2016

Association Between HAART and Metabolic Syndrome Components Among HIV-Positive Adults in Southeastern Nigeria

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Walden University
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Abstract

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MA, Michael Okpara University of Agriculture, 2004

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

November 2016

Abstract

Highly active antiretroviral therapy (HAART) contributes to metabolic disorders and the growing prevalence of metabolic syndrome (MetS) in human immunodeficiency virus (HIV)-infected patients. Hypertension, obesity, and hyperglycemia (components of MetS) are risk factors for cardiovascular disease. Studies have shown that HIV patients on HAART have a 2-fold risk of dying from MetS. There are no such studies in Umuahia; hence the need for this study to fill this gap. Using a sample size of 192 medical records of HIV-infected patients in Federal Medical Centre, Umuahia, and applying metabolic syndrome theory, this study examined the relationships among types of HAART regimen, duration of HAART and hypertension, obesity, and hyperglycemia among HIV-infected adult patients. The records were stratified into 4 by duration of HAART. Chi-square test was used to determine associations between the nonparametric variables, whereas multiple logistic regressions were used to estimate the odds ratios. Odds of hypertension were more than 18-fold (OR = 18.52, 95% confidence interval [CI] = 5.464, 42.50) at >12 months on HAART, whereas odds of obesity was more than 5-fold (OR = 5.43, 95% CI = 2.227, 13.158) at >12 months. Odds of hyperglycemia were more than 14-fold at >12 months compared with <12 months on HAART. Statistical significance was achieved with duration of HAART for hypertension and hyperglycemia ($p < .05$) but none with types of HAART ($p < .05$). Being male, older age, and duration of HAART were associated with odds of metabolic syndrome components. This knowledge provides a base for population-based intervention programs for the HIV-positive population undergoing antiretroviral therapy in the Umuahia metropolis.

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Acknowledgements

I would like to express my profound gratitude to God, the almighty for the protection and guidance throughout my studies. I would also like to offer my heartfelt appreciation to my committee chair, Dr. Wen-Hung Kuo, my committee member, Dr. Hebatullah Tawfik, and my URR member, Dr. Patrick Tschida for their mentorship and untiring guidance throughout my dissertation study. A big thank you goes to my husband and children for being very supportive, understanding, and encouraging during this journey.

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Chapter 1: Introduction

Access to highly active antiretroviral therapy (HAART) significantly reduced the rate of human immunodeficiency virus (HIV) infection-related mortality and morbidity (Berhane, Yami, Alemseged, Yemane, Hamza, Kassim, & Deribe, 2012). The advent of HAART in the management of HIV-positive patients in 1996 brought about a significant reduction in the annual mortality rates in the HIV-positive population from more than 29% to less than 2% in a space of 10 years (May, Sterne, & Costagliola, 2006). However, new concerns have arisen regarding the adverse effects of HAART on the metabolic system of HIV-infected patients (Muhammad, Sani, & Okeahialam, 2013). According to Muhammad et al., observed metabolic abnormalities such as hyperlipidemia, insulin resistance, high blood pressure, and fat redistribution constitute major risk factors for cardiovascular disease (CVD). These abnormalities are said to be components of the metabolic syndrome (MetS). However, variation exists in the risk factors by population characteristics and racial differences (Grundy, Cleeman, Daniels, Donato, Eckel, et al., 2005; Ngatchoua, Lemogouma, Ndobob, Yiagnignib, Tiogoub, et al., 2013).

I examined the relationship among HAART regimen and hypertension, obesity, and diabetes as metabolic syndrome components, and I examined the association among duration of HAART regimen and hypertension, obesity, and diabetes as metabolic syndrome components. The incidence of metabolic syndrome and CVD in the HIV-positive population can be reduced and prevented through informed population–based intervention programs if the right attention is drawn to these modifiable risk factors.

In this chapter, I introduce the study topic and the overview of the study. In the first section of this chapter, I summarize relevant, recent literature relating HAART with hypertension, obesity, and diabetes as metabolic syndrome components. I also provide insights into the problem addressed in this study, the purpose of the study, research questions, and the hypotheses. In the second section, I introduce the theoretical concepts that formed the framework of the study; I summarize metabolic syndrome theory; and I describe the nature of research, definitions, scope of the study, delimitations, and limitations. I also highlight the significance of this study for the advancement of public health through positive social change.

Background

HIV is a lentivirus of the retrovirus family. The acquired immunodeficiency syndrome (AIDS) virus infects the individual through various routes of transmission and then invades the host's immune system (Agyemang-Yeboah & Nkum, 2012). The infected person's immune system is thus compromised, thereby creating room for life-threatening opportunistic infections (Agyemang-Yeboah & Nkum, 2012). According to Agyemang-Yeboah & Nkum, the virus has the potential of surviving in body fluids and be transmitted from person to person.

Using anti-HIV drugs in the treatment of individuals infected with HIV is termed *antiretroviral therapy* (World Health Organization [WHO], 2014). The therapy is a cocktail of at least three drugs that reduces or suppresses the replication of the HIV. The combined therapy is popularly called HAART (WHO, 2014). A combination of three drugs is used to reduce the possibility of the virus developing resistance to the drugs

(WHO, 2014). Using cocktail of medicines confers the unique quality that can stop the HIV disease progression (WHO, 2014). The drug combination reduces the rates of disease progression and mortality in this population of patients, thereby improving the quality of life of these patients (WHO, 2014). Using HAART in HIV infection management has led to increased prevalence of diabetes mellitus, insulin resistance, lipoatropy, fat redistribution, dyslipidemia, hypertension, hepatic steatosis (Currier, 2014), and arterial stiffness (Ngatchou et al., 2013). These metabolic syndrome components in conjunction with other factors according to Stein and Hsue (2012) increase the risk for CVD.

According to Zhou, Wang, and Yu (2014), common pathways exist between CVD and metabolic syndrome that are shared by patients with metabolic syndrome. These pathways include defective glucose metabolism, increased oxidative stress, hypercoagulability, and endothelial damage. In addition, hypertension and insulin resistance are components of metabolic syndrome that most times coexist (Zhou, Schulman, & Zeng, 2012). Furthermore, insulin also induces vasorelaxation through stimulation of nitric oxide in the endothelium in addition to its metabolic effects (Zhou et al., 2012). Similarly, Schulman and Zhou (2009) demonstrated that insulin resistance contributed to the development of CVD and hypertension in cardiovascular tissues.

Several studies in the United States, Europe, and Canada investigated the incidences of CVD. The studies compared CVD in HIV-infected patients and persons without HIV infection (Chow, Regan, Feske, Meigs, Grinspoon et al., 2012) and CVD in HIV-infected patients on HAART and HIV-infected patients not on HAART (Durand,

Sheehy, Baril, Lelorier, & Tremblay, 2011; Freiberg, Chang, Kuller, Skanderson, Lowy et al., 2013; Lang, Mary-Krause, Cotte, Gilquin, Partisani et al., 2010). Their findings confirmed increased rates of cardiovascular events in HIV-infected patients who took HAART. In a similar study, the risk of heart attack and stroke was two to four times increased by hyperglycemia—a component of metabolic syndrome (Alberti, Eckel, Grundy, Zimmet, Cleeman et al., 2009). The management of chronic diseases such as diabetes mellitus, hypertension, and CVD in HIV-positive patients adversely affects the quality of life and increase the financial burden on the patient as well as the health care system (Centers for Disease Control and Prevention [CDC], 2013).

HAART and Metabolic Syndrome Prevalence

Due to the adverse metabolic effects such as increased blood pressure, dyslipidemia, and insulin resistance associated with HAART regimen, there have been reported cases of increased incidences of cardiovascular disorders in this group of the population (Guaraldi, Stentarelli, Zona, Orlando, Carli et al., 2010; Palios, Kadoglou, & Lampropoulos, 2012). Guaraldi et al. reported a 26% increase in risk for myocardial infarction in their study. Other reported adverse effects of HAART include arterial wall stiffness (Ngatchou et al., 2013) and coronary artery calcium (CAC) (Guaraldi et al., 2010). The reported adverse effects of HAART play a role in the development of atherosclerosis and increased risk for myocardial infarction (Guaraldi et al., 2010; Ngatchou et al., 2013). The growing concern for increasing prevalence of metabolic abnormalities and risk of CVD among HIV-positive patients on HAART has necessitated several observatory cohort studies (Durand, Sheehy, Baril, Lelorier, & Tremblay, 2011;

Guaraldi et al., 2010; Muhammad et al., 2013; Ngatchou et al., 2013; Omech, Sempa, Castelnuovo, Opio, Otim et al., 2012) to determine the prevalence of metabolic syndrome. The studies also established the relationship between HAART and metabolic syndrome components, and the incidence of CVD among the HIV-positive population. These studies on the prevalence of metabolic abnormalities and risk of CVD among the HIV-positive population validate reports that metabolic syndrome prevalence varies by population, race/ethnicity, and age (Muhammad et al., 2013; Ngatchou et al., 2013). Although the prevalence of metabolic syndrome may vary by race/ethnicity and increase with age, the studies showed that other modifiable risk factors vary within and between populations (Razzouk & Muntner, 2009).

In the United States, data from the National Health and Nutrition Examination Survey (NHANES) was used to monitor and estimate the U.S. population (Beltrán-Sánchez, Harhay, Harhay, & McElligott, 2013). Increased concern regarding the prevalence of metabolic syndrome has prompted the CDC to conduct series of cross-sectional studies every 2 years to assess prevalence rate of metabolic syndrome in the U.S. population (Beltrán-Sánchez, Harhay, Harhay, & McElligott, 2013). However, in Nigeria there are no such continuous studies that assess the prevalence rate of metabolic syndrome.

In the NHANES studies, during physical examinations, blood samples were collected and analyzed to determine the presence of metabolic syndrome components using the harmonized definition of metabolic syndrome that defined *metabolic syndrome* as the presence of three or more of the metabolic syndrome components (Alberti et al.,

2009). The results showed an estimate of 25% metabolic syndrome prevalence rate (Mozumdar & Liguori, 2011). A similar study conducted among a British cohort of middle-aged men estimated the prevalence of metabolic syndrome to be 26% (Wannamethee, 2008). The studies of Mozumdar and Liguori; Wannamethee have contributed in validating the reports that prevalence of metabolic syndrome varies between and within populations. Razzouk and Muntner (2009); Rosolova and Nussbaumerova (2011) also showed that there are different rates of disease progression and that metabolic syndrome is a marker for metabolic abnormalities. Furthermore, the studies by various researchers showed that there are arrays of designs and methods used to determine the prevalence and presence of metabolic syndrome in various populations (Alberti, Eckel, Grundy, Zimmet, Cleeman et al., 2009; Mozumdar & Liguori, 2011; Muhammad et al., 2013; Ngatchou et al., 2013; Wannamethee, 2008).

The growing increase in the prevalence of metabolic syndrome and its components has been attributed to physical inactivity, unbalanced food intake, and the use of HAART in the HIV-positive population (Paula, Falcão, & Pacheco, 2013). Thus, this study focused on a group of certain metabolic factors associated with risk for cardiovascular disease. These metabolic factors include high blood pressure, obesity, and elevated blood glucose levels, (Alberti et al., 2009). Thus, the presence of any three or more of the five factors (elevated blood glucose levels, abnormal blood lipid levels, elevated triglyceride, high blood pressure, and obesity) is termed *metabolic syndrome* (Alberti et al., 2009). Grundy et al. (2005) defined *metabolic syndrome* as the presence of at least three of the five of metabolic syndrome components: (a) elevated triglycerides

≥150; (b) low high-density lipoprotein cholesterol <40 for men <50 for women; (c) elevated blood pressure of ≥130/≥85 mm Hg; (d) fasting blood glucose >100 mg/dL; (e) body mass index (BMI) of ≥30 kg/m^2. However, only elevated blood pressure, elevated blood glucose, and obesity as metabolic syndrome components were employed in the study. Based on the guidelines of the National Cholesterol Education Program's (NCEP) Adult Treatment Panel (ATP) III, the following criteria were adopted in this study: (a) elevated blood pressure of ≥130/≥85 mm Hg or treatment for hypertensive; (b) fasting blood glucose >100 mg/dL, or antidiabetic treatment; (c) BMI ≥30 kg/m^2 (Anon, 1998; WHO, 2015).

The observations by the NCEP and other researchers (Guaraldi et al., 2010; Ngatchou et al., 2013) reported that metabolic syndrome is a multiple component risk factor for cardiovascular disease and it is, therefore, deserving of more attention, especially as it concerns diet and lifestyle in the HIV-positive population.

Problem Statement

The introduction of HAART in the management of HIV infection has significantly reduced morbidity and mortality rates in HIV-positive patients (Berhane et al., 2012). However, HAART has created a new burden of metabolic disorders that are risk factors for CVD in these categories of patients (Kiage, Heimburger, Nyirenda, Wellons, Shashwatee et al., 2013).

Metabolic syndrome is a major public-health and medical challenge that is on the increase globally (Alberti & Zimmet, 2005). In Africa, diabetes a component of MetS affects more than 14 million people, and it is expected that by 2030, 28 million

individuals will be affected (International Diabetes Federation [IDF], 2011). In Nigeria, reports showed that MetSprevalence rate among diabetic patients is more than 80% (Okafor, 2012). According to Alberti and Zimmet, metabolic syndrome patients have increased risk of myocardial infarction up to three- to 4-fold, of stroke up to two- to 4-fold, and a 2-fold risk of dying from these metabolic syndrome components.

HAART has been linked to the development of metabolic syndromes (Muhammad et al., 2013). According to Friis-Moller, Sabin, & Weber (2007) and Muhammad et al., metabolic syndrome components increases the risk of cardiovascular disease, heart attack, and stroke. Other known risk factors for metabolic syndromes include protease inhibitors (PIs); nucleosides reverse transcriptase inhibitor(s) (Wu et al., 2012); cigarette smoking; the effect of chronic inflammation related to the infection, and advancing age (Steinhart & Emons, 2004). PIs target the HIV-1 PR and inhibit its enzymatic activity thereby preventing the cleavage of the Gag and Gag-pol that bring about the production of noninfectious virus particles (Adamson, 2012).

