America	1.2 million [760 000 – 2 million]	54 000 [9600 – 130 000]	23 000 [9100 – 55 000]	0.60% [0.4% – 1.0%]
Western and Central Europe	730 000 [580 000 – 1 million]	27 000 [14 000 – 49 000]	8000 [4800 – 17 000]	0.30% [0.2% – 0.4%]
Eastern Europe, Central Asia	1.5 million [1.1 – 1.9 million]	110 000 [67 000 – 180 000]	58 000 [41 000 – 88 000]	0.80% [0.6% – 1.1%]
Caribbean	230 000 [210 000 – 270 000]	20 000 [16 000 – 25 000]	14 000 [11 000 – 16 000]	1.10% [1.0% – 1.2%]
Middle East and North Africa	380 000 [280 000 – 510 000]	40 000 [20 000 – 66 000]	27 000 [20 000 – 35 000]	0.30% [0.2% – 0.4%]
Oceania	74 000 [66 000 – 93 000]	13 000 [12 000 – 15 000]	1000 [<1000 – 1400]	0.40% [0.3% – 0.5%]
Total	33 million [30.3 – 36.1 million]	2.7 million [2.2 – 3.2 million]	2 million [1.8 – 2.3 million]	0.80% [0.7% – 0.9%]

[Source: *Report on the global AIDS epidemic 2008*, August 2008]

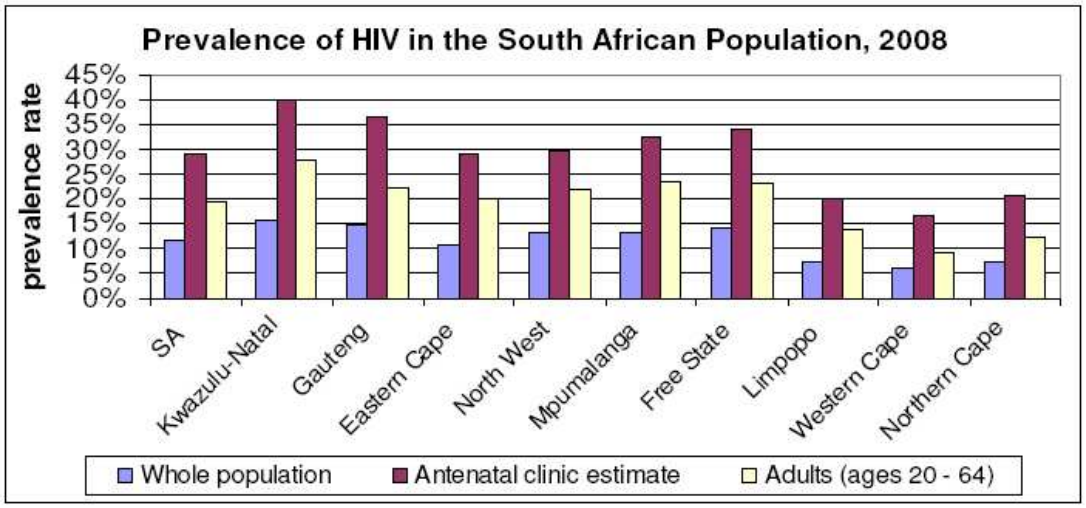
South Africa has been deemed the country with the highest prevalence of HIV in the world, with over 5 million people infected with the virus, which accounts for more than 10% of the countries' total population (9). The prevalence of

HIV/AIDS in the province of Gauteng is estimated 15% of the population in that province. (The province where this study has been conducted) (Figure 2.1)



Figure 2.1: Republic of South Africa

The prevalence of HIV in South Africa is described in Figure 2.2.



(ASSA2003 (full) AIDS and Demographic model available on: www.actuarialsociety.org.za)

Figure 2.2: Population distribution on HIV Prevalence in South Africa

Highly active antiretroviral therapy (HAART) has been used as treatment for people infected with HIV. Highly active antiretroviral therapy has significantly improved the life-expectancy of people living with HIV in that it restores

immune system functions, and suppress viral load replications (4). HAART can be divided into five drug classes: protease inhibitors (PI) (indinavir, ritonavir, fosamprenavir, saquinavir, tipranavir and darunavir), Nucleoside reverse transcriptase inhibitors (NTRIs) (Stavudine, zidovudine, lamivudine, abacavir, didanosine, tenofovir and emtricitabine), non-nucleoside reverse transcriptase inhibitors (NNTRIs) (sfaviranz and nevirapine), entry class inhibitors (fusion inhibitors: enfuvirtide; and CCR5 inhibitors: maraviroc) and integrase inhibitors (raltegravir) (4).

The increase use of (HAART) among patients with HIV infection has led to increasing reports of metabolic diseases such as diabetes, hypertension, dyslipidaemia, obesity (1;13). The Table 2.2 depicts some of the known adverse effects associated with HAART (14). These metabolic diseases is underpinned by insulin resistance, which has been found to be an adverse side effect of protease inhibitors (4;15-17).

Table 2.2: HIV regiment and associated adverse effect

Regiment	Associated Adverse side effect
IDV + ZDV + 3TCIDV + d4T	patients developed abnormal accumulation of fat over shoulders and neck (buffalo hump); increased breast size and abdominal girth
3TC + d4T + IDV	Swelling in breast noted, chest measurement increased; therapy continued and chest size increased 5 months post-IDV initiation; associated with breast pain; oedematous skin encompassing breasts, increased abdominal girth, thinning of buttocks and thighs.
HIV-infected patients with buffalo hump receiving RTIs with a PI (IDVor NFV)	DEXA showed that patients with buffalo hump had significantly greater proportion of truncal fat than control patients
ZDV + 3TC + IDV (800 mg three times daily)	Fat wasting in arms, buttocks, and legs along with central obesity and enlargement of cervicodorsal fat pad. DEXA confirmed loss of body fat. No changes in muscle mass or strength. No abdominal organomegaly, mass, or ascites. Changes progressed over 19 months of monitoring; Normal fasting morning plasma cortisol; elevated TG, cholesterol, C peptide concentrations; impaired glucose tolerance
Two NRTIs + One PI; Two NRTIs Specific drugs and dosages not stated	significant breast enlargement in women (>2 bra sizes), increase in abdominal girth, reduction in fat mass of calves and thighs, no changes in total body weight; DEXA showed redistribution of body mass due to changes in fat tissues not involving bone or muscle tissues. Fat redistribution more frequently with triple therapy including a PI than with duo therapy with NRTIs. Women with fat redistribution shows cytokine pattern (high IL-12, low IL-10 and TNF) not seen in women without fat redistribution, but no differences between groups observed with respect to plasma cortisol, ACTH, GH, C-peptide, testosterone, prolactin, glucose, cholesterol, or TG levels.

Adapted from Graham 2000

2.2 METABOLIC DISEASES

The metabolic diseases such as hypertension diabetes mellitus, obesity and hypercholesterolemia are predominantly found in developed countries. However, the prevalence's are gradually increasing in the developing countries. There are various factors contributing to this, such as urbanization and western lifestyle. Recently the HIV and its treatment are also linked to that.

2.2.1 METABOLIC DISEASES AMONG HIV INFECTED PATIENTS

Longer duration of protease inhibitor therapy, HIV stage (those who started on HAART later on in the course of their disease) as well as increased CD4 count and decreased viral load are associated with the risk of developing diabetes mellitus, dyslipidaemia and hypertension (1). Demographic and anthropometric characteristics such as age, gender and ethnicity was found to be associated risk factors of the mentioned metabolic diseases (1;3).

Older age and male gender were significantly associated with dyslipidaemia in study of a cohort of 900 HIV positive patients (1). It was also found that the risk of developing diabetes mellitus increased with older age and when patients on HAART were overweight or obese (17).

2.3 DIABETES AND ABNORMAL GLUCOSE METABOLISM

The prevalence of diabetes in the general population in South Africa is estimated at between 2.8% and 3% and is expected to increase to 3.9% by 2025; this expected increase is linked to the worldwide increase in obesity. (18).

2.3.1 DIABETES AMONG HIV POSITIVE PATIENTS

Glucose metabolism alterations are frequent in HIV-positive individuals treated with ART and give impetus to insulin resistance, impaired glucose tolerance, and diabetes mellitus (3;19). As a result of that, the incidence of

diabetes mellitus is increasing in the HIV infected population more than that of the general population, even in the absence of the concomitant problem of obesity (20). Both in vitro and clinical studies have shown that PI even after a single dose can induce insulin resistance (4;21) which underlies many metabolic conditions including type 2 diabetes *(4;22)*

One study have illustrated that the prevalence of diabetes mellitus in PI recipients with lipodystrophy have increase from 2% to 7% after 14 months observation (23). The overall prevalence of glucose disorders in HIV-infected patients treated with HAART, which includes diabetes mellitus, impaired fasting glucose and impaired glucose tolerance, was found to be at 25% for that particular study (23).

Prospective studies have reported that 10% of HIV infected patients treated with HAART developed diabetes during 4 years of follow-up (4;24).

2.4 DYSLIPIDAEMIA

Dyslipidaemia has been noted as one of the major contributing factors of cardiovascular diseases in the South African population and is expected to be exacerbated by the increase of diabetes and obesity, also known as diabesity (25). The prevalence of lipid abnormalities in South Africa has not been determined in a population samples, by means of a national survey or by other data collecting tools, although smaller random studies has been conducted (25).

2.4.1 DYSLIPIDAEMIA AMONG HIV POSITIVE PATIENTS

Increasing incidence of dyslipidaemia has been recognised among HIV infected individuals. HIV infection *per se* is associated with lipid alteration including total cholesterol and it components (low HDL- and LDL-cholesterol and hypertriglyceridaemia) (4). The use of HAART has been associated with

elevation of serum lipids above that of its pre-treated levels, except for HDL cholesterol (1;26).

The prevalence of dyslipidaemia in HIV infected patients ranges from 28% to 80% and includes hypertriglyceridedaemia (40-80%), hypercholesterolemia (10-50%) and mixed forms (26). Insulin resistance has been considered the link between dyslipidaemia and other metabolic disturbances within metabolic syndrome such as abdominal obesity, diabetes, heat diseases, hypertension (4).

There has been no association found between CD4 lymphocyte count or viral load and lipid abnormalities (27). Due to the high incidence of dyslipidaemia and its potential long term morbidity in this population, it is deemed necessary to screen HIV patients on HAART for lipid abnormalities (27).

2.5 HYPERTENSION

Hypertension in South Africa is a very common condition and is a risk factor for cardiovascular diseases. There are various definitions of hypertension such as South African guidelines for Hypertension, WHO etc. The most widely used definition is that of the systolic blood pressure of > 140 mmHg and diastolic pressure of > 90 mmHg. People who are hypertensive are usually unaware of that they have this condition unless their blood pressure has been measured at a healthcare facility (28). According to the second South Africa Demographic and Health Survey (29), the reported prevalence of hypertension in men was 9% and 19% in women, but this prevalence rose significantly when they were identified as either hypertensive (blood pressure ≥ 140/90 mmHg) or on hypertension medication, to 40% in men and 51% women for the age group 15 and older (29). This analysis was made by means of making use of the South African hypertension guidelines and the WHO international Society of Hypertension Guidelines for the Management of Hypertension that suggest that a person can be classified as being hypertensive with a blood pressure BP≥ 140/90 mmHg, and/or taking anti-hypertensive medication (28).