In response to these emerging burdens of metabolic abnormalities among HIV-positive patients treated with HAART, several researchers conducted cross-sectional observational studies that observed that metabolic syndrome components are prevalent in HIV-positive patients on HAART (Alvarez, Salazar, & Galindez., 2012; Berhane et al., 2012; Hansen, Petersen, Haugaard, Madsbad, Obel et al., 2009; Muhammad et al., 2013; Omech et al., 2012;). In Nigeria, Muhammad et al. reported 21% prevalence of metabolic syndrome among HIV-positive patients on HAART. Wu et al. (2012) also found in their study conducted in Taiwan that a metabolic syndrome was developed in approximately

one quarter of HIV-infected patients on HAART. In Wu et al.'s study, 210 (26.2%) of 877 HIV-positive patients developed metabolic syndrome. The results also showed an association among prolonged exposure to HAART, PIs; nucleoside reverse transcriptase inhibitor(s), and metabolic syndrome OR of 1.78 (95% confidence interval [CI], 1.03–3.07), 1.96 (95% CI, 1.13–3.42), and 1.91 (95% CI, 1.11–3.30), respectively (Wu et al., 2012). Hansen et al. conducted a similar cross-sectional study in the department of infectious diseases, Hvidovre Hospital, Denmark. The results of the study showed that 27% of a total of 566 HIV-positive patients treated with various antiretroviral drug classes developed a metabolic syndrome (Hansen et al., 2009). Furthermore, Alencastro et al. in their cross-sectional study in southern Brazil also confirmed that metabolic syndrome was prevalent in southern Brazil. In the same vein, Friis-Moller et al. demonstrated in their data collection on adverse events of anti HIV drugs Data Collection on Adverse Events of Anti-HIV Drugs (DAD) study that association exists between antiretroviral therapies and cardiac risk factors (Friis-Moller et al., 2007). This reported association is partly responsible for the increase in the rate of myocardial infarction. Increased rate of myocardial infarction was demonstrated by an increase in relative risk (RR) for myocardial infarction with the use of protease inhibitor (1.16; 95% CI, 1.10–1.23; $p \leq .001$) after controlling for dyslipidemia, diabetes, and hypertension. Studies also showed that there is a greater risk of myocardial infarction and CVD in HIV-positive patients treated with HAART than are non–HIV-infected persons who are not on HAART (Friis-Moller et al., 2003; Triant, Lee, Hadigan, & Grinspoon, 2007; Grinspoon, 2009). The underlying causes according to Grinspoon are multifactorial that include risk

factors such as the effect of chronic inflammation related to HIV infection, adverse metabolic effects of antiretroviral therapy, and cigarette smoking (Grinspoon, 2009).

HIV infection activates the inflammatory pathways that change the endothelial cells to prothrombotic from their phenotype, which result in increased carotid intima thickness (Dagogo-Jack, 2008). This phenomenon occurs as a consequence of the direct activation of the endothelial cells by HIV and explains why HIV increases the risk for CVD (Dagogo-Jack, 2008). Similarly, in HIV-infected individuals, tumor-necrosis factor (TNF) Receptors 1 and 2, high sensitive C-reactive protein, and abnormal fat distribution contribute to impaired glucose homeostasis (Brown, Tassiopoulos, Bosch, Shikuma & McComsey, 2010). Metabolic dysfunction such as dyslipidemia, lipodystrophy, insulin resistant, and diabetes occur as a result of the administration of antiretroviral therapy (Dagogo-Jack, 2008).

Adverse metabolisms according to Steinhart & Emons (2004) lead to the development of hypertriglyceridemia, hypercholesterolemia, low high-density lipoprotein cholesterol levels, high low-density lipoprotein cholesterol level, insulin resistance, and hyperglycemia. These are components of metabolic syndrome and they present challenges in the treatment process, and also creates a burden on the finances of these individuals (Steinhart & Emons, 2004). Although several studies on metabolic syndrome in HIV-positive patients on HAART, and the risk of CVD has been conducted in Brazil, Denmark, Taiwan, the United States, Ethiopia, and Cameroon, similar studies are limited in Nigeria. A few studies in the northeastern and northwestern Nigeria examined the relationship between HAART and metabolic syndrome, with a view of its effect on

cardiovascular health in HIV-positive patients (Denue, Muazu, Gashau, Mbo, and Ajayi, 2012; Muhammad et al., 2013; Ogundahunsi, Oyegunle, Ogun, Odusoga, & Daniel, O. J., 2008). However, such studies are yet to be conducted in Umuahia metropolis. Hence, this study sought to fill this gap in the existing literature and examine the relationship between HAART regimen and hypertension, obesity, diabetes as metabolic syndrome components with a view to identifying the risk of CVD among HIV-positive adults 18 years and older on HAART in this study area (Federal Medical Centre, Umuahia,southeast Nigeria).

Purpose of the Study

The purpose of this retrospective quantitative study was to examine the relationship among HAART regimen and hypertension, obesity, and diabetes as metabolic syndrome components among HIV-positive patients 18 years and older, after ruling out the presence of these three variables at baseline. I also sought to examine the relationship among duration of HAART regimen and hypertension, obesity, and diabetes as metabolic syndrome components after controlling for age, gender, and CD4+ cell count. To determine the prevalence of hypertension, obesity, and diabetes as metabolic syndrome components among HIV-positive patients 18 years and older attending the clinic at the Federal Medical Centre, Umuahia Abia State, Nigeria, I used medical chart reviews including baseline data.

This study's findings will help identify cardio metabolic risk factors attributed to the side effects of antiretroviral therapy. I hope that this study will contribute to preventing additional burdens of chronic diseases such as hypertension, obesity, and

diabetes in the study population through intervention programs, and I hope the findings will help reduce the cost of health care; encourage positive, healthy lifestyles; and improve the quality of life of HIV-positive patients on HAART.

Research Questions and Hypotheses

I attempted to answer two main research questions and sub questions, with corresponding research hypotheses (H_a), and null hypotheses (H_0) as listed below.

RQ1: Type of HAART Regimen

RQ1A: Is there an association between HAART regimen and elevated blood pressure (hypertension) as a metabolic syndrome component among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

H_0: HAART regimen does not increase the odds of hypertension.

H_a: HAART regimen increases the odds of hypertension.

RQ1B: Is there an association between HAART regimen and obesity as a metabolic syndrome component among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

H_0: HAART regimen does not increase the odds of obesity.

H_a: HAART regimen increases the odds of obesity.

RQ1C: Is there an association between HAART regimen and elevated blood glucose level (hyperglycemia) as a metabolic syndrome component among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

H_0: HAART regimen does not increase the odds of hyperglycemia.

H_a: HAART regimen increases the odds of hyperglycemia.

RQ2: Duration of HAART Regimen

RQ2A: Is there an association between duration of HAART regimen and hypertension among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

H_0: Duration of HAART regimen does not increase the odds of hypertension.

H_a: Duration of HAART regimen increases the odds of hypertension.

RQ2B: Is there an association between duration of HAART regimen and obesity among HIV-positive patients 18 years and older in Umuahia, Southeast Nigeria?

H_0: Duration of HAART regimen does not increase the odds of obesity.

H_a: Duration of HAART regimen increases the odds of obesity.

RQ2C: Is there an association between duration of HAART regimen and elevated blood glucose (hyperglycemia) level among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

H_0: Duration of HAART regimen does not increase the odds of hyperglycemia.

H_a: Duration of HAART regimen increases the odds of hyperglycemia.

Theoretical Foundation and Conceptual Framework

Epidemiological studies are prompted by observations of events and phenomena that explore relationships between hosts (Kamanger, 2012). These could be chemical, physiological or biological factors. Epidemiological studies focus on looking for causes of diseases by linking exposures to risk of developing diseases (Kamanger, 2012). Thus, investigational studies involving infectious diseases such as HIV/AIDS focus on a single causal factor. However, the situation is different with chronic diseases that focus on the

relationship between several factors such as environmental, host behaviors, and physiological changes (McKenna & Collins, 2010). According to the University of Toronto (n.d.), HIV disease is also being viewed as a chronic, long-term disease that has been evaluated by the rising prevalence of disability among HIV-positive patients.

HIV is a multisystem infection that affects different systems of the body such as the cardiorespiratory, the musculoskeletal, and neurological systems (University of Toronto, n.d). HIV infection is further complicated by antiretroviral therapies including HAART, which cause undesirable side effects, thereby affecting the day-to-day activities and quality of life of HIV-positive patients (University of Toronto, n.d). As a result, to prevent or delay chronic diseases attributed to the side effects of HIV infections and antiretroviral therapy, it is recommended that intervention programs that include lifestyle and behavioral changes be developed (CDC, n.d.).

The physiologic changes that predispose infected patients to the development of CVD as a result of exposure to HAART are described by the metabolic syndrome theory (American Diabetes Association [ADA], n.d.). Metabolic syndrome theory is the foundation on which this study was based. Reaven (1988) proposed the metabolic syndrome theory first by describing the metabolic and physiologic changes observed in patients with diabetes type 2 diabetes mellitus (DM2) that leads to CVD. The syndrome is based on malfunctioning of insulin in the body system that results in insulin resistance. Furthermore, the observed association between obesity and hypertension attracted the inclusion of increased risk of hypertension in obese individuals in the metabolic syndrome theory. Also, Wilcox (2005) posited that changes in protein metabolism, fat

metabolism, and elevated blood sugar levels were responsible for insulin resistance. Thus, metabolic syndrome is characterized by elevated blood sugar levels, elevated blood pressure, enlarged waist circumference, elevated triglyceride levels, and low HDL cholesterol (Alberti et al., 2009; Wilcox, 2005). I discuss the metabolic syndrome theory further in Chapter 2.

The positivistic theoretical approach that uses deductive reasoning was also a framework for this study (Institute of Medicine [IOM], 2003a, p. 2). I discuss this topic further in Chapter 2. The deductive reasoning focuses on the relationships between variables such as the environment and the individuals' health (Liehr & Smith, 1999). These approaches promote the identification of challenges encountered in the treatment process and encourage the development of programs that promote positive behavioral changes that lead to healthy lifestyles.

Nature of the Study

This study was a quantitative, cross-sectional study. Quantitative studies focus on establishing relationships between the independent and dependent variables (Creswell, 2009). This study is in line with the focus of quantitative studies to determine the prevalence of hypertension, obesity, diabetes as metabolic syndrome and examined the association among HAART regimen and hypertension; HAART regimen and obesity; and HAART regimen and diabetes among HIV-positive patients 18 years and older in Umuahia, southeastern Nigeria. This study used the observational study design and cross-sectional data collection method. This study was a retrospective study of prospectively collected data of HIV-positive patients 18 years and older managed for HIV infection

between January 2009 and January 2013 at the Federal Medical Centre, Umuahia, Abia State, Nigeria. According to Hess (2004), in retrospective studies, the baseline state, intervention, and outcome are collected from existing data collected for purposes other than the study. I used the observational study design because it is a quantitative option that enables the comparison of pre-existing groups (HAART and non-HAART) retrospectively without doing any intervention (Al Amoor, 2013). I chose a cross-sectional design because the study determined the prevalence of hypertension, obesity, and diabetes as metabolic syndrome components, and I collected samples from the population at the one-time point only (Crosby, Diclemente, & Salazar, 2006). The secondary data of patients' treatment record included information at baseline before antiretroviral therapy (ART) initiation, previous laboratory results, ART history, clinical manifestations of metabolic syndrome, and sociodemographic characteristics. The methods used for the study was adapted from the studies of Berhane et al. (2012); Denue, Muazu, Gashau, Mbo, & Ajayi (2012); Diouf, Cournil, BaFall, Ngom-Gueye, Eymard-Duvernay et al. (2012); Muhammad et al. (2013); and Tadewos, Addis, Ambachew, & Banerjee, (2012). I discuss the methods in detail in Chapter 3.

I divided my target population into four strata (those cases not on HAART, those on HAART for 6 months, 12 months, and those on HAART for >12 months) from where I collected my samples. I used the pre or non-HAART cases as controls. The proportionate stratified random sampling was employed. This stratified technique required dividing the population into subgroups or strata, and then the final subjects selected consecutively from the different strata (Explorable.com, n.d.).

Using the G*Power 3.1.9.2 statistical power analysis software, the *z* test, logistic regression statistical test, binomial distribution, a power of 0.80, α of 0.05, and effect size (as odds ratio) of 2.333333, I calculated the sample size to be 186. I made up the sample size to 192 and then allocated 48 subjects to each stratum (Berhane et al., 2012). I chose the effect size as odds ratio because the dependent variable in the study is binary (Wilson, 2015).

I used Statistical Package for Social Sciences (SPSS) version 23 to analyze my data, and I used descriptive statistics to determine the prevalence of metabolic syndrome components. Furthermore, I used multiple logistic regressions to examine the association between HAART regimen and the metabolic syndrome components. I used multiple logistic regressions because according to Szklo and Nieto (2014), multiple logistic regression is used to examine relationships between the predictor variables, and the outcome (dependent) variables while allowing the control for possible confounders. Multiple logistic regressions are also used when the dependent or outcome variable is binary (Szklo & Nieto, 2014). In this study, the outcome of interests is presence or absence of hypertension; presence or absence of obesity; presence or absence of diabetes mellitus.

The *metabolic syndrome components* (hypertension and diabetes) were defined according to the guidelines of the National Cholesterol Education Program (NCEP) ATP III (Grundy, et al., 2005), whereas *obesity* was defined according to WHO (2015) criteria. The following criteria were used: (a) elevated blood pressure of ≥130/≥85 mm Hg or treatment for hypertensive; (b) BMI ≥25kg/m^2 is overweight; BMI ≥30kg/m^2 are obese;

(c) fasting blood glucose >100 mg/dL, or antidiabetic treatment. The dependent variables (hypertension, obesity, diabetes) were categorized as presence = yes or absence = no. The independent variables were categorized as pre-HAART, HAART regimen at 6 months, HAART regimen at 12 months, and HAART regimen >12 months. The measures included fasting blood glucose test, blood pressure measurement, and weight and height measurements. I included age, gender, and CD4+ cell count as confounding variables.

Statistical significance of odds of those with metabolic syndrome components and those without a component were determined by $p < .05$ and 95% CIs. Rejection of the null hypotheses supported statistical significance for hypertension, obesity, and diabetes. I provided details of the methods in chapter three.

Definitions

I used the following definitions in this study:

Highly active antiretroviral therapy (*HAART*): A cocktail of a minimum of three classes of antiretroviral drugs─PIs, nonnucleoside reverse transcriptase inhibitors (NNRTIs), and nucleoside reverse transcriptase inhibitors (NRTIs).

Metabolic syndrome (*MetS*): MetS is a combination of any three of the five metabolic syndrome components (hyperglycemia, hypertension, hypertriglyceridemia, low HDL cholesterol, and central obesity) (Grundy et al., 2005).

Hyperglycemia: *Hyperglycemia* as defined by the ATP III guidelines is elevated blood glucose level above 100 mg/dL (NCEP, 2002).

Hypertension: *Hypertension* as defined by ATP III guidelines is elevated blood pressure greater or equal to 130/85 (NCEP, 2002).

Obesity: *Obesity* was defined as BMI ≥ 30 kg/m^2 (WHO, 2015).