2.5.1 HYPERTENSION AMONG HIV POSITIVE PATIENTS

HIV-infected patients are at a higher risk of developing hypertension compared to the general population. The prevalence of hypertension in HIV infected people is 29% and occur more in older men than in women (30). Body mass index (BMI), in this group has been reported to be significantly higher in the hypertensive individuals compared to the normotensive group (25.8 vs. 23.6 kg/m^2 (30).

The prevalence of hypertension in HIV infected patients that is on HAART was found to be 21% in one study (31). Hypertension was found to be more prevalent in males than in females (17;30;31).

It was also noted that the time interval between the onset of symptoms and the establishment of components of hypertension such as, pulmonary hypertension was approximately six months which is in contrast with diagnoses of pulmonary hypertension in which that time has been reported as 2.5 years (31;32). Therefore, the HIV infected patients on HAART should be monitored closely for hypertension.

2.6 OBESITY

Obesity has become a global epidemic with an estimated 1.3 billion people overweight or obese (31;33). The developed countries have higher prevalence obesity and overweight than developing countries, with the United States with a prevalence of 26.6% in men and 32.2% in women above 20 years of age. The epidemic is however on the increase in the developing countries. The second South African Demographic and Health Survey (SADHS), undertaken in 2003 and published in 2004, indicates that the prevalence of obesity for adult men is 9% and 23% for adult women while the prevalence of overweight is found to be at 21% for men and 29% for women (29).

2.6.1 OBESITY AMONG HIV POSITIVE PATIENTS

The prevalence of Obesity in HIV infected individuals was reported at 14% and was found to be more common in women than in men. A CD4 lymphocyte count ≥ 200 cells/µL count is associated with an increase in BMI. (15)

2.7 METABOLIC SYNDROME

Metabolic syndrome which is affecting the general population in epidemic proportions is commonly associated with increase cardiovascular risk (34). The risk of metabolic syndrome has been found to be greater in HIV infected patients compared with that of the general population because of the higher prevalence of lipid and glucose abnormalities (35)

2.7.1 METABOLIC SYNDROME AMONG HIV POSITIVE PATIENTS

The prevalence of metabolic syndrome in HIV infected individuals has been reported at 14% to 20.8% (4;35). In a study population of 881 HIV infected patients it was found that progression to metabolic syndrome occurs within three years after the initiations of antiretroviral therapy and the incidence of this syndrome was significantly associated with an increased risk of diabetes mellitus and cardiovascular diseases (3).

The age and gender risk- adjusted risk of having metabolic syndrome in HIV infected patients was twice as great as that in HIV-negative control patients (5;35;36).

The development of metabolic syndrome in patients treated with HAART is an inevitable consequence of long-term successful HAART (37). Therefore, the HIV-infected patients on HAART must be monitored for metabolic syndrome in order to manage this added burden of disease effectively.

2.8 SUMMARY OF THE CHAPTER

South Africa is afflicted by a quadruple burden of disease, including HIV/AIDS, cardiovascular diseases, infectious parasitic disease, malignant neoplasm and injuries (12). The review of literature confirms that metabolic and morphological changes, as a result of the prolong use of HAART, are prevalent among HIV positive individuals. Thus, the quadrants between the cardiovascular diseases as described above and the HIV/AIDS will blur more in future as more HIV-infected patients are expected to receive HAART.

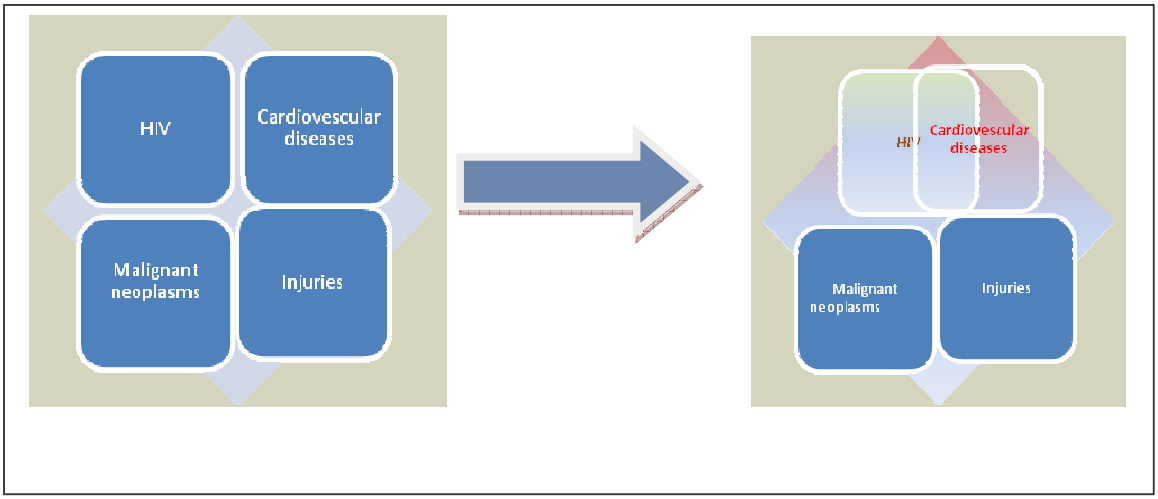


Figure 2.3: Projected burden of disease due to the effect of HAART

The mechanism of developing of metabolic diseases among HIV infected individuals is not yet well understood.

Furthermore, the burden of metabolic disease among HIV infected individuals on HAART has not been fully explored in South Africa.

CHAPTER 3

METHODOLOGY

The methodology used for this study was selected on the basis of its aims and objectives. In this chapter the following are discussed: setting, scope, study design and research tools.

The motivation for this study was driven by the need to estimate the burden of HIV associated metabolic diseases in public hospitals in South Africa, which has one of the highest prevalence of HIV/ AIDS in the world. In this chapter the study design, scope, study population, sample size calculation, research tools, the data collection, the pilot study, analysis and statistical methods are described.

3.1 STUDY DESIGN

The study design was a cross-sectional study of HIV positive patients that have developed metabolic disorders, specifically looking at diabetes, hypertension, obesity and dyslipidaemia.

3.2 SETTING

This study was conducted at the Charlotte Maxeke Johannesburg Academic Hospital (JHBH) in the Gauteng province of South Africa (Figure 3.1)



Figure 3.1: The Province of Gauteng

The JHBH have a HIV clinic which caters for the HIV positive patients Southern surrounding areas of Johannesburg. This hospital has been chosen because it is one of the first hospitals in South Africa to have been accredited to roll-out ARV treatment. Thus, the mean number of years for patients that were recruited was three years.

3.3 SCOPE

This study was a prospective study on HIV positive patients attending the JHBH HIV clinics.

3.4 STUDY POPULATION

The study population was the HIV positive patients at the JHBH HIV clinic that was on HAART for more than one year at the time of the study. Patients that were not on HAART or that were on HAART for less than a year was excluded. Only patients between the ages of 18 and 45 years were recruited for this study. This was due to the fact that metabolic diseases general occurs in people above the age 45 years and thus the HAART might have little impact on the development of metabolic diseases. Patients under the age of

18 years can only participate, provided that permission was obtained from their parents or guardians.

3.5 SAMPLE SIZE

Sample size was calculated using Statcalc (Epi-Info version 6) based on:

- a study population of 1500
- expected prevalence of 50%, and
- worst acceptable result of 45%
- α of 0.05 and β of 0.8.

A sample size of 304 was required to achieve the above parameters.

Study variables

The following variables were collected for each patient:

- Demographic information – gender and age (The DISA system does not record the patients ethnicity)
- Metabolic disorders: types and prevalence
- Duration of HAART
- Diabetes: blood sugar
- Cholesterol triglyceride, HDL-cholesterol
- Body mass index and waist circumference
- Blood pressure measurements

The sources of the above variables are listed in Table 3.1.

Table 3.1: Data source for variables

Objectives	Variables	Data Source
2	age	
2	gender	
	Waist Circumference	Patient file
	BMI (kg/m^2)	Patient file
	Systolic Blood pressure	Patient File
	Diastolic Blood pressure	Patient File
1	total cholesterol	DISA*Lab & Patient file
	LDL cholesterol	DISA*Lab & Patient file
	Triglycerides	DISA*Lab & Patient file
	HDL Cholesterol Male	DISA*Lab & Patient file
	HDL Cholesterol female	DISA*Lab & Patient file
1	Glucose	DISA*Lab & Patient file
	HBA1c	DISA*Lab & Patient file

- Metabolic syndrome: For the purpose of this study metabolic syndrome is defined according to the international diabetes federation (IDF) criteria, which includes waist circumference >80 cm in women and >94 cm in men plus two of the following: triglycerides > 1.7 mmol/l, HDL <1.29 mmol/l, systolic blood pressure ≥130 mmHg, or diastolic blood pressure ≥ 85 mmHg. No data for fasting glucose were used as these are not done routinely.
- Hypertension: For the purpose of this study hypertension was defined as blood pressure > 140/90 and / or if the patient were on hypertensive medication.
- Diabetes mellitus: For the purpose of this study diabetes mellitus was defined as an HBA1C > 7% or a random glucose ≥ 11.1 mmol/l.
- Dyslipidaemia: For the purpose of this study hypercholesterolemia was defined as Total Cholesterol (TC) > 5.0 mmol/l, (TC ≥ 6.2 mmol/l IDF criteria for MS), LDL Cholesterol (LDL) ≥ 4.1 mmol/l, HDL Cholesterol (HDL) ≤ 1.2 mmol/l, Triglycerides ≥ 1.7 mmol/l

3.6 DATA COLLECTION

The data was collected over three months period (January 2009 to March 2009) by means of reviews of the patients files and the NHLS laboratory information system (DISA*LAB) using the patients' hospital-numbers. The researcher visited the HIV clinic of the JHBH each day of the study period. He approached the patients who fulfil the inclusion criteria and obtained their consent to do laboratory blood tests and anthropometric measurements.

Patients receiving HAART for more than one year, at the time of the study was asked to volunteer to have their anthropometric measurements taken and their blood drawn for relevant tests. The laboratory tests that were done for these patients include HIV viral loads, CD4 lymphocytes counts, Lipograms, Glysated Haemoglobin (HbA1c) and random glucose test.
Data collection tools are described below in Table 3.2.

Table 3.2: Data Collection tools

Tools name	**Data Collection tool**
Patient clinical records	1
Metabolic profile of HIV patients	2
HIV related tests	2

3.7 DATA ANALYSIS

The hospital-numbers of the HIV-infected patients was supplied by the management of the JHBH-HIV clinic. The collected data was recorded by making use of Microsoft access. Each patient's information regarding their age, sex, BMI, waist and Hip circumferences and the interested laboratory results (HBA_1C, random sugars, Lipograms including TC, HDL, LDL and plasma triglycerides) was recorded.

Patients' results were obtained from the NHLS laboratory information system

and were verified against their respective hospital patient files.
All data was analysed using standard statistical software Epi-info version 6.0.

Following descriptive statistics was reported:

- continuous variables with normal distribution: mean and standard deviation
- Other continuous variables: median and interquartile range, and
- Nominal and ordinal variables: proportion and range.