Assumptions

The first assumption in this study was that data is an accurate representation of the HIV population in Umuahia metropolis because of the location of the study center, and the population of clientele that patronizes the center (Federal Medical Centre, Umuahia). The hospital is a tertiary hospital that has an antiretroviral therapy clinic (ART clinic) that serves as a referral center for several communities, from where patients requiring ART care are referred (FMC Umuahia, 2014). The second assumption was that data on hypertension, obesity, and diabetes would be available in the patients' treatment charts in the medical records (FMC Umuahia, 2014). Laboratory test results were abstracted directly from the medical records. A third assumption was that blood pressure, weight, height, and blood glucose level tests were measured at baseline and thereafter. A fourth assumption was that blood glucose tests results were documented with the fasting test status according to the WHO recommendation (WHO, 2006).

Scope and Delimitations

This study was limited to and dependent on previously collected data from patients' treatment records to establish the prevalence of hypertension, obesity, and hyperglycemia; and the relationship between HAART and diabetes, HAART and obesity, and HAART and diabetes. In addition, the study was dependent on information documented during the examination at baseline. This study was further limited to the frequency of laboratory investigations in line with the frequencies of patients' visits to the clinic. With regard the dependent variables (hypertension, obesity, and diabetes); the

study was limited to the definition by ATP III and WHO guidelines, as well as the antiretroviral drug combination used in the facility. The study was also limited to markers of metabolic syndrome components such as hyperglycemia, and hypertension, as well as the CD4 cell counts, weight measurements, and height measurements. Covariates were limited to gender, age, and CD4+ cell count.

The study population included HIV-positive patients 18 years and older who attended the ART clinic in FMC, Umuahia, southeast Nigeria between January 2009 and December 2013. The outcome of this study may be generalizable to the infected population in Nigeria. Muhammad et al. (2013) used the HAART regimens that are mostly used in sub-Saharan Africa in their study. They reported that their cohort study was representative of the participating community. Similarly, this cohort study will use the same HAART regimen.

Limitations

The limitations that apply to retrospective cohort studies also apply to this study. Also applicable are the limitations that apply to medical chart reviews (Hess, 2004; Wang et al., 2010). These limitations include reliance on information provided by patients on family history and accuracy of documented records of patients. These could lead to recall bias. In addition, incomplete critical data such as laboratory test results could be a limitation in this study (Hess, 2004); selection bias as a consequence of the relationship between exposed and unexposed patients to the outcome of interest (Aschengrau & Seage, 2008, p. 267). According to Aschengrau and Seage, in retrospective cohort studies, selection bias occurs when the outcome of interest is related to the exposed and

unexposed individuals. Other limitations would include difficulty in controlling confounders and bias as a result of nonrandomization and blinding (Hess, 2004). However, these limitations can be managed. To minimize loss of validity and loss of reliability caused by selection bias, I used the same criteria for the selection of cases and controls, and I managed bias due to nonrandomization by using a control group made up of individuals with diseases (Aschengrau & Seage, 2008, p. 282).

Significance

This study is unique because it addressed an area of research that focuses on the relationship between HAART and metabolic syndrome components, which has been understudied in southeastern Nigeria. The burden would be enormous if HIV-infected individuals come down with other chronic diseases such as hypertension, diabetes or hyperlipidemia that are characteristics of metabolic syndrome, and risk factors for CVD (Palios, Kadoglou, & Lampropoulos, 2012). In addition, having to treat the additional chronic illnesses not only poses problems in the treatment process but can be an enormous financial burden for the individual (CDC, 2013). Thus, the results obtained in this study could provide insights into the factors that contribute to developing metabolic syndrome in HIV-infected individuals, with a view of developing intervention programs on lifestyle changes (diet and exercise) to prevent metabolic syndrome while on antiretroviral drugs. These intervention programs could minimize the risk for cardiovascular disease, reduce patients' medical expenditures, and cost of health care generally, thereby promoting positive social change by improving the quality of life of these groups of individuals.

Summary

The management of infected patients and reduction of HIV/AIDS epidemic in the developing nations using HAART is not without a price (Denue et al., 2012). The price includes metabolic abnormalities. These lead to certain risk factors for CVD (Paula et al., 2013). Metabolic syndrome components (hypertension, obesity, diabetes, elevated triglycerides ≥150 mg/dL, low HDL cholesterol <40 mg/dL in men, <50 mg/dL in women) are increasingly becoming important factors in the treatment of HIV-positive patients globally (Paula, Falcão, & Pacheco, 2013; Subbaraman, Chaguturu, Mayer, Flanigan, & Kumarasamy, 2007). Wu et al. (2012) found in their study that a metabolic syndrome was developed in about a quarter of HIV-infected patients on HAART. However, there may be variations in the distribution of the adverse effects of metabolic syndrome between developed and developing nations (Subbaraman et al., 2007). These differences distribution are due to host genetic makeup (Subbaraman et al., 2007), diet, physical inactivity, and obesity (Paula et al., 2013) as independent risk factors for metabolic syndrome. Although there is the consensus that metabolic syndrome components are modifiable and associated with HAART regimen and cardiovascular disease, several studies showed that the relationship between HAART and metabolic syndrome components differs in diverse populations and regimen (Razzouk & Muntner, 2009; Rosolova & Nussbaumerova, 2011; Wu et al., 2012). Identification of risk factors could form the basis to develop and provide intervention programs for the target population. Thus, this study examined the relationship between types of HAART regimen and hypertension, types of HAART regimen and obesity, and types of HAART regimen

and hyperglycemia. The study also examined the relationship among duration of HAART regimen and hypertension, duration of HAART regimen and obesity, and duration of HAART regimen and hyperglycemia among HIV-positive adults 18 years and older in Umuahia, southeastern Nigeria. I conducted this study with a view of identifying the risk of CVD in HIV-positive adults on HAART in this study area to inform preventive interventions that could promote positive social change. The prevalence of hypertension, obesity, and diabetes was also determined.

I review the literature that includes the framework that directed the study in Chapter 2. I also discuss studies that demonstrate the prevalence of hypertension, obesity, and diabetes among the HIV-positive population on HAART in Chapter 2. In addition, I review recent literature that demonstrates the association among HAART, hypertension, hyperglycemia, and obesity as metabolic syndrome components in Chapter 2. Furthermore, I discuss in detail studies that used secondary data and I describe their methods in Chapter 2.

Chapter 2: Review of the Literature

HAART considerably increases the risk for MetS and CVD in HIV-infected patients (Kiage et al., 2013; Tadewos et al., 2012). The prevalence of metabolic disorders is on the increase (Berhane et al., 2012; Muhammad et al., 2013). The increasing prevalence has made management of HIV infection with HAART a cause for concern globally (Paula et al., 2013; Subbaraman et al., 2007). Risk factors for metabolic syndrome components include HAART regimen, duration of HAART regimen, age, and gender (Grinspoon, 2009). Other modifiable risk factors for metabolic syndrome components include smoking status, physical inactivity, diet, and obesity (Paula, Falcao, & Pacheco, 2013). Cross-sectional studies confirmed that metabolic syndrome components are prevalent among HIV-positive patients on HAART in Nigeria (Muhammad et al., 2013) and other developing nations (Berhane et al., 2012; Malangu, 2014; Tadewos et al., 2012). However, there has not been any study on the analysis of the relationship between HAART and metabolic syndrome in this study population in Umuahia metropolis to date.

The purpose of this study was to: (a) examine the relationship among types of HAART regimen and hypertension, obesity, and diabetes mellitus among HIV-positive patients 18 years; (b) examine the relationship between duration of HAART regimen and hypertension, obesity, and hyperglycemia as components of metabolic syndrome among HIV-positive patients 18 years; (c) determine the prevalence of hypertension, obesity, and hyperglycemia as components of metabolic syndrome among HIV-positive patients

18 years and older attending the clinic at the Federal Medical Centre, Umuahia southeast Nigeria.

In this literature review, I present the hypothetical model approach that promotes the approach to the practice of public health (Institute of Medicine [IOM], 2003). This approach provides the foundation for the application of theories at the individual level and the population level (IOM, 2003). In the hypothetical model, it is assumed that all exposures and disease outcome are linked (IOM, 2003). In this chapter, I present the metabolic syndrome theory that explains the relationship among HAART, hypertension, obesity, and hyperglycemia, and the relationship among duration of HAART regimen, hypertension, obesity, and diabetes mellitus (American Diabetes Association [ADA], n.d.).

I review studies that demonstrate the prevalence of hypertension, obesity, and diabetes mellitus as components of metabolic syndrome among the HIV-positive population on HAART. Recent literature that demonstrates the association between HAART, hypertension, obesity, and diabetes mellitus as components of metabolic syndrome are discussed as well in this chapter. Details of studies that used secondary data and that described their methods are also reviewed in this section. The dependent variables are hypertension, obesity, and hyperglycemia (presence or absence of each of the variables). The independent variables are HAART regimen and duration of HAART regimen (HAART at 6 months, HAART at12 months, and HAART >12 months). Confounding variables include age, gender, and CD4+ cell count. I also discuss the gaps in knowledge and how this study proposes to address the gaps and improve the overall

health of HIV-positive patients on HAART in this chapter. Finally, I summarize the sections of Chapter 2 in the summary section.

Literature Search Strategy

Search strategies used for this literature review included peer-reviewed journal articles retrieved from Google advanced search engine, published lectures, dissertations retrieved from Walden University Library, and databases such as PubMed, MEDLINE, and Cumulative Index to Nursing & Allied Health Literature (CINAHL). Key search terms included *prevalence*, *HAART*, *diabetes*, *metabolic syndrome*, and *HIV-infection*. The search terms were used individually as well as in combinations. Only peer-reviewed articles from databases that returned abstracts of articles in the past 5 years with search key terms were included. Using the previous 5 years range was to ensure relevant reviews. However, articles from databases that returned abstracts beyond five years related to theoretical framework and constructs were included. The search was further narrowed down by adding the words Umuahia, Abia state Nigeria. Queries of peer-reviewed articles 2009 and beyond that returned recent relevant studies related to the prevalence of diabetes, hypertension, obesity, metabolic syndrome, HAART, and HIV infection were included. Further scanning of article titles returned several other relevant articles for full-text reviews with authors, references, and publications.

Theoretical Foundation and Conceptual Framework

The first step in identifying factors that affect health is by conducting epidemiological studies which are prompted by observational phenomenon and events (Kamanger, 2012). These events could be triggered by biological, chemical, or

physiological factors found in the physical environment. As a result, observational studies focus on exposures and disease occurrence by exploring the different associations found among variables. The associations include the relationship between disease-causing agents, host and the environment (epidemiology triangle) as regards infectious diseases (Ferng, n.d., p 4). Conversely, as regards chronic diseases, the focus is on the physiologic changes of the host that occur as a result of the relationship between host behavior and the environmental factors (McKenna & Collins, 2010). A combination of theories that include the "systems theory" and the metabolic syndrome theory were used in this review.

The CDC's "systems theory" has its focus on understanding the fundamental interactions of all the different make-ups of the system (Ferng, n.d., p 5). The system is said to be made up of the agent, host characteristics, and environmental factors (epidemiology triangle) (Ferng, n.d., p 5). In this system, the agents are classified into biological, chemical, and physical; while the factors that affect the susceptibility of the individual to causative agents include gender, lifestyle, race, socioeconomic status, and age (Ferng, n.d., p 5). Furthermore, the theory of chronic diseases in the population is also supported by observational studies (IOM, 2003b). However, regarding chronic diseases, this theory provides the foundation that chronic diseases evolve from exposures to a combination of genetic, behavioral, and environmental factors (IOM, 2003b). The rates and types of chronic diseases may differ across populations due to genetic and behavioral characteristics peculiar to the different populations (IOM, 2003b). These various features play significant roles in influencing the disease risk factors in

populations, which in turn provoke series of events that leads to morbidity and mortality if not prevented. Hence, public health focuses on interrupting the chain of events that leads to morbidity and mortality through ecological epidemiology studies using exposure data (IOM, 2003b).

In summary, the "systems theory" examines the different components or factors that influence health at the population level (Ferng, n.d., p 5). Since individuals make up populations, the same environmental and societal factors affect individual behavior. Thus, social, economic status, age, ethnicity, geographic location, gender, and economic policies influence individual health by shaping individual behavior (Kaplan, 1989). Although there is knowledge on the theoretical concepts of individual health about population health, there is the need to close the gap that exists in the understanding of why there are variations in the rates of chronic disease (Kaplan, 1989). Researchers conducted epidemiologic studies to compare and contrast risk factors that are associated with chronic diseases in populations to fill this gap. Population level intervention programs that target reduction of chronic diseases are then developed based on the outcomes of the epidemiologic studies.

Metabolic Syndrome Theory

The metabolic syndrome theory is based on the clustering of metabolic abnormalities that increase the risk of CVD (Alberti et al., 2009; Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004; Mente, Yusuf, Islam, McQueen, Tanomsup et al., 2010). According to Reaven (1988), hypertension, dyslipidemia, and hyperglycemia are among several risk factors that cluster together in most cases. Reaven observed that this

type of clustering is a complex system composed of several individual risk factors for CVD, and named it Syndrome X. Reaven however excluded central obesity as a component of syndrome X. In contrast to Reaven's observation of the clustering of metabolic risk factors, other researchers used the term metabolic syndrome (Alberti et al., 2009; Grundy et al., 2006; Mente et al., 2010). Reaven postulated that insulin resistance underlies Syndrome X and then used the term "insulin resistance syndrome" (Reaven, 1988). After that, Reaven proposed that the clustering of metabolic syndrome components: increased levels of triglyceride, low levels of high-density lipoproteins, glucose intolerance, increased levels of low-density lipoproteins, and increased blood pressure increased the risk of CVD. Epidemiological studies showed that metabolic syndrome occurs in different ethnic groups (Stem, 1997; Zimmert, 1992).

Metabolic syndrome is characterized by elevated blood pressure (hypertension), hyperglycemia (elevated blood sugar levels), obesity, and dyslipidemia (abnormal lipid levels) (Alberti et al., 2009; Grundy et al., 2004; Grundy, 2006). In defining metabolic syndrome, several criteria that included clinical outcomes, therapeutic interventions, metabolic components, the risk for clinical outcomes, clinical criteria for diagnosis and pathogenesis were considered (Grundy et al., 2004). According to the National Cholesterol Education Program (NCEP) (2002), it was viewed that the main clinical outcome of metabolic syndrome is the CVD and that several risk factors were observed in persons that developed CVD (Grundy et al., 2004). The 1979 Framingham study showed that hyperglycemia and hypertension increased the risk for CVD (Kannel & McGee, 1979). Thus, a conclusion drawn from the Framingham study was that there is a greater

risk of developing adverse clinical conditions when multiple risk factors are involved than when only a single risk factor is involved (Framingham risk equation) (Grundy et al., 2004).