Following analytical statistics was reported

- For two samples and one variable:
    - Continuous variables with normal distribution: t test
    - Other continuous variables: Mann-Whitney's test
    - Nominal and ordinal variables: Chi-Square test
- For two samples and two variables: Analysis of Variance
- Logistics regression was used to determine the factors influencing the prevalence of metabolic syndrome

3.8 PILOT STUDY

A pilot study, on retrospective data, was conducted to test the feasibility of the study. The JHBH HIV clinic database was used to screen 194 patient's files of patients that have received HAART for more than one year. The pilot study indicated that 115 (59.28%) of 194 patients were tested for the relevant metabolic disease. The pilot study further indicated that the relevant data for the project was very scanty. The anthropometric data for most the patients (90%) were also not complete. The Table 3.3 depicts this sparseness the laboratory data of the patient's that were screened.

Table 3.3: laboratory data for patients on HAART prior 2006

Number of Patients files screened	Laboratory tests	Total (%)
194	Total no of relevant metabolic tests	115 (59.28)
194	Random Glucose	7 (3.6)
194	Fasting Glucose	2 (1.0)
194	Glysated Haemoglobin (HBA1c)	3 (1.6)
194	LDL cholesterol	8 (4.1)
194	HDL cholesterol	8 (4.1)
194	Triglycerides	50 (25.8)
194	Total cholesterol	62 (31.9)

The paucity of data prompted the researcher to obtain further permission to collect the required data prospectively from patients' files.

3.9 ETHICAL CONSIDERATIONS

This project was approved by the committee for Human Subjects Medical (M081154) and the Management of Johannesburg Hospital. (Annexure A and B)

CHAPTER 4

RESULTS

The results obtained from the analysis of the data are described in this chapter.

4.1 STUDY SAMPLE

A total of 345 study participants partook in the study but only 304 patients had all the relevant metabolic tests done. The study population consist of 237 (77.9%) female and 67 (22%) male participants.

4.2 DEMOGRAPHIC INFORMATION

The study participants comprised of patients at the JHBH HIV clinic that were on HAART treatment for more than one year at the time of the study and between the ages of 18 and 45 years. Age was distributed normally and the mean age for the study group was 35.8 ± 5.3 years. The mean number of years that patients were receiving HAART is 3.2 ± 2.4 years. The mean number of years that male and female participants received HAART did not differ very much with a mean of 3.14 years for female and a mean of 3.53 years for male. The range of the study group was between 23 and 45 years of age.

Table 4.1: Age distribution and the period on HAART

	Total (Mean ±SD)	**Female (Mean ± SD)**	**Male (Mean ±SD)**
Sample size	304	237	67
Age	35.8 ±5.3	37.4 ± 4.4	35.4 ± 5.5
Number of HAART Years	3.2±2.4	3.1±1.5	3.53±4.3

4.3 ANTHROPOMETRIC MEASUREMENTS

Among the 304 participants, 152 (50%) met the criteria for IDF abdominal obesity threshold levels, that includes 7 (10%) men that had a waist circumference > 94 cm and 145 (61%) women that had a waist circumferences > 80 cm. Less patients however, met the threshold levels for the NECP (ATP) III criteria, in that only 88 (30%) of participants, including 4 (6%) men and 84 (34%) women met the criteria of a waist circumference > 88 cm for women and 102 cm for men.

Table 4.2: Anthropometric Measurements

	Total (Mean ±SD)	**Female (Mean ± SD)**	**Male (Mean ±SD)**
Waist (cm)	84.2 ± 11.5	84.8 ± 12.0	82 ± 9.7
HIP (cm)	99.5 ± 11.5	100.8 ± 12.1	94.7 ± 6.9
Weight (kg)	66.8 ± 13.5	66.6 ± 14.1	67.7 ± 10.9

4.4 BODY MASS INDEX

The World Health Organization (WHO) standards were used to categorise body mass index. Table 4.3 depicts the distribution of the weight categories for the sample population. The mean BMI of the study group was 25.15 ± 5.3 kg/m^2 with a mean BMI for women of 25.76 ± 5.6 kg/m^2 and men mean BMI = 23.07 ± 3.2 kg/m^2. There is no correlation between BMI and Viral load (Spearman's correlation ρ = 0.01; p=0.95). Therefore a high BMI is associated with a low viral load. There is a significant positive correlation between BMI and CD4 lymphocyte count (Spearman's correlation ρ =0.12; p =0.02). Therefore, BMI is associated with higher CD4 lymphocyte count.

Table 4.3: Body Mass Index (BMI=kg/m^2)

Category	Total (%)	Female (%)	Male (%)
Obese (BMI≥ 30 kg/m^2)	51 (16.8%)	47 (19.8%)	4 (5.9%)
Over weight (BMI≥ 25 < 29.9 kg/m^2)	87(28.6%)	73 (30.8%)	14 (20.9%)
Normal Weight (BMI≥ 18.5<24.9 kg/m^2)	145 (46.8%)	97 (40.9%)	48 (71.6%)
Under weight (BMI<18.5 kg/m^2)	15 (4.9%)	13 (5.5%)	2 (2.9%)

4.5 DYSLIPIDAEMIA

The International Diabetes Federation (IDF) was used to categorise the lipid profiles as depicted in Table 4.4. The mean total cholesterol (TC) levels for the study group were 4.7± 1.0 mmol/l. On the IDF definition of TC> 6.2 mmol/l there was more women that met this criteria than men. The prevalence for hypercholesterolemia (TC ≥ 5 mmol/l, the clinical cut-off as determined by the National Health Laboratory Services (NHLS)) is 35.5% (n=108) for the study group, (n=83) 35% women and 37% (n=25) in men. The overall mean for HDL–cholesterol was 1.2 ± 0.4 mmol/l and the overall mean for LDL cholesterol was 2.8 ± 0.9 mmol/l.