Abnormalities of adipose tissue, obesity, and insulin resistance are said to be potential causes of metabolic syndrome (Villamar, Albuja, & Salas, 2011). Independent factors such as molecules of hepatic origin, immunologic origin, as well as the vascular origin are also said to mediate metabolic syndrome components (Villamar, Albuja, and Salas, 2011). However, it is said that both genetic and acquired factors regulate each risk factor for metabolic syndrome. According to Grundy et al. (2004), metabolism of lipoprotein is strongly modulated by variations in the genes. These variations in genes result in the dyslipidemia being expressed in response to obesity or insulin resistance. In the same vein, blood sugar levels are regulated by the insulin-secretory capacity and insulin sensitivity. Other independent contributory factors that mediate metabolic syndrome components include hormonal changes, aging, and pro-inflammatory state (Grundy et al., 2004).

Reaven (1988) observed the association between elevated blood pressure and hyperinsulinemia. He also noted that there was an association between hypertension and obesity that was frequent (Reaven, 1988). This frequent association according to Reaven was attributed to fluid retention and increase in circulating catecholamine produced in hyperinsulinemia, as a result of the over stimulation of the sympathetic nervous system. On the other hand, Kaplan's attention was on the relationship between DM2 and body fat distribution (Kaplan, 1989). Kaplan attributed abdominal/central obesity or adiposity to

the association between DM2, body fat distribution, hypertriglyceridemia, and hypertension. Kaplan further argued that the incidences of DM2 and CVD are increased by abdominal obesity (Kaplan, 1989). Furthermore, Wang, Goalstone, and Drazin (2004), linked the limited ability of insulin to confer protection on blood vessels from forming atherogenic plaque to the association between hypertension and insulin resistance. According to Grundy et al. (2004), insulin resistance may lead to elevated blood pressure through different mechanisms. Also, production of low-density lipoprotein triglycerides is enhanced by hyperinsulinemia which subsequently increases triglycerides levels.

Definitions of *Metabolic Syndrome*

The WHO (1999) provided a working definition of metabolic syndrome as the presence of insulin resistance identified by: DM2, impaired fasting glucose or impaired glucose tolerance in addition to any 2 of the following: High blood pressure (≥140 mm Hg systolic or ≥90 mm Hg diastolic) and/or antihypertensive medication, plasma triglycerides ≥150 mg/dL (≥1.7 mmol/L), HDL cholesterol ≥35 mg/dL (0.9 mmol/L) in men or ≥39 mg/dL (1.0 mmol/L) in women, BMI ≥30 kg/m^2 and/or waist-hip ratio >0.9 in men, >0.85 in women, and microalbuminuria (Urinary albumin excretion rate) ≥20 µgm/minute (WHO, 1999). WHO defined *type 2 diabetes mellitus* as fasting glucose >126 mg/dl (7.0 mmol/L) and a 2-hour oral glucose tolerance test (2-h OGTT) ≥200 mg/dl (11.1 mmol/L); impaired glucose tolerance (IGT) as normal fasting and a 2-hour oral glucose tolerance test ≥140 mg/dL (7.8 mmol/L).

The International Diabetes Federation (IDF), 2006) defined metabolic syndrome based on the presence of increased waist circumference (abdominal obesity) in addition

to at least two of five of metabolic syndrome components. In defining abdominal obesity, IDF took the different ethnic groups into account. The European men whose waist circumferences are ≥94 cm (37 inches) and European women with waist circumferences ≥80 cm (31.5 inches) are considered as having abdominal or central obesity (IDF, 2006). However, central obesity was defined differently as waist circumference ≥102 cm (40 inches) in European men and ≥88 cm (35 inches) in European women; ≥90 cm (35 inches) in Asian American men and ≥80 cm (32 inches) in Asian American women by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) (American Heart Association, 2014). Similarly, Adult Treatment Panel (ATP) III (National Cholesterol Education Program (NCEP) (2002) defined metabolic syndrome as the presence of any three of the five components of metabolic syndrome without attributing any preference to any of the metabolic syndrome components. These observed differences in the definition of metabolic syndrome created challenges in the evaluation of the association between DM2 and metabolic syndrome within and across populations (IDF, 2006). However, the ATP III guidelines with ethnicity-specific values of waist circumference were adopted by most organizations to harmonize the criteria for defining metabolic syndrome (Alberti et al., 2009).

Table 1

New International Diabetes Federation Definition of Metabolic Syndrome Components

Metabolic syndrome components	Cut points
Elevated fasting plasma glucose	(FPG) ≥100 mg/dL (5.6 mmol/L) or treatment of previously diagnosed type 2 diabetes
Elevated blood pressure	systolic BP ≥130 or diastolic BP ≥85 mm Hg or treatment of previously diagnosed hypertension
Decreased HDL cholesterol	<40 mg/dL (1.03 mmol/L) in males <50 mg/dL (1.29 mmol/L) in females or specific treatment for the lipid abnormality
Elevated triglyceride	≥150 mg/dL (1.7 mmol/L) or treatment for abnormal lipid level
BMI	≥30 kg/m^2

Note. HDL= High density lipoprotein*, BP*= Blood pressure, *FPG*= Fasting plasma glucose, *BMI* = Body mass index.

Source: Adapted from International Diabetes Federation (2006)

Table 2

ATP III Definition of Metabolic Syndrome Components

Risk Factor	Measurement	Cut Points
Waist circumference central obesity[a]	Men	>102 cm (≥40 inches)
	Women	>88 cm (≥35 inches)
Elevated blood pressure[a]	Systolic blood pressure	≥130 mm Hg
	Diastolic blood pressure	≥85 mm Hg
Low HDL cholesterol[a]	HDL cholesterol	
	Men	< 40 mg/dl (<1.03 mmol/l)
	Women	< 50 mg/dl (<1.29 mmol/l)
Elevated triglycerides[a]	Triglycerides	≥150 mg/dl (>1.7 mmol/l)
Elevated fasting glucose	Fasting glucose	
	Current[b]	≥100 mg/dl (>5.6 mmol/l)
	Former[a]	≥110 mg/dl (>6.1 mmol/l)

Note. *ATP III* = Third Adult Treatment Panel, cm = centimeters, mm Hg = millimeters Mercury, mg/dl = milligrams per deciliter, HDL = high-density lipoprotein, mmol/l = millimoles per liter. [a]ATP III guidelines (National Cholesterol Education Program, 2002) [b]ATP III guidelines modified to meet American Diabetes Association guidelines
Source: (Alberti et al., 2009).

Definitions of *HAART*

HAART is defined as the use of two nucleosides or nucleotide reverse transcriptase inhibitor (NRTI/NRTI) in combination with a non-nucleoside reverse transcriptase inhibitor (NNRTI), the use of two NRTIs and a protease inhibitor (PI) or the use of three NRTIs (Department of Health and Human Services [DHHS], 2004).

Mechanisms of Action of HAART

Metabolic changes such as elevated blood pressure, dyslipidemia, and insulin resistance, which are components of metabolic syndrome, frequently been associated with individuals infected with HIV on HAART (Palios et al., 2012). These metabolic changes have resulted in a rise in the incidence of cardiovascular disorders among HIV-infected patients (Palios et al., 2012). According to Friis-Moller, Sabin, and Weber (2003), the use of HAART in HIV-infected patients has increased the risk of myocardial infarction by 26%.

The adverse effect of HAART on the arterial wall is said to be the underlying mechanism behind myocardial infarction in HIV-infected individuals (Hsue, Hunt, & Wu, 2009). However, other reports have implicated HIV infection through chronic progressive inflammation, immunodeficiency, and endothelial cell dysfunction in the development of atherosclerosis (Francisci, Giannini, & Baldelli, 2009; Hsue, Hunt, & Schnell, 2009). It is, therefore, important to understand the underlying mechanisms of the HAART-induced metabolic syndrome to enable the designing of effective interventions to control cardiovascular diseases in this population.

The liver centrally regulates lipid homeostasis. It is also the first organ that ingested medicines including HAART come into contact (Zha, Studer, Zha, Hylemon, Pandak et al., 2011). The ApoE endocytosis pathway converts lipids into chylomicrons in the intestines, and finally ends up in the liver (Zha et al., 2011). Triglycerides (TGs) and cholesterol are packaged in the liver into very low-density lipoproteins (VLDL) for onward transport to peripheral tissues (Zha et al., 2011). Following lipase hydrolysis, VLDLs and TGs are then taken up by adipose tissue and muscle. The lipoproteins that are left known as intermediate density lipoproteins (IDL) are either converted to low-density lipoproteins by lipases or endocytosis by cells. Lipids and cholesterols are sent back to the liver by peripheral tissues to prevent overloading of LDL and signaling the liver to stop further production of VLDLs, proteins. However, this pathway is said to be affected by HAART (Zha et al., 2011).

The activation of the inhibition of sterol regulatory element-binding protein-1 (SREBP-1) in the liver, the protease-mediated breakdown of Apo lipoprotein-B, the formation of very low-density lipoproteins, and lipase activity reduction are the potential mechanisms underlying protease inhibitor (PI) associated dyslipidemia (Liang et al, 2001; Ranganathan & Kern, 2002). One of the side effects of HAART is insulin resistance (Palios et al., 2012). According to Haugaard, Andersen, and Storgaard (2004), PIs affect insulin sensitivity through the IRS-1 phosphorylation and glucose uptake from adipocytes. Insulin signaling is mediated by the protein Akt (Zha et al., 2011). But the insulin signaling action is inhibited by PIs which induce cellular insulin resistance. Furthermore, Lee, Rao, and Grunfeld (2005) found a decrease in peripheral glucose

uptake with PIs use. In the same vein, lipodystrophy causes impairment of insulin feedback on B-cells, resulting in the dysfunction of B-cell. Thus, increase in visceral fat and reduction in subcutaneous fat independently contribute to hyperinsulinemia and insulin resistance in HIV-infected patients on HAART (Palios et al., 2012). Lipolysis caused by antiretroviral drugs is also another way through which insulin resistance is developed in HIV-infected patients on HAART (Grinspoon, 2003).

Application of Metabolic Syndrome Theory (MST)

The application of metabolic syndrome is very apparent in several epidemiological studies (Beltrán-Sánchez et al., 2013; Berhane et al., 2012; Dimodi et al., 2014; Ervin, 2009; Feleke, Fekade, & Mezegebu, 2012; Mhlabi, 2011; Villamar et al., 2011; Wu et al., 2012). Metabolic syndrome has been applied to studies that examined relationships between HAART and hypertension, obesity, diabetes.

This study focuses on the relationship between HAART and Metabolic syndrome components (hypertension, obesity, diabetes). HAART causes malfunctioning of the metabolic system (Muhammad et al., 2013). HAART leads to insulin resistance and subsequently DM2 (Abebe, Kind, Belay, Gebreegziabxier, Challa et al., 2014). HAART also leads to abnormalities of adipose tissues that result in obesity (Villamar et al., 2011). Thus, adapting the MST will provide a good understanding of the relationship between HAART and hypertension, obesity, diabetes.

Prevalence of Metabolic Syndrome Components

The epidemiological construct of metabolic syndrome components in individuals living with HIV is associated with varying permutations of risk factors that present with

unique treatment strategies and clinical implications (Ferrannini, 2007). To assess the prevalence of metabolic syndrome and its components in populations, researchers apply the appropriate study design and methods such as cross-sectional study design used in this study. Cross-sectional studies according to (Crosby, Diclemente & Salazar, 2006) are used to determine the prevalence of disease within a population at a one-time point only. Researchers have raised concern over increased rates of metabolic syndrome and CVD in HIV-infected population, thereby making metabolic syndrome a major public issue (Biron, Bobin-Dubigeon, Volteau, Piroth, Perre et al., 2012; Ervin, 2009; Feleke et al., 2012). Researchers reported the prevalence of metabolic syndrome components among HIV-positive patients, and the relationship to HAART in several population-based cross-sectional studies (Beltrán-Sánchez et al., 2013; Berhane et al., 2012; Diouf et al., 2012; Feleke et al., 2012; Sachithananthan, Loha, & Gose 2012; Wu et al., 2012).

In Ethiopia, Sachithananthanet al. (2012) conducted a retrospective study and examined the prevalence of diabetes Mellitus, hypertension, and lipodystrophy in HIV patients receiving HAART in Sodo Government hospital in southern Ethiopia. Sachithananthan and colleagues recruited one hundred and seventy-six subjects from patients' electronic database and analyzed data using descriptive statistics, Chi-square, bivariate analysis, and multivariate logistic regressions. They recorded 8% (95% CI, 4.1–11.9) prevalence of diabetes mellitus and 15.9% (95% CI, 10.5–21.3) hypertension. They, however, found that the prevalence of hypertension (p = .007, COR: 5.73; 95% CI, 1.46–22.58) in those with Lipohypertrophy was significantly higher (Sachithananthanet al., 2012).

In a similar cross-sectional study in Senegal, Diouf et al. (2012) examined the prevalence of diabetes and hypertension, and the relationship between diabetes, hypertension and antiretroviral treatment among HIV-positive patients. The authors found that 28.1% of the 242 subjects had hypertension while 14.5% had diabetes. Using multivariate logistic regressions, they also concluded that there was an association between diabetes and long duration of ART (≥119 months), elevated cholesterol levels, increased BMI, and older age. They, however, found that high triglycerides levels, increased BMI, and older age were associated with increased risk of hypertension.

In Albania, Kolpepaj, Shkurti, Nake, Harxhi, Kolici et al. (2015) conducted a study that investigated the metabolic problems associated with HIV treatment; focusing on HAART –linked lipodystrophy and central obesity. The authors used multivariate analysis to examine the associations and found that alteration of adipocytes, amplified metabolic action in different adipose tissues, and imperfect lipogenesis, resulted to HAART-linked lipodystrophy.

Prevalence of Metabolic Syndrome Components in Developing Countries

According to Gaziano, Bitton, Anand, Abrahams-Gessel and Murphy (2010), there is an increase in the number of persons with metabolic syndrome components in developing countries in the past couple of decades. Gaziano et al.; Gersh, Sliwa, Mayosi, and Yusuf (2010); Mohan & Deepa (2006) observed the increase in the rates of morbidity and mortality caused by CVD. The prevalence of metabolic syndrome in developing countries as published by various studies ranged from 30.7% in Cameroon (Dimodi et al.,

2014), 15% in China, 19% in Malaysia 20% in Indian using the ATP III definition of metabolic syndrome (Mohan & Deepa, 2006).

In Cameroon, Dimodi et al. (2014) examined the prevalence of metabolic syndrome and its individual components among HIV-positive patients in a prospective cross-sectional study. The study was conducted with 492 infected patients 20 years and older on antiretroviral therapy. Findings of the study showed 32.8% and 30% prevalence of metabolic syndrome using the IDF and ATP III criteria respectively (p = .0001). They also found the prevalence of metabolic syndrome to be 36% and 23.4% in patients receiving HAART and HAART-naive patients (p = .0001) respectively (Dimodi et al., 2014). The prevalence of the individual components was: abdominal obesity (40.5%; 26.9% (IDF and ATP III respectively); hypertriglyceridemia (55.5%), low HDL cholesterol (42.5%), systolic hypertension (38.2%) diastolic hypertension (28.5%), and hyperglycemia (31.2%; 1.3% p = .0001) (Dimodi et al., 2014). The study established that prevalence of metabolic syndrome is dependent on the use of HAART, and the type of HAART used.

Similar results were reported by Wu et al. (2012). Wu and colleagues reported 26.2% metabolic syndrome of a total of 877 HIV-positive patients on HAART in a cross-sectional study conducted in a hospital in Taiwan. Wu and colleagues also reported an association between prolonged exposure to HAART, PIs, NRTIs, and MetS (OR, 1.78; 95% CI, 1.03–3.07); (OR, 1.96; 95% CI, 1.13–3.42), and (OR, 1.91; 95% CI 1.11–3.30) respectively (Wu et al., 2012).

Prevalence of Metabolic Syndrome Components in Developed Countries

The prevalence of metabolic syndrome in developed countries is similar to that in developing countries as observed by several researchers (Beltrán-Sánchez et al., 2013; Ervin, 2009; Hansen et al. 2009; Lauda, Mariath, & Grillo, 2011). Ervin (2009) studied the NHANES data from 2003 to 2006 that examined U.S adults 20 years and older as participants. Ervin reported metabolic syndrome prevalence of 34%, and that metabolic syndrome increased with age but differed by ethnicity. Ervin concluded that metabolic syndrome varied by population (Ervin, 2009). Hansen et al., in a similar study reported a metabolic syndrome prevalence of 27% in a retrospective HIV cohort study in Denmark. In the same vein, Lauda et al. (2011) reported a metabolic syndrome prevalence of 20.9% of which 18.5% were male, and 23.5% were female in a cohort of 249 HIV-infected individuals 18 and older in Brazil. These studies all point to the increasing burden of metabolic syndrome prevalence among the HIV-positive population, and that prevalence cut across race/ethnicity and region both in the developing and developed nations.

When compared with countries in the developed world, the extent and degree of adverse drug reactions related to HAART in developing countries have made the process of dealing with HAART toxicity pivotal in the care and management of HIV (Kumarasamy, VenKatesh, Cecelia, DeValeenal, Lai et al., 2008; Mills, Cooper, Seely & Kanfe, 2005). Though Wu et al. (2012); Berhane et al. (2012) reported an association between prolonged exposure to HAART and metabolic syndrome in Taiwan and Ethiopia respectively, Hansen et al. (2009) on the other hand, reported no association between the presence of metabolic syndrome and HAART duration in Denmark.

The severity of adverse effects could be related to the high prevalence of other underlying disease conditions such as tuberculosis, malnutrition, anemia, and the concomitant use of herbal medications with some individuals presenting with advanced HIV disease at their initial hospital visit in developing countries (Mills, Cooper, Seely, & Kanfe, 2005).

Effects of HAART on Blood Pressure

There is growing evidences that HIV-infected patients on HAART are at greater risk of heart disease and stroke as a result of elevated blood pressure (Arruda Junior, Lacerda, Moura, Albuquerque, Filho et al., 2010; Denue et al., 2012; Palacios et al., 2006). Blood pressure according to NHLBI (2011a) is the force the heart exerts to pump blood into the vascular system of the body. The heart is said to require more force to pump blood efficiently in the system when there is resistance in the vascular system (NHLBI, 2011a).

Investigations in Maiduguri, Nigeria affirmed the high prevalence (31.7%) of hypertension among HIV-positive patients on HAART (Denue, et al., 2012). Denue and colleagues examined the impact of HAART on blood pressure after two years of commencement of HAART in a cohort of 227 patients. They used $\chi 2$ test or Fisher's exact test to analyze categorical variables and used the paired Student's t-test to compare baseline data with data 2 years after commencement of HAART. The result showed a rise in blood pressure with time 3.47±15.21 vs. -0.71±16.28 (p = .08), 1.81±10.12 vs. 1.0±11.39 (p = .625) and 1.67±14.14 vs. 1.71±12.08 (p = .982). The authors thus suggested periodic measurement of blood pressure and treatment where necessary of

HIV-positive patients on HAART. Prevalence of hypertension with longer duration of antiretroviral use was also reported by Arruda Junior et al. (2010) in a study in Brazil. They also reported 25.6% hypertension prevalence, 14% pre-hypertension, and 40.5% normotension (controls) in the participants, and concluded that there is a need for measures to control factors such as unhealthy diet and excessive weight gain (Arruda Junior et al., 2010). Palacios et al. (2006), in a prospective study of 95 HIV-infected patients placed on HAART regimen reported 26% prevalence of hypertension. They recommended periodic measuring and treatment where necessary of HIV-infected patients on HAART.

Effects of HAART on Body Fat Distribution

Despite the benefits of HAART in reducing HIV levels in infected patients, exposure to HAART is said to affect body fat distribution in HIV-infected patients, and also increases the risk of CVD (Brown et al., 2009). The body store fat underneath the (subcutaneous fat), and in the viscera (Reaven, 2011). The subcutaneous fat provides insulation for the body, while the visceral fat provides a source of quick energy (Reaven, 2011). Abdominal adiposity (central obesity) is said to be associated with excessive accumulation of visceral fat and also associated with the metabolic syndrome (Reaven, 2011). WHO defined obesity based on the body mass index (BMI) (WHO, 2015). *Obesity* was defined as BMI $\geq$30kg/m^2, overweight as BMI $\geq$25kg/m^2, BMI 19-24.9kg/m^2 as the normal range, and BMI <19kg/m^2 as being underweight. BMI according to WHO (2015) is the weight of an individual in kilograms divided by the square of the individuals' height in meters (kg/m^2).

In Jimma, southwest Ethiopia, Berhane et al. (2012) evaluated the prevalence of lipodystrophy (fat metabolism disorder) and metabolic syndrome among HIV-positive individuals on HAART. They reported lipodystrophy prevalence of 12.1% in a sample of 313 HIV patients 18 years and older. The study also revealed that taking the antiretroviral therapy for 12 months and more was associated with metabolic syndrome male (AOR = 4.2; 95% CI = 1.24, 14.23) and female (AOR = 2.30; 95% CI = 1.0, 5.27). Berhane and colleagues also found that taking the antiretroviral therapy for the longer duration of 12 months and more was independently associated with HIV-lipodystrophy (AOR = 3.59; 95% CI = 1.03, 12.54) (Berhane et al., 2012).

Sharma, Bynum, Schneider, Cox, Tien et al. (2014) followed 1177 HIV-positive women in a prospective study for 15 years to examine changes in BMI after being initiated on HAART regimen. The authors used the multivariate mixed-effects ordinal logistic regression to estimate the degree of association of exposure with post-HAART BMI. Sharma and colleagues reported that 39% of the women had normal BMI before the commencement of HAART, but 40% of them became overweight, while 47% became obese, and 27% morbidly obese at some point. This point to the hypothesis that duration of HAART increases the odds of obesity

Effects of HAART on Glucose Metabolism

Glucose is a source of energy to body tissues, and a major factor in metabolism (Merriam-Webster, 2015). It is transported into tissue cells by insulin (Merriam-Webster, 2015). Insulin also regulates the amount of glucose that circulates in the body (Schneider, 2014). In situations when there is insulin resistance, insulin is unable to control the

amount of circulatory glucose, thereby resulting in elevated glucose in the blood stream resulting in diabetes mellitus (Schneider, 2014). Thus, elevated blood glucose is a marker for insulin resistance. Insulin resistance according to Bastard et al. (2006) determines the production of excess adipokine leading to dysfunction of the endothelia. The endothelial dysfunction leads to metabolic syndrome and diabetes mellitus with a progression of endothelial damage (Bastard et al., 2006). Thus, the progression of endothelial damage, as well as thrombosis and inflammation of the endothelia results in the production of atherosclerotic plaques in the wall of the vessels (Bastard et al., 2006).

Insulin resistance and increased rate of diabetes mellitus have been associated with HAART (Abebe et al., 2014; Brown, et al., 2005; Chukwuanukwu, Manafa, Ugwu, Onyenekwe, Oluboyo et al., 2013). In Nigeria, Chukwuanukwu et al. determined the prevalence of DM in HIV-infected patients on HAART using a sample of 150 patients. The patients were grouped into two groups of 50 patients each according to the drug regimen; first line drugs (lamivudine, nevirapine, combivir, combipack, and efavirenz); second line drugs (truvada and aluvida) and a third control group of 50 patients not on HAART. The authors reported a prevalence of 6% diabetes mellitus with the second line regimen, 0% prevalence with the first line regimen, and 10% prevalence of impaired glucose intolerance (Chukwuanukwu et al., 2013). Similar results were reported by Abebe et al. (2014) in Addis Ababa Ethiopia, where they examined the association between antiretroviral treatment and hyperglycemia and dyslipidemia among 126 HIV-infected patients on HAART in the Burayu health center. The results showed that hyperglycemia was 7.9% prevalent in the HAART initiated group and 5.6% prevalent in

the non-HAART group. However, they recorded no significant difference between HAART initiated and the HAART-naive group ($p = .45$).

Similarly, Butt, McGinnis, Rodriguez-Barradas, Crystal, Simberkoff et al. (2009) reported 21.4% ($p < .0001$) prevalence of diabetes in HIV-infected patients on HAART compared to 14.9% HIV-infected patients at baseline in the veterans aging cohort study (VACS) prospective study of 3,327 HIV-infected patients and 3,240 HIV-uninfected subjects (controls) in the U.S. They also reported that HIV was associated with the use of NRTI, NNRTI therapy and that NRTI; NNRTI therapy increased the risk for diabetes in HIV-infected individuals (Butt et al., 2009). These reports all support the hypothesis that HAART increases the odds of diabetes mellitus (hyperglycemia).

Metabolic Syndrome and Cardiovascular Disease

The risk for CVD is substantially increased by HIV infection and HAART (Kingsley et al., 2008; Triant et al., 2007). Cardio-metabolic outcomes in patients living with HIV infections and combination antiretroviral therapy have being established by several studies (Kingsley, Cuervo-Rojasc, Muñozc, Palellad, Post, Budoff, Kingsley, Palellad, Witt et al., 2008; Post, Budoff, Kingsley, Palella, Witt et al., 2014; Triant, Lee, Hadigan, & Grinspoon, 2007). The independent association of the aforementioned cannot be overemphasized as studies have established the association of HAART with insulin resistance, elevated serum triglycerides (TG), low-density total and lipoprotein cholesterol (TC & LDL-c) (Fontas, van Leth, Sabin, Friis-Moller, Rickenbach et al., 2004; Jones, Sawleshwarkar, Michailidis, Jackson, Mandalia et al., 2005; Passalaris, Sepkowitz & Glesby, 2000). Similarly, increases in the level of LDL-C has been reported

to be associated with the thickening of the arterial walls (atherosclerosis), CVD, coronary heart disease, and coronary artery disease resulting in myocardial infarction and stroke (Roger, 2011).

The relationship between metabolic syndrome and CVD has been demonstrated by several researchers in Nigeria (Muhammad et al., 2013), Zambia (Kiage et al., 2013), and Addis Ababa (Feleke et al., 2012). Muhammad et al. evaluated the cardiovascular risks among patients on HAART in a cross-sectional study of HIV patients placed on HAART for six months and above, and HAART naïve group in Aminu Kano Teaching Hospital, Nigeria. The researchers found that there was an increased proportion of cardiovascular risk in individuals placed on HAART. The incidence of hypertension in patients exposed to HAART was approximately eight times higher when compared to the non-exposed, 17% and 2% respectively ($p < .001$) (Muhammad et al., 2013). The study established significant correlations in cardiovascular risk factors such as metabolic syndrome, obesity and hypercholesterolemia in patients treated with HAART. Kiage et al. on the other hand conducted a retrospective study of 210 HIV-positive patients 16.5 - 60 years old using the dataset from the diet, genetic polymorphisms in lipid-metabolizing enzyme genes, and antiretroviral therapy-related dyslipidaemia (DGPLEAD) in Lusaka, Zambia from January to December 2007. The researchers found that there was an association between cardiometabolic risk markers and combined anti-retroviral therapy regimen; changes in cardiometabolic risk markers and duration of combined anti-retroviral therapy regimen. Furthermore, Feleke et al. (2012) explored the risk factors and prevalence of cardiovascular complications and chronic metabolic abnormalities in a

cross-sectional study in Addis Ababa. The authors reported the prevalence of hypertriglyceridemia as 15.2%, lipid density lipoprotein cholesterol as 54.2% and the prevalence of hypercholesterolemia as 38.2%. They also reported that the prevalence of hyperlipidemia was considerably high 56.9% (319) amongst study participants. Feleke et al. further established a significant association in the development of hypertriglyceridemia, lipohypertrophy and lipoatrophy in individuals exposed to HAART for duration of at least a year or more and reiterated the importance of monitoring adverse events in patients on HAART for metabolic abnormalities.

Summary

Metabolic syndrome is based on the premise that three or more of the five components are present (NCEP, 2002). Metabolic syndrome is composed of a combination of hypertension, obesity (central obesity), elevated blood sugar, and dyslipidemia. In this study, I used hypertension, obesity, and hyperglycemia as metabolic syndrome components. These components are risk factors for CVD. Although according to Reaven (2011), metabolic syndrome is not a risk assessment tool, it explains the relationships that exist between metabolic abnormalities and clinical outcomes.

Exposure of HIV-infected individuals to antiretroviral therapy predisposes them to abnormal glucose metabolism and dyslipidemia, with low HDL cholesterol and hypertriglyceridemia predominating in HIV-related metabolic syndrome (Fontas et al., 2004). Non standardization of measurement while capturing clinical details of patients give room for bias in the assessment of the prevalence of metabolic syndrome argued Worm, Friis-Moller, Bruyand, Monforte, Rickenbach et al. (2010). For this reason, Worm

et al. suggested that laboratory measurements be conducted two times consecutively and that prevalence of metabolic syndrome should be based on this in cohort studies.

Assessing metabolic syndrome components in populations can go a long way in determining the most prevalent component. This knowledge can help form the platform on which effective prevention and intervention programs that adopt lifestyle changes to reduce the prevalence of metabolic syndrome and CVD. I discuss in detail the methods used in this study to determine the prevalence of hypertension, obesity, and hyperglycemia; and examined the relationship among HAART, hypertension, obesity, and hypertension as metabolic syndrome components in Chapter 3.