Table 4.4: Lipid Profiles

Category	Total (%)	Female (%)	Male (%)
Total Cholesterol >6.2 mmol/l	24(8%)	18(6%)	6(2%)
HDL <1.29 mmol/l Female	138(58%)	138(58%)	0
HDL <1.04 mmol/l male	24(36%)	0(0)	24 (36%)
Triglycerides>1.7 mmol/l	90(30%)	61(26%)	29(14%)
LDL > 4.1 mmol/l	32(10%)	27(11%)	5(7%)
Patients lipid lowering drugs	25(8.2%)	16(5.8%)	9(13.4%)

4.6 BLOOD SUGARS AND DIABETES

Only 1% of the study population had random glucose levels higher than 11.1 mmol/l and same percentage that had an HbA1c >7%. All these patients were more than 30 years of age. No patients were tested for fasting glucose.

Table 4.5: Blood Sugars

Category	Total (%)	Female (%)	Male (%)
HbA1c >7%	4(1%)	4(2%)	0
Random Glucose >11.1 mmol/l	4(1%)	4(2%)	0

4.7 HYPERTENSION

Hypertension (systolic / diastolic ≥ 140/90 mmHg and / or on hypertension medication) was reported at 16% in this study population and was more prevalent in males (17.9%) than in females (13.9%).

Body weight was significantly associated with systolic and diastolic blood pressure (Spearman's correlation ρ =0.26; p <0.001 and Spearman's correlation ρ =0.23; p <0.001 respectively). Similarly, body mass index was significantly associated with systolic and diastolic blood pressure (Spearman's correlation ρ =0.21; p <0.001 and Spearman's correlation ρ =0.20; p <0.001 respectively).

Table 4.6: Blood Pressure

Category	Total (%)	Female (%)	Male (%)
Systolic/Diastolic >140/90 mmHg	18 (6%)	12(5%)	6(9%)
Systolic/Diastolic >140/90 mmHg + Hypertension drugs	11(3.6%)	7(2.9%)	4(5.9%)
Systolic/Diastolic >140/90 mmHg with no Hypertension medication (Undiagnosed)	7(2.3%)	5(2.1%)	2(3%)
Total Patients on Hypertension medication	43(14%)	33(13.9%)	10(14.9%)
Total Hypertensive Patients	50(16%)	38(16.03)	12(17.9%)

Systolic >130 / Diastolic > 85 mmHg (IDF criteria for MS)	43(14%)	29(12%)	14(21%)

4.8 METABOLIC SYNDROME

Table 4.7 indicates that 20.4% of participants met the metabolic syndrome criteria for IDF definitions. At least two features of metabolic syndrome, excluding their waist circumferences that was in the non-metabolic range, were present in 17 (25%) men and 48 (20%) women respectively, in the study group.

Table 4.7: Metabolic syndrome according to IDF criteria

	Total	**Female**	**Male**
IDF	62(20.4%)	57(24.1%)	5(7.5%)

4.9 FACTORS INFLUENCING METABOLIC SYNDROME

The logistic regression analysis shows a significant association between the various variables and metabolic syndrome ($P < 0.0001$). The age has a positive association and the women had more chance of developing metabolic syndrome. The CD4 count had near significant association. However, viral load and period on HAART had no significant association with metabolic syndrome.

4.10 HIV RELATED LABORATORY TESTS

The majority of the patients 263(86.2%) had a CD4 lymphocyte count for ≥ 200 x 106 cells/l, which includes 212(89.5%) women and 51(76.1%) men.

Table 4.8: CD4 lymphocyte count

Laboratory Test	**Total (Mean ±SD)**	**Female (Mean ± SD)**	**Male (Mean ±SD)**
CD4 lymphocyte (10^6 cells/l)	416.1± 203.7	441.9±208.9	323.4±152.4

Most of the patients HIV viral load tests results were less than detectable; viral load < 40 copies /µl.

Table 4.9: HIV RNA Viral load

Category	**Total (%)**	**Female (%)**	**Male (%)**
LDL (VL< 40 RNA copies/ ml)	255 (84)	201 (85)	54 (81)
Viral Load VL≥ 40 RNA copies/ ml	49 (16)	36 (15)	13 (19)

CHAPTER 5

DISCUSSION

In this chapter, the results obtained in the previous chapter is discussed and compared with other published studies.

5.1 INTRODUCTION

This study was an attempt to explore the burden of metabolic diseases among HIV patients that received HAART for period of more than one year at JHBH HIV clinic.

The findings in this report are based on data that was collated from patients' anthropometric measurements, metabolic and HIV related laboratory tests results. The data was collected from consented patients of whom their anthropometric and laboratory tests results were obtained. Only patients that were older than 18 years and younger than 45 years and on HAART for more than one year, at the time of the study was allowed to partake in the study. A total number of 345 patients volunteered but only 304 patients participated in the study.

5.2 RISK FACTORS AND PREVALENCE OF METABOLIC DISEASES AMONG HIV PATIENTS

It is well documented that the use HAART has significantly decreased the morbidity and mortality rate of HIV infected individuals (26). The South African Government, however only made these drugs available in 2004, hence the mean number of years that male and female patients were on HAART, for this study was 3.5 and 3.1 years respectively. The prolong use of HAART (that contains PI), age, sex, increased CD4 count and decreased viral load is associated with increased risk of developing metabolic diseases, (such as

obesity, Hypertension, diabetes mellitus, dyslipidaemia, and metabolic syndrome) (1;3;17).

The present study confirms that these metabolic diseases are more prevalent in women, except for hypertension where the prevalence were higher in men than in women. The concentration levels of HIV viral load for the majority of patients (84%) were within the undetectable limits (VL<40 copies / µl) along with 86.2% of the patients that had their CD4 lymphocyte ≥ 200 X 10^6 cells/l. These ranges for CD4 lymphocytes and viral loads was reported to be optimum levels for the impetus of the relevant metabolic diseases (38;39).