Chapter 3: Research Method

This purpose of this retrospective quantitative study was to use medical records/treatment charts to examine the relationships between types of HAART regimen and hypertension, types of HAART regimen and obesity, and types of HAART regimen and hyperglycemia. The study's purpose was also, to examine the relationship between duration of HAART regimen and hypertension, duration of HAART regimen and obesity, and duration of HAART regimen and hyperglycemia. In addition, the purpose was to determine the prevalence of hypertension, obesity, and hyperglycemia among HIV-positive patients 18 years and older attending the clinic at the Federal Medical Centre, Umuahia, Nigeria.

I discuss the study design and methods in this chapter. I review the research questions and I provide the rationale for using descriptive statistics to determine the prevalence of hypertension, obesity, and hyperglycemia. In this chapter, I also explain why I used multiple logistic regressions to examine the relationship among HAART regimen, hypertension, obesity, and hyperglycemia.

Furthermore, I detail the study population, sample, and sample procedures, and I describe the data collection methods and data analysis. In addition, I discuss the measures I took to minimize bias and strengthen the internal and external validity in this section. I also explain the procedures I followed to gain access to data and protect the study participants.

Research Design and Rationale

My aim in this study was to answer two major research questions and a series of sub questions on the relationship among HAART regimen, duration of HAART regimen and hypertension, obesity, and diabetes as metabolic syndrome components.

RQ1: Type of HAART Regimen

RQ1A. Is there an association between types of HAART regimen and elevated blood pressure (hypertension) among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

RQ1B. Is there an association between types of HAART regimen and obesity among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

RQ1C. Is there an association between types of HAART regimen and elevated blood glucose level (hyperglycemia) among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

RQ2: Duration of HAART Regimen

RQ2A. Is there an association between duration of HAART regimen and hypertension among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

RQ2B. Is there an association between duration of HAART regimen and obesity among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

RQ2C. Is there an association between duration of HAART regimen and elevated blood glucose level among HIV-positive patients 18 years and older in Umuahia, southeast Nigeria?

The first question focuses on the relationship among HAART regimen and hypertension, obesity, diabetes as metabolic syndrome components. I used the quantitative research methods in this study. Quantitative methods use numerical data that are analyzed statistically to explain phenomena that occur in the world (Burns & Grove, 2005, p. 23.) According to Burns and Grove, this method is used to describe variables and determine cause-and-effect interactions between variables. Also, according to Creswell (2009), quantitative studies focus on establishing relationships between the independent and dependent variables. As in this study, HAART and duration of HAART are the independent variables, while hypertension, obesity, and hyperglycemia are the dependent variables). Also, to answer this question, the cross-sectional data that was collected at one point in time was the basis for determining the prevalence of hypertension, obesity, and hyperglycemia among HIV-positive patients in this study.

As indicated in Chapter 1 of this dissertation thesis, the quantitative option enables the comparison of pre-existing groups (ART and non-ART) retrospectively without doing any intervention (Al Amoor, 2013). According to Crosby, Diclemente and Salazar (2006), cross-sectional studies that use data drawn from the population at a one-time point only are used for prevalence studies. Furthermore, to establish whether HAART regimen increases the odds of high blood pressure, obesity, and hyperglycemia, the presence of HAART regimen before the onset of these metabolic variables, were observed. Likewise, the temporal association between the onset of high blood pressure, obesity, hyperglycemia and HAART regimen were confirmed by comparing the

prevalence of risk factors in the individuals who did and did not develop high blood pressure, obesity, and hyperglycemia (Nicholols, & Moler, 2010).

The second question is whether there is an association among duration of HAART regimen and high blood pressure, duration of HAART regimen and obesity, duration of HAART regimen, and diabetes as components of metabolic syndrome in the study population. Prevention programs can be strengthened if the focus is on reducing risk factors that can bring about enormous health problems. As a result, knowing whether the duration of HAART regimen increases the odds of hypertension, obesity, and hyperglycemia is necessary. Thus, understanding the risk factors that predict these metabolic syndrome components in HIV-positive patients in Umuahia will prevent or delay development of metabolic syndrome components in the study population, as well as enable population specific intervention programs to be brought closer to the community (Howard, Rodriguez, Bennett, Harris, Hamman et al., 2002).

Relationships among HAART and high blood pressure, obesity, and hyperglycemia were determined by the odds ratios and the respective *p* - values and 95% CIs for each independent variable. Independent variables include HAART regimen and duration of HAART regimen. The independent effects of each variable on these metabolic syndrome components were analyzed using multiple logistic regression models when other covariates were controlled. It was assumed that in multiple logistic regression analysis, the logit (natural logarithm of the odds of the outcome) changes linearly with multiple independent variables. Multiple logistic regressions also assume that the outcome is a binomial distribution (Katz, 2006). The assumption for a binomial

distribution was met in this study since the outcome was presence or absence of hypertension; absence or absence of obesity; presence or absence of hyperglycemia. Furthermore, to meet the second assumption of logit changes with multiple independent variables, I divided continuous variables such as age into categorical groups to create dichotomous variables. According to Katz, multiple covariates could be categorical or continuous.

Table 3
Study Variables

Variable type	Variable name	Potential response	Level of measurement
Dependent	Hypertension	Presence of hypertension = 1 Absence of hypertension = 0	Nominal
Dependent	Obesity	Presence of obesity = 1 Absence of obesity = 0	Nominal
Dependent	Diabetes	Presence of diabetes = 1 Absence of diabetes = 0	Nominal
Independent	HAART	Lam, stav, nvp = 1 Comb, nvp = 2 Comb, efv =3 Truv, efv = 4	Nominal
Independent	Duration of HAART	Pre HAART = 0 <6 months = 1 6–12 months = 2 >12 months = 3	Nominal
Covariate	Age	18–29 =1 30–50 = 2 >50 = 3	Nominal
Covariate	Gender	Male =1 Female = 2	Nominal
Confounder	CD4+ cell count	10–200 =1, 201–350 = 2 351–500 = 3, >500 = 4	Nominal

Note. HAART = Highly active antiretroviral therapy, Lam = Lamivudine, stav = Stavudine, nvp = Nevirapine, comb = Combivir, efv = Efavirenz, Truv = Truvada.

In this study, I used existing data from medical charts/ records of HIV-positive individuals. I sought permission from the Health Research Ethics Committee of Federal Medical Centre (FMC) Umuahia to access the medical records of the patients, to use data. Medical record review according to Wickson-Griffiths, Kaasalainen, Ploeg, and McAiney (2014) is a method used in collecting retrospective data, collecting data for research and occupational therapy for performance analysis and quality assessment. The retrospective methodology involves looking back in time into events (Panacek, 2007) as is the case in this study where I will be looking into the medical records of my study population. According to Hess (2004), in retrospective studies, the baseline state, intervention, and outcome are collected from existing data collected for purposes other than the study. Retrospective designs are useful when evaluating or assessing palliative and end -of-life care, and when it's hard or impossible to answer research questions prospectively (Hess, 2004).

Although the analysis of secondary data retrospectively eliminates the cost and time of designing, funding, and implementing compared to conducting prospective cohort studies; retrospective cohort studies do have some limitations or challenges (Wickson-Griffiths et al., 2014). Some of the limitations of medical chart review in retrospective studies include incomplete and inaccurate documentation, incomplete data, missing charts, lack of binding to the study purpose, and inconsistency in the coding of chart information (Wickson-Griffiths et al., 2014). These limitations according to Wickson-Griffiths et al. may threaten the overall validity and reliability of this study.

Population and Sampling

This study was conducted in the Federal Medical Centre (F.M.C) Umuahia, southeast Nigeria. F.M.C Umuahia is a 327-bed tertiary hospital centrally located and easily accessible. It is the only federal hospital in Abia state. The facility draws patients and clientele predominantly from the southeast and south-south part of the country (Nwadinma, 2013). The facility provides specialized services including HIV services for both outpatients and inpatients. HIV services became available in Nigeria in the year 2004. However, HIV services in the facility commenced in the year 2006. The facility runs an outpatient antiretroviral clinic.

In this facility-based retrospective study, the population source was HIV-infected patients 18 years and older managed for HIV infection between January 2009 and December 2013 in F.M.C., Umuahia. Because organized antiretroviral therapy unit (ART) was established in January 2009, I used January 2009 as my study start date. Umuahia is the capital of Abia state in south-eastern Nigeria and located at latitude 5, 5333 (531’59.988’’N) and longitude 7, 4833 (728’59.988’’E). It has a population of 359,230 people as of the last Nigerian census in 2006 and has Igbo as the traditional language (The GPS Coordinates.net., n.d.). Umuahia is comprised of Umuahia North and Umuahia South local government areas.

Sampling Procedures

The method for sampling was adapted from the study of Berhane et al. (2012). The proportionate stratified random sampling techniques were employed. To achieve a representative sample of a population, it is imperative to randomly select the samples

(Frankfort-Nachmias & Nachmias, 2008). This stratified technique requires dividing the population into subgroups or strata, and the final subjects are then selected sequentially from the different strata (Explorable.com, n.d.). The stratified sampling technique helps to highlight particular subgroups within the population. It is also employed in studies that involve population with various attributes, as well as studies that observe existing relationships (Explorable.com, n.d.) as is the case with this study. This technique was chosen to evaluate the relationship between HAART regimen and development of high blood pressure, obesity, hyperglycemia because of the variableness of the characteristics of the target population. Each stratum was assigned the same sample size by the proportionate stratified random sampling where the same sampling fraction is allocated to each stratum (Explorable.com, n.d.).

Sampling Frame and Sample Size

I stratified my target population into four to accommodate all the categories of HIV-positive individuals assessing treatment in the clinic (Pre-ART, those who took HAART for six months, those who took HAART for twelve months, and those who received HAART for twelve months and above) from where I collected the samples. More so, eligible patients came for check-ups and refilled every three months, but did their blood tests every six months. The pre- HAART cases were infected individuals who were not eligible for antiretroviral therapy because their CD4+ cell count was above 350 cells/mL thresholds for eligibility and served as the control group. Based on the assumptions that the outcome is binary and that there is a linear relationship between the

predictors and the log of the outcome variables (Field, 2009), power analysis to determine the sample size a priori was done.

I used the G*Power 3.1.9.2 statistical power analysis software for the power analysis (Faul, Erdfelder, Buchner, & Lang, 2009). The power analysis was carried out to determine the sample size with the following parameters of the G* Power software: The Z test, logistic regression statistical test, binomial distribution, a power of 0.80, α of 0.05, and effect size as odds ratio of 2.333333 (Figure 1). I used the odds ratio because the outcome variable is binary (Karabi, 2012). I calculated the sample size to be 186, but the sample size was rounded to 192 (48 subjects per stratum). Samples were then allocated to the strata proportionately (Berhane et al., 2012).

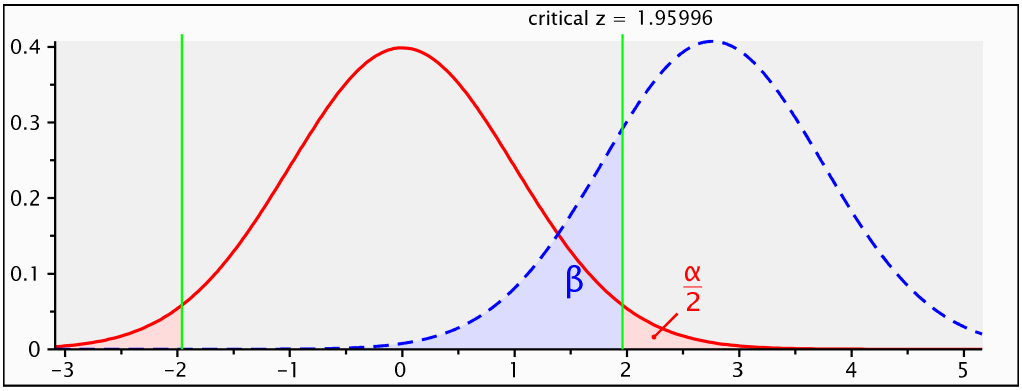

Figure 1. G-power analysis required sample size a priori.

Note. *z* tests - Logistic regression, tail(s) = two, odds ratio = 2.3333333
α = 0.05, power = 0.80, distribution = binomial, critical *z* = 1.9599640
total sample size = 186.

Inclusion and Exclusion Criteria

The population for the study included medical records of adult HIV patients 18 years and older; those who adhered to taking HAART; those who had no abnormal blood glucose, BMI, and elevated blood pressure at baseline. I excluded the medical records of those below 18 years. The records of those who had elevated blood glucose, blood pressure, and abnormal BMI at baseline were also excluded from the study. Also excluded from the study were those whose records indicated pregnancy.

Data Collection Instrument and Measurement of Patients' Samples

Information regarding age, sex, date of HAART initiation, type of HAART received, duration of HAART regimen, weight, height, blood pressure, CD4+ cell count, and fasting blood glucose were abstracted from the medical records of patients' using an abstraction form (Villamar et al., 2011). Blood pressure was measured using Reiseter Exacta sphygmomanometer (Rudolf Reiseter, Jungingen, Germany). Fasting blood glucose was measured using Selectra Junior chemistry auto analyser (ELITech Clinical Systems, Netherlands). Weight and height were measured using GT 131-120 health scale (Skyline Medical Equipment).

Data Access and Collection Process

I sought permission and approval of the study from the Institutional Review Board (IRB) of Walden University following approval for data collection from medical records of patients by the Health Research Ethics Committee (HREC) of F.M.C. Umuahia. I removed every form of identifier that could link the patient to the study to

protect patients' rights to confidentiality in agreement with the Helsinki Declaration (World Medical Association [WMA], 2008).

Data Validity

Data validity addresses the accuracy of the data (Creswell et al., 2009). According to Creswell et al., the manner of data collection (internal factors) can interfere with the validity of data. Data validity can be sectioned into internal and external validity (Cook & Campbell, 1979, p. 5.). Internal validity borders on the soundness of the design and analysis such as reliability of instrument and statistics, environment variables control, and characteristics of participants while external validity borders on the question of generalizability (Cook & Campbell, 1979, p. 5.). This includes the generalizability of the effect of the study to populations, measurement variables, treatment variables, and settings (Cook & Campbell, 1979, p. 5.).

Since confidence in a study can be achieved with only valid data (Creswell et al., 2009), I ensured data validity and reduced external threats to validity by determining whether data was stored electronically or by a paper chart. I also found out the type of information that was recorded as suggested by Hall, Schroder, and Weaver (2002). I also ensured data validity as stated by Engel, Henderson, Fergenbaum, and Colantonio (2009) by using trained data entry clerks in the medical records department of the ART clinic to abstract data from patients' records. Furthermore, Engel et al. noted that the layout and content of the abstraction form could enhance the reliability of the data abstraction form. As a result, response fields on the abstraction form followed the order as it appeared in the records. To further enhance data validity, I coded the variables numerically and

aligned the response fields visually. I also justified to the right with no blank spaces to avoid transcription and data entry errors as suggested by Banks (1998).

Statistical Power for Analysis

The margin of error also known as alpha (α) level or level of statistical significance is important when conducting epidemiologic studies and it is set a priori (Frankfort-Nachmias, & Nachmias, 2008). The alpha level is the level of error allowed to reject a true hypothesis (Frankfort-Nachmias, & Nachmias, 2008). Statistical significance is very vital in testing a statistical hypothesis. It plays a very crucial role in determining when to reject or accept a null hypothesis (Meier, Brudney, & Bohte, 2011). Thus, a *p*-value of 0.05 (probability) is equivalent to a chance of 1 in 20 of rejecting a true hypothesis. By tradition, a *p*-value > .05 supports the null hypothesis and is not statistically significant. On the other hand, a *p*-value < .05 is considered statistically significant and does not support the null hypothesis (Frankfort-Nachmias, & Nachmias, 2008). Based on this, the level of significance was set at 0.05. Furthermore, to have substantive and replicable results, the appropriate effect size must be applied as Frankfort-Nachmias, & Nachmias posited. According to Kelley & Preacher (2012), the quantitative measure of the strength of a phenomenon is the effect size. In addition, to prevent type II error with logistic regression, I set the power (1-β) at 80% with 95% Confidence interval (CI).

Statistical Analysis

Data that I extracted from the medical records were imputed manually into Microsoft Excel. I then exported the data into SPSS version 23 for analyses after

inspection and cleaning by excluding all missing data and used only records with complete data for the analysis as stated by Frankfort-Nachmias, and Nachmias (2008). I conducted descriptive statistics on my data and determined the prevalence of hypertension, obesity, and hyperglycemia using frequency distribution of demographic, laboratory, and clinical values. I also used the Chi-square test for independence ($\chi 2$) to determine the association between categorical variables according to the methods of Berhane et al. (2012). In addition, I used bivariate logistic analyses to identify predictors of hypertension, obesity, and hyperglycemia. Thereafter, I used the multivariate logistic regression analyses to analyse the independent variables that showed significant associations ($p < .05$) with the bivariate analyses. Furthermore, I used the multiple logistic regressions to estimate odds and odds ratio and controlled the effect of confounding variables. Multiple logistic regressions enabled me to examine the relationship between types of HAART regimen and high blood pressure, types of HAART regimen and obesity, and types of HAART regimen and hyperglycemia (Denue et al., 2012; Diouf et al., 2012). According to Kaneko et al. (2011); Wang et al. (2010), high blood pressure, obesity, and diabetes vary by characteristics of the population, and that gender, ethnicity, family history, differences in age, and smoking status contributes to differences in metabolic syndrome. These factors can alter the effects of HAART regimen on the dependent variables without being the direct cause of the outcome, thereby confounding the effect size of the dependent variables (Kaneko et al., 2011). Thus, preventing the effect of confounders informed the choice of multiple logistic regressions. Multiple logistic regressions allow controlling for confounding variables

(Szklo, & Nieto, 2014). According to Szklo and Nieto, multiple logistic regressions is used to examine relationships between the predictor variables, and the outcome (dependent) variable while allowing controlling for possible confounders. Multiple logistic regression is also used when the dependent or outcome variable is binary (Szklo, & Nieto, 2014). In this study, the outcome of interest is presence or absence of hypertension, presence or absence of obesity, and presence or absence of diabetes. The predictor variables (independent variables) are types of HAART regimen and duration of HAART regimen. However, using the directed acyclic graph (DAG), only age, and gender were included as covariates, $CD4^{+}$ cell count was included as confounder. High blood pressure, obesity, and hyperglycemia were analyzed independently by creating dummy variables using the ATP III criteria (NCEP, 2002).

In my data analysis, I included age and gender as covariates because they are patient variables, and they are related to the outcome variables only. However, I included CD4+ cell count that represents the immune status of the patient as a confounder because CD4+ cell count is related to both the exposure and the outcome (StraightHealthcare, 2015). According to StraightHealthcare, covariates are patient variables that could be related or not related to the study outcome. But when the covariates are related to both the exposure and outcome, they become confounders.

Study Variables

In this study, I derived the variables based on abstracted clinical information and laboratory test results from the medical records of HIV-infected individuals. I coded the outcome variables as presence of hypertension = 1, absence of hypertension = 0, presence

of obesity = 1, absence of obesity = 0, presence of hyperglycemia = 1, absence of hyperglycemia = 0. However, I coded the predictor variables (types of HAART regimen and duration of HAART regimen) at five and four levels respectively: pre- HAART (control) = 0, the use of lamivudine, stavudine, nevirapine = 1; the use of combivir, nevirapine = 2; the use of combivir, efavirenz = 3; the use of truvada, efavirenz = 4; baseline = 0, HAART regimen for 6 months = 1, 12months = 2, >12 months = 3.

Summary

In this study, I analyzed data from medical records of HIV patients. The aims of this study are to: (a) examine the relationship among types of HAART regimen and hypertension, obesity, and hyperglycemia among adult HIV positive patients 18 years and older attending the clinic in F.M.C. Umuahia, Nigeria; (b) examine the relationship among duration of HAART regimen, hypertension, obesity, and hyperglycemia among adult HIV positive patients 18 years and older attending the clinic in F.M.C. Umuahia, Nigeria; (c) determine the prevalence of hypertension, obesity, and hyperglycemia among adult HIV positive patients 18 years and older attending the clinic in F.M.C. Umuahia, Nigeria. The study was limited to: (a) data available in patients' medical records; (b) data that met the inclusion criteria of 18 years and older; (c) records that showed no evidence of abnormal blood glucose level, BMI, and hypertension at baseline.

The effects of HAART on blood pressure, BMI, and blood sugar level were analyzed using logistic regression analysis. I based statistical significance on $p < .05$ and 95% CIs. I took steps to ensure validity by minimizing bias, and also controlled confounders. Following approval of this study by the Walden University IRB and

approval to access patients' medical records by HREC of F.M.C Umuahia, I then collected data, cleaned, coded, and analyzed data. Thereafter, I analyzed data statistically and present results in Chapter 4.

Chapter 4: Results

The purpose of this study was to analyse data from the treatment records of HIV-positive individuals accessing treatment in the ART clinic in Federal Medical Centre (FMC), Umuahia quantitatively. In this study, I determined whether types of HAART regimen and duration of HAART regimen significantly affect the odds of hypertension, obesity, and hyperglycemia in HIV-positive individuals. The aim of this study was to answer two research questions: (a) what is the relationship among types of HAART regimen and hypertension, obesity, and hyperglycemia as metabolic syndrome components in HIV-infected individuals? ; (b) What is the relationship among duration of HAART regimen and hypertension, obesity, and hyperglycemia as metabolic syndrome components in HIV-infected individuals? I also sought to determine the prevalence of hypertension, obesity, and hyperglycemia among HIV-positive individuals receiving treatment at the ART clinic in FMC Umuahia in this study.

In this chapter, I report the baseline descriptive and demographic characteristics of the sample population first. Then, I report the results of univariate analyses that justified the inclusion of covariates in the bivariate logistic model. Furthermore, I report the results of the multivariate logistic model after determining their individual effect on the outcome variables. In addition, I report the results of the multivariate logistic model after including age, gender, and CD4+ cell count to control their effect. I also summarize, tabulate, and report the findings of all statistical analysis about each hypothesis.

Data Access and Acquisition and Characteristics of Study Population

Data Access and Acquisition

I sought for and obtained approval to access patients' treatment records from the FMC HREC. The HREC approval number for the study is (FMC/QEH/G.596/Vol.10/166. Data collection and analysis for this study could start only when I got approval to carry out this study by Walden University's IRB. The Walden University's IRB approval number for the study is 04-08-16-0322042. I requested for Data from the medical records of all HIV-positive patients that accessed treatment in the ART clinic in FMC Umuahia between January 2009 and December 2013. I then used only the records that met the inclusion criteria. I further derived variables as listed under study variables in Chapter 3.

I coded all responses as described in Table 3 under study variables, and I limited the responses for the covariates to age and gender, and limited confounders to CD4+ T lymphocyte cell count. I limited the responses because other variables like family history of hypertension, family history of diabetes, alcohol use and cigarette smoking status of patients were not captured in the patients' medical records. I also, used the term hyperglycemia instead of type 2 diabetes mellitus because there was no sufficient information such as Hb1C test, and information on the use of antidiabetic medication in the records of patients.

Characteristics of Study Population

In this retrospective study, I defined the sample size as the total number (n= 192) of treatment records of HIV-infected patients 18 years or older enrolled in the ART clinic

between January 2009 and December 2013 that met the inclusion criteria. Meanwhile, for the purpose of this study, I regarded the treatment records as participants, and I dichotomized continuous data for hypertension, obesity, and hyperglycemia using the ATP III criteria for hypertension and hyperglycemia and WHO criteria for obesity, as described in Chapter 3 (Tables 3 and 2, respectively). I also categorized age, CD4+ cell count, and WHO disease staging after obtaining their individual means. It is important to note that all the participants in the HAART group adhered to their regimen. Frequencies (number and percent) of the characteristics of the pre-HAART regimen control group and HAART regimen group collected from January 2009 to December 2013 are presented in Table 4.

Table 4 shows the characteristics of the pre-HAART and HAART group. The sample size was 192 treatment records of HIV-positive patients 18 years and older. The sample was stratified into four groups, based on the duration of HAART regimen as follows: (a) pre-HAART (Control) = 48; (b) HAART group- 6months = 48; (c) HAART group -12 months = 48; (d) HAART group- >12 months = 48. In some comparison, I grouped three HAART groups as one single "HAART group" (Table 4). The pre-HAART group consisted of only patients who were yet to commence the HAART regimen, whereas the HAART group consisted of HIV-positive patients on the HAART regimen. Of the 48 participants in the pre-HAART control group, 18 (12.5%) were males, whereas 30 (26.8%) were females. The age ranged between 18 years and 57 years. The mean value for age was 35.3years, with the majority of the participants in the 18-29 and 40-50 years groups (Table 4). There was no participant on HAART regimen in the pre-

HAART group. The immune statuses of patients as presented by CD4+ T lymphocyte cell count range was 201 cells/mL—> 500 cells/mL. The WHO HIV disease staging of all participants were below stage 3. Obesity was 12.5% prevalent with a mean BMI of 25.5. There was no observed presence of hypertension (0.0%) and hyperglycemia (0.0%) in the pre- HAART group (Table 4). Of the 144 participants in the HAART group, 59 (41.0%) were males whereas 85(59.0%) were females. The age ranged between 23 years and 65 years, with a mean value of 38.7 years. The majority of the participants were in the age group 30-39 years (39.6%). In the HAART group, there were 82 (28.5%) participants on the lamivudine, stavudine and nevirapine regimen; 158 (54.9%) were on the combivir and nevirapine regimen, while 24 (8.3%) each were on the combivir and efavirenz, truvada and efavirenz regimen respectively. Obesity and hyperglycemia occurred in 16% and 31% of the participants respectively. Systolic hypertension was 73.4 %, with a mean value of 142.2 mm Hg; diastolic hypertension was 26.6%, with a mean value of 93.4 mm Hg. The average value for BMI was 23.4 kg/m^2, whereas the average value for fasting blood sugar was 85.9 mg/dL.

Table 4
Characteristics of the Pre-HAART and HAART Group

Variable	Pre-HAART Frequency N	(%)	Mean value	HAART group Frequency N	(%)	Mean value
Overall	48	(25%)	-	144	(75%)	-
Gender						
Male	18	(37.5)	-	59	(41.0)	-
Female	30	(62.5)	-	85	(59.0)	
Age group (years)						
18-29	15	(10.4)	35	21	(14.6)	38.7
30-39	14	(9.7)		57	(39.6)	
40-50	15	(10.4)		54	(37.5)	
>50	0.4	(8.3)		12	(8.3)	
Type of HAART						
Lam,stav,nvp	0.0	(0.00)	-	82	(28.5)	-
Comb,nvp	0.0	(0.00)		158	(54.9)	
Comb,efv	0.0	(0.00)		24	(8.3)	
Truv,efv	0.0	(0.00)		24	(8.3)	
CD4+ cell count (cells/mL)						
10-200	0.0	(0.00)	707	101	(35.1)	281
201-350	0.0	(0.00)		113	(39.2)	
351-500	82	(56.9)		42	(14,6)	
>500	62	(43.1)		32	(11.1)	
WHO disease staging						
<3	48	(100)	1	253	(87.8)	1
>2	0.0	(0.00)		35	(12.2)	
Hypertension(mm Hg)						
SBP (mm Hg)	0.0	(0.00)	-	41	(73.4)	142.2
DBP (mm Hg)	0.0	(0.00)		35	(26.6)	93.4
BMI (Kg/m^2)						
Obesity	18	(12.5)	25	16	(5.6)	23.4
FBS (mg/dL)						
Hyperglycemia	0.0	(0.00)	-	31	(10.8)	85.9
Duration of HAART						
Baseline	0.0	(0.00)	-	0	(0.00)	-
6 months	0.0	(0.00)		48	(33.3)	
12months	0.0	(0.00)		48	(33.3)	
>12 months	0.0	(0.00)		48	(33.3)	

Note. Hypertension and hyperglycemia were defined according to *ATP III* criteria (NCEP, 2002). Obesity was defined according to WHO criteria (WHO, 2015). %= Percent, N=Number. Lam = Lamivudine, Stav = Stavudine, Nvp = Nevirapine, Comb = Combivir, Efv = Efavirenz, Truv = Truvada. SBP= Systolic blood pressure, DBP= Diastolic blood pressure.

Results

Prevalence of Metabolic Syndrome Components

To identify the prevalence of hypertension, obesity, and hyperglycemia, I excluded records of patients that showed baseline examination measurements within hypertensive, obesity, and hyperglycaemic range. Thereafter, I used descriptive statistics analysis to determine the prevalence of hypertension, obesity, and hyperglycemia. Total prevalence for the pre- HAART and HAART groups are presented in Table 5. Moreover, the prevalence of hypertension, obesity, and hyperglycemia stratified by gender and age in the HAART regimen group are presented in Table 6. I used the chi-square test ($\chi 2$) for independence to determine relationships between the duration of HAART regimen and hypertension, duration of HAART regimen and obesity, duration of HAART regimen and hyperglycemia using the 4 x 2 $\chi 2$ model.