5.3 DIABETES

The prevalence of diabetes in HIV infection is expected to vary from one population to another as being modified by factors such as genetic susceptibility, obesity rates and sedentariness (40). Only 4(1%) of the study population had an HbA1c>7% and random glucose > 11.1 mmol/l, and all of them were also women. This is much lower than the reported diabetes of 23% to 40% for HIV positive patients (23). Prospective studies have reported that 10% of HIV infected patients treated with HAART developed diabetes during 4 years of follow-up (4;41). The prevalence of hyperglycemia for a study done in 1440 HIV-infected patients was reported at 2% (42).

The prevalence for diabetes and glucose impairment for this study was also lower than both the national and provincial prevalence for women that have diabetes in the general population of SA and Gauteng.

Diabetes mellitus was reported to be at 2.9% nationally for the age group between 35-44 years and 3.5% for the province of Gauteng in 2003 (29). The prevalence of diabetes mellitus for the same age category for this study was found to be n=3 (2.32%) of women. None of the four patients that were diagnosis with diabetes mellitus in this study was on HAART for more than 4 years.

5.4 OBESITY AND OVER WEIGHT

The data for this study suggest that obesity and overweight is more prevalent among women than in men. This data correlates with previous reported data (15). BMI≥ 30 kg/m^2 is associated with increased CD4 Lymphocyte count and decreased viral load as what was reported previously (15). The prevalence for obesity for this study (16.8%) was higher than that reported for patients on HAART at 14% (15).

However, the prevalence for obesity for women (20.9%), for the ages between 35 and 44 years, for this study group is much lower than that of the reported 35.4% obesity for women between the ages of 35-44 years in general population for South Africa (29). The prevalence for obesity in the Gauteng province was found to be 30.1% in 2003 (29), which is also higher than the prevalence for this study group. In 2003 the SADHS reported that obesity in South Africa was more prevalent among older women and men and that the prevalence among women, African, Coloured and Asian were most likely to be equal to be obese (29). Due to the race composition of the patients JHBH HIV clinic it was not possible to affirm these findings.

5.5 HYPERTENSION

Hypertension in South Africa is a very common condition and is a risk factor for cardiovascular diseases. According to the second South Africa Demographic and Health Survey (SADHS 2003), the total national prevalence of hypertension in men was 40% and 51% in women for the age group 15 and older and the prevalence for the Gauteng province was 9.2% for men and 21.2% for women (29).

HIV infected patients are at a higher risk of developing hypertension compared to the general population (30). Patients were classified as hypertension when they had a blood pressure reading (BP) ≥140/90 mmHg and / or were on hypertension medication. The data for this study indicates

that 16% of the study population met this criterion and is therefore said to be hypertensive. This prevalence of hypertension in this HIV infected patients is much lower than the 29% that what was previously reported for HIV positive patients (30). More men (17.9%) than women (16.03%) were classified as being hypertensive. This study found that 7 (2.3%) of this study population was undiagnosed for hypertension as they were not on anti-hypertension medication.

The prevalence of hypertension in this study group was lower for women (15%) and higher for men (24%) than that found in the general population of South Africa, where the national prevalence for women and men between the ages of 35 and 44 were, 18.8% and 8.8% respectively (28;29). The prevalence is higher for men in the Gauteng province where the prevalence was 9.2 % for men and still lower for women where the prevalence were 21.3% in 2003 in the same age category (29).

5.6 DYSLIPIDAEMIA

Lipid metabolism abnormalities have been increasingly recognized among HIV-infected patients treated with HAART (1;26). Dyslipidaemia is therefore very common among HIV positive people that are on (HAART) (27;39) and the prevalence ranges between 33% and 82% (26;27). The prevalence of dyslipidaemia in our study group ranges between 10% for LDL > 4.1 mmol/l and 58% for HDL<1.29 in women. The prevalence of triglycerides>1.7 mmol/l was 34% compared with the documented prevalence ranges between 43% and 66% (3;27). Data from a prospective cohort study reported that 19% of patients develop hypertriglyceridedaemia and 24% of patients develop hypercholesterolemia after 5 years of HAART (3). In the current study the prevalence for hypercholesterolemia is 35%. This prevalence is much higher than the reported 19.4 % for Black Africans in South Africa (43). The data for this study did not find any association between CD4 lymphocyte count or HIV viral load and lipid abnormalities. This is also a reinforcement of previous reported data (27;39).

The presences of lipid abnormalities in this study were more prevalent in women than in men.

The prevalence for dyslipidaemia in South Africa has not been determined in a random population sample through national surveys (25). Various studies have been conducted in smaller regional surveys (25); however the data was not used to draw any comparisons as these regions were all outside the province of Gauteng.

5.7 METABOLIC SYNDROME

Metabolic syndrome which is affecting the general population in epidemic proportions is commonly associated with increase cardiovascular risk (34). By using the IDF criteria for metabolic syndrome, 20.4% of the patients can be classified as being positive for metabolic syndrome. Many patients who were not classified as having metabolic syndrome had at least two metabolic syndrome components, including low HDL and BP ≥ 130/85 mmHg but did not meet the criteria for the waist circumferences. Women had a higher prevalence of metabolic syndrome than men.

The prevalence of metabolic syndrome, among HIV positive patients, in an international cohort study, was reported at 14% using the IDF criteria and 18% using the NCEP (ATP) III criteria (6). The prevalence for metabolic syndrome in this study group is much higher than the reported data for HIV patients (6;37).

The data suggest that age and female gender is associated with the development of metabolic syndrome among HIV patients on HAART. CD4 count had a near significant association, while viral load and period on HAART had no significant association with the development of metabolic syndrome.

By comparing this findings with that of prevalence studies done in the general population of South Africa the prevalence according to the IDF criterion was lower 20.4% vs. 24.8% (37;44).

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

This chapter concludes the research report and draws conclusion from the research data in relation to the aim of the study and makes recommendations regarding the need to test HIV positive patients for metabolic related disease. The limitations of the study are also articulated and recommendations for further studies that stems from the limitations is also made.

6.1 CONCLUSIONS ACCORDING TO THE OBJECTIVES OF THE STUDY

The following conclusions are made according to the findings of this study:

Objective 1: Determination of the prevalence of metabolic diseases (hypertension, diabetes, obesity and dyslipidaemia) in patients attending the HIV clinics at JHBH

This study found that the prevalence of diabetes mellitus is 1%, hypertension is 16%, obesity is 16.8%, and hypercholesterolemia is 35.5% among HIV positive patients in the age group 18 to 45 years and on HAART medication for more than one year.

Objective 2: Determination of the prevalence of metabolic syndrome among patients attending the HIV clinics at JHBH

This study found that the prevalence of metabolic syndrome, according to the IDF criteria, is 20.4% among HIV positive patients that is on HAART medication for more than one year and between the age of 18 and 45 years.

Objective 3: Determination of the association between specific risk factors (such as: age, gender, CD4 lymphocyte count, viral load) and metabolic syndrome in HIV infected patients

This study found that the development of metabolic syndrome was positively associated with age and that female gender has a greater chance of developing metabolic syndrome. CD4 had a near significant association. However viral load and the period on HAART had no significant association with the development of metabolic syndrome.

6.2 LIMITATIONS

The findings of this study may not be generalisable to all age categories and all racial groups, as the majority of the sample were mainly black African females.

Metabolic syndrome for this study was defined without fasting glucose tests done for the patients and was determined based on the remaining parameters, i.e. waist circumferences, low HDL, elevated plasma triglycerides and BP ≥ 130/85 mmHg.

Furthermore, there were no age and sex match controls included i.e. patients that were HIV negative and patients that were HIV positive, but not on HAART.

6.3 FURTHER RESEARCH

The following is proposed for further research:

1. A randomized control study to compare a) HIV positive patients on HAART with b) HIV positive patients without HAART medication and c) HIV negative patients to estimate the true effect of HIV and HAART on the

prevalence of metabolic diseases and metabolic syndrome.

2. A longitudinal study among HIV patients on HAART to establish the incidence of metabolic diseases and metabolic syndrome.

6.4 SUMMARY OF THE STUDY

The findings of this research indicate that there is a high prevalence of metabolic syndrome among HIV patients that is on HAART for more than one year in this study group.

These metabolic diseases are negatively correlated with CD count and viral load and were more frequent in women than in men, except for hypertension. Literature review indicates that the development of metabolic disorders is associated prolong use of HAART in HIV positive patients.

It is therefore recommended that a longitudinal study needs to be conducted to monitor all patients on HAART, at the JHBH HIV clinic for metabolic disorders.

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APPENDICES

APPENDIX A: ETHICAL CLEARANCE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Julius

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M081154**
PROJECT	Metabolic Diseases amongst Human Immunodeficiency Virus (HIV) Positive Patients attending theJohannesburg Hospital
INVESTIGATORS	Mr HP Julius
DEPARTMENT	School of Public Health
DATE CONSIDERED	08.11.28
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 08.12.12 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr M Kawonga

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX B: PERMISSION FROM THE JOHANNESBURG ACADEMIC HOSPITAL

Private bag X39, Johannesburg 2000, South Africa
Tel: + 27 (0) 11 488 4911, Fax: + 27 (0) 11 643 1612
www.johannesburghospital.org

Gauteng Department of Health

Office of the CEO
Enquiries: M. Motjelele
(011): 488-3785
(011) 488-3753

22 December 2008

Attention: Mr. H. P. Julius

Dear. Mr. Julius,

RE: Permission to Undertake Research on metabolic diseases amongst Human Immunodeficiency Virus (HIV) positive patients attending the Johannesburg hospital

Permission is provisionally granted for you to conduct the above research as described in your request provided:

1. Ethics approval is obtained.
2. Johannesburg hospital will not in anyway incur or inherit costs as a result of the said study.
3. Your study shall not disrupt services at the study sites.
4. Strict confidentiality shall be observed at all times.
5. Informed consent shall be solicited from patients participating in your study.

Please liaise with the Head of Department and Unit Manager or Sister in Charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

I wish you success in your studies.

Yours sincerely

Dr. S. B. Mfenyana
Acting Chief Executive Officer

APPENDIX C: AMENDMENTS TO THE TITLE OF THE REPORT

Faculty of Health Sciences
Medical School, 7 York Road, Parktown, 2193
Fax: (011) 717-2119
Tel: (011) 717-2745

Reference: Ms Tania Van Leeve
E-mail: tania.vanleeve@wits.ac.za
13 May 2009
Person No: 0506409W
TAA

Mr HP Julius
3 Boles Street
Hamburg
Hoodepoort
1724
South Africa

Dear Mr Julius

Master of Public Health (Health Policy and Management): Change of title of research

I am pleased to inform you that the following change in the title of your Research Report for the degree of has been approved:

From:	**The burden of metabolic disease amongst HIV positive patients attending the Johannesburg Hospital.**
To	**The burden of metabolic disease amongst HIV positive patients on HAART attending the Johannesburg Hospital**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX D: DATA COLLECTION TOOLS

Patient Clinical Records (Data Collection Tool 1)

Study Number	Sex	Age	period on PI	BMI(kg/m^2)	Waist Circumferences (cm)	Blood pressure (mmHg)

Metabolic Profiles of HIV patients (Data collection tool 2)

Study Number	Random Glucose reading (mmol/l)	HBA1c	Total Cholesterol (mmol/l)	HDL-cholesterol (mmol/l)	LDL Cholesterol (mmol/l)	Triglycerides (mmol/l)	CD4 Count	Viral Load