The crosstabs I conducted were between HAART regimen for 6 months, 12 months, >12 months duration, and at baseline; and the presence or absence of each dependent variable (hypertension, obesity, and hyperglycemia). Results are presented in Table 7. The relationship between types of HAART regimen and metabolic syndrome components is shown in Table 8. The relationship between metabolic syndrome components and gender of patients on HAART is presented in Table 9, while the relationship between metabolic syndrome components and age is shown in Table 10. Odds ratios for hyperglycemia by type of HAART regimen is shown in Table 11. Relationships between the type of HAART regimen and the individual components were determined using $\chi 2$ and shown in Table 8. Statistically, significant associations were

determined by a $p = < .05$. Variables with statistically significant associations were further included in bivariate logistics regressions to determine the odds ratios (ORs) for the individual variables. Results of the ORs are presented in Tables 11 and 12 respectively. After obtaining statistically significant ORs with each component, a final model was run with each component adjusted for all covariates to identify the adjusted effect of each independent variable on the dependent variables, while non-statistically significant variables were excluded from the final model. Results of final model are presented in Table 13.

Table 5
Prevalence of Metabolic Syndrome Components in the Pre HAART and HAART Group

	Pre-HAART		HAART	
Variable	**Value (N)**	**Percent (%)**	**Value (N)**	**Percent (%)**
Hypertension	0.0	0.0	48	33.3
Obesity	18.0	12.5	16	5.6
Hyperglycemia	0.0	0.0	31	10.8

Note. Hypertension and hyperglycemia were defined by *ATP III* criteria (NCEP, 2002). Obesity was defined according to WHO criteria (WHO, 2015).

There was no prevalence (there were no cases) of hypertension and hyperglycemia in the pre-HAART control group (Table 5). However, in the HAART group, hypertension and hyperglycemia were 33.3% and 10.8% prevalent respectively (Table 5). The prevalence of obesity in the control group and HAART groups were 12.5% and 5.6% respectively (Table 5). Obesity was 6.9% higher in the pre- HAART control group than the HAART group (5.6%) (Table5).

In this study, the prevalence of hypertension in males (56.3%) is higher than in females (43.8%) (Table 6). Similarly, males were more likely to become obese (15.0%) than females (8.3%). Furthermore, hyperglycemia was 6% higher in males (25%) than in females (19%). Results also showed that prevalence of hypertension increase with age. In the 18─29 year age group, prevalence was 19.0% and in the 30─39 year group, prevalence was 19.3%. Prevalence rose to 29.6% in the 40-50 group and nearly doubled (58.3%) in the >50 year age group. Obesity prevalence was 8.8% in the 30-39 year age group, 16.7% in the 40─50 age groups, and 16.7% in the >50 age group. However, there was no obesity in the 18─29 age groups. Though hyperglycemia had a similar prevalence trend as obesity, there was 19.0% prevalence of hyperglycemia in the age group 18─29. Hyperglycemia prevalence was 17.5% in the age group 30-39; 27.8% in age group 40-5; and 16.7% in the >50 age group (Table 6).

Table 6

Metabolic Syndrome Components Prevalence in Patients on HAART Regimen by Gender and Age

Variable	Gender				Age group (years)							
	Male		Female		18-29		30-39		40-50		>50	
	%	(N)	%	(N)	%	(N)	%	(N)	%	(N)	%	N
Hypertension	56.3	(27)	43.8	(21)	19.0	(4)	19.3	(11)	29.6	(16)	58.3	(7)
Obesity	15.0	(9)	8.3	(7)	00.0	(0)	8.8	(5)	16.7	(9)	16.7	(2)
Hyperglycemia	25.0	(15)	19.0	(16)	19.0	(4)	17.5	(10)	27.8	(15)	16.7	(2)

Note. Hypertension and hyperglycemia were defined according to *ATP III* criteria (NCEP, 2002). Obesity was defined according to WHO criteria (WHO, 2015). %= Percent, N= Number

Tables 7 and 8 present the relationships between duration of HAART regimen and metabolic syndrome components and type of HAART regimen and metabolic syndrome components respectively. At baseline, there were no cases of hypertension (0.00%), obesity (0.00%), and hyperglycemia (0.00%). However, at six months, the prevalence of hypertension was 10.4%; obesity was 4.2%, and hyperglycemia was 6.3%. Furthermore, at 12 months on HAART regimen, the prevalence increased to 35.4% for hypertension, 12.5% for obesity, and 18.8% for hyperglycemia. Similarly, the prevalence of hypertension and hyperglycemia were almost doubled with HAART regimen for >12 months (54.2% and 39.6%), respectively. However, obesity was 16.7% prevalent at >12 months (Table 7).

The $\chi 2$ (20.813) for hypertension and its corresponding $p < .001$ (Table 7) showed that there was a statistically significant association between hypertension and duration of HAART regimen. The effect size (Cramer's V = 0.380) for the association was large. The $\chi 2$ (24.353) and $p < .001$for obesity signified a statistically significant association between obesity and duration of HAART regimen. The effect size of 0.54 was large (Table 7). Similarly, $\chi 2$ for hyperglycemia was 63.08 and $p < .001$ also showed a statistically significant association between hyperglycemia and duration of HAART regimen. The effect size 0.468 was also large (Table 7).

Table 7
Relationship Between Duration of HAART Regimen and Metabolic Syndrome Components

Variable	Baseline % (N)	6months % (N)	12months % (N)	>12months % (N)	χ2	*p*-value	Effect size
Hypertension	0.00 (0)	10.4 (5)	35.4 (17)	54.2 (26)	20.813	<0.001***	0.380
Obesity	0.00 (0)	4.2 (2)	12.5 (6)	16.7 (8)	24.354	<0.001***	0.291
Hyperglycemia	0.00 (0)	6.3 (3)	18.8 (9)	39.6 (19)	60.91	<0.001***	0.468

Note. Hypertension and hyperglycemia were defined according to *ATP III* criteria (NCEP, 2002). Obesity was defined according to WHO criteria (WHO, 2015). %= Percent, N= Number, χ2= Chi-square test, *** = Significant

When stratified by types of HAART regimen, patients on the LAM, STAV, and NVR regimen, 8.5% patients were obese, 20.7% were hypertensive, and 15.9% had hyperglycemia. Also, with patients on the COMB, NVP regimen, 3.8% were obese, 9.5% hypertensive, and 6.3% of the patients had hyperglycemia. Similarly, 4.2%, 12.5%, 12.5% of patients on the COMB, EFV regimen were obese, hypertensive, and had hyperglycemia respectively. Furthermore, with the TRUV, EFV regimen, there was obesity prevalence of 8.3%, hypertension was 12.5%, and hyperglycemia was 20.8% (Table 8). The $\chi 2$ and *p*-values for hypertension, obesity, and hyperglycemia were ($\chi 2$ = 3.108, p = .375; $\chi 2$ = 2.761, p = .430; $\chi 2$ = 7.824, p = .045) respectively (Table 8).

Results showed that there were no statistically significant associations between obesity and type of HAART regimen; hypertension and type of HAART regimen ($p >$ .05). However, there was a statistically significant association between hyperglycemia and type of HAART regimen ($p < .05$) the association had a moderate effect size 0.167 (Table 8). Types of HAART regimen was not included in the final regression models for hypertension and obesity because there was no statistically significant association between types of HAART regimen and hypertension, and types of HAART regimen and obesity. It is important to note here that where the assumption for Chi-square was violated, the likelihood ratio was used instead as was the case for hyperglycemia.

Table 8
Relationship Between Types of HAART Regimen and Metabolic Syndrome Components

Variable	Lam,stav,nvp % (N)	Comb,nvp % (N)	Comb,efv % (N)	Truv,efv % (N)	χ^2	*p*- value	Effect size
Hypertension	15.9 (13)	6.3 (10)	12.5 (3)	20.8 (5)	3.108	0.375	Nil
Obesity	20.7(17)	9.5 (15)	12.5 (3)	12.5 (3)	2.761	0.430	Nil
Hyperglycemia	8.5 (7)	3.8 (6)	4.2 (1)	8.3 (2)	7.824	0.045*	0.167

Note. *Hypertension* and *hyperglycemia* were defined according to *ATP III* criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). %= Percent, N= Number, χ2= Chi-square test, * = Significant, Lam=Lamivudine, stav= Stavudine, nvp = Nevirapine, efv= Efavirenz, Truv= Truvada.

Research Questions

The first research question was based on whether there is a relationship between types of HAART regimen and metabolic syndrome components. The second research question focused on whether there is a relationship between duration of HAART regimen and metabolic syndrome components. To answer these research questions one and two, I used the $\chi 2$ test to determine the associations between HAART regimen and metabolic syndrome components and duration of HAART regimen and metabolic syndrome components. I also used logistic regressions to identify bivariate odds ratio for hypertension, obesity, and hyperglycemia with and without each covariate and independent variable. This model was appropriate to determine the direction of the association with each of the dependent variable (hypertension, obesity, and hyperglycemia), and to determine if the independent variables were predictors of the outcome, and to know the odds of developing hypertension, obesity, and hyperglycemia. In addition, I used multiple logistics regression that included all covariates, but excluded non-significant variables as the final model. Results of the final regression model are presented in Table 13. All continuous variables were categorized. Results of the $\chi 2$ tests are shown in Tables 7 and 8. The relationship between metabolic syndrome components and gender of patients on HAART is presented in Table 9, while the relationship between metabolic syndrome components and age of patients on HAART is shown in Table 10. The bivariate logistic regression analyses are presented in Tables 11 and 12.

Results of the $\chi 2$ test showed that there was no statistically significant association between types of HAART regimen and hypertension ($\chi 2 = 3.108$, $p = .375 > .05$, Table

8). As a result, types of HAART regimen were excluded from the bivariate logistics regression to determine odds of hypertension. Types of HAART regimen were also excluded from the bivariate logistics regression to determine odds of obesity because there was no significant association between types of HAART regimen and obesity ($\chi 2 = 2.761$, $p = .430$) (Table 8).

The relationship between metabolic syndrome components and gender of patients on HAART is presented in Table 9. The Chi-square test for hypertension was 57.600 and its corresponding $p < .001$. The $\chi 2$ showed that gender is statistically significantly related to hypertension. The effect size for the association was large (0.447). Chi-square for obesity was 16.941, $p = .002$, $< .05$. This indicated that gender was statistically significantly related to obesity. The association also had a medium effect size (0.243). Similarly, $\chi 2$ for hyperglycemia was 34.739, p-value $< .001$. This $\chi 2$ result implied that gender is statistically significantly related to hyperglycemia. The effect size was 0.347 (Table 9). Results justified the inclusion of gender as a covariate in the final model.

The relationship between metabolic syndrome components and age of patients on HAART is presented in Table 10. The $\chi 2$ test for hypertension was 55.122 and its corresponding $p < .001$. This showed that age is statistically significantly related to hypertension. The effect size for the association was large (0.425). Chi-square for obesity was 21.510, $p = 0.03$, $< .05$ indicated that age was statistically significantly related to obesity. The association had a medium effect size (0.221). Similarly, $\chi 2$ for hyperglycemia was 33.740, $p = < .001$. This $\chi 2$ result implied that age is statistically

significantly related to hyperglycemia. The effect size was 0.351 (Table 10). Results justified the inclusion of age as a covariate in the final model.

Table 9
Relationship Between Metabolic Syndrome Components and Gender of Patients on HAART

Variable	Chi-square (χ2)/ Likelihood ratio	*p*-value	Effect size	Significance
Hypertension	57.600	< .001	0.447	S
Obesity	16.941	.002	0.243	S
Hyperglycemia	34.739	< .001	0.347	S

Note. *Hypertension* and *hyperglycemia* were defined according to ATP III criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). S= Significant,

Table 10
Relationship Between Metabolic Syndrome Components and Age of Patients on HAART

Variable	Chi-square ($\chi 2$)/ Likelihood ratio	*p*-value	Effect size	Significance
Hypertension	55.122	< .001	0.425	S
Obesity	21.510	< .03	0.221	S
Hyperglycemia	33.740	< .001	0.351	S

Note. *Hypertension* and *hyperglycemia* were defined according to *ATP III* criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). S= Significant.

ORs of hyperglycemia with the COMB and NVR; COMB and EFV; TRUV and EFV regimen were 1.14 (95% CI, 0.526, 2.463); 3.11 (95% CI, 1.393, 6.944) and 1.13 (95% CI, 0.257, 5.00) respectively (Table 11). These ORs indicated that patients on COMB and NVR regimen are 1.14 times odds of hyperglycemia, those on COMB and EFV are 3.11 times odds of hyperglycemia, and those on TRUV and EFV 1.13 times odds of having hyperglycemia, compared with patients on LAM, STAV, NVP (reference group). Results showed that COMB and EFV regimen was statistically significantly related to hyperglycemia ($p = 0.006 < .05$) (Table 11). However, I found COMB/ NVR regimen and TRUV/ EFV regimen statistically not significantly related to hyperglycemia ($p = 0.742$ and $p = 0.867$), respectively $p > .05$. Also, I could not predict the relationship between LAM, STAV, NVP regimen and the dependent variables using the model.

The OR for hypertension at 12 months duration of HAART regimen was 3.10 (95% CI, 1.299, 7.352). This OR showed that patients are 3.10 times odds of developing hypertension when on HAART regimen for 12 months. Odds ratio of 9.62 (95% CI, 3.205, 28.57) at >12 months indicated that patients on HAART for more than 12 months are 9.62 times odds of developing hypertension. Results also showed that duration of HAART was statistically significantly related to hypertension ($p = .011 < .05$). Furthermore, after controlling for the covariates, there were increases in the unadjusted ORs for hypertension from 3.1(95% CI, 1.299, 7.352) (Table 12) to AOR = 4.15(95% CI, 1.949, 8.849) at 12 months and from OR 9.6 (95% CI, 3.205, 28.57) to AOR = 18.52 (CI, 5.464, 42.50) at >12 months (Table 13). Duration of HAART was still statistically

significantly related to hypertension $p < .001$). The R^2 was 0.498, signifying that 49.8% of the variance could be explained.

Table 11
Odds Ratio (OR) for Hyperglycemia by Types of HAART Regimen

Variable	Types of HAART	OR(95% CI)	*p*- value	Sig	R^2
Hyperglycemia					
	Lam,stav,nvp	referent	-	-	0.816
	Comb,nvp	1.14 (0.526, 2.463)	0.742	NS	
	Comb,efv	3.11 (1.393, 6.944)	0.006	S	
	Truv,efv	1.13 (0.257, 5.000)	0.867	NS	

Note. *Hypertension* and *hyperglycemia* were defined according to ATP III criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). S= Significant, NS= Not significant. OR=Odds ratio, CI= Confidence interval, Sig=Significance, Lam=Lamivudine, stav= Stavudine, nvp = Nevirapine, efv= Efavirenz, Truv= Truvada.

Table 12
Odds Ratio (OR) for Metabolic Syndrome Components by Duration of HAART Regimen

Variable	Duration on HAART (months)	OR	95% CI	*p*- value	Sig	R^2
Hypertension						
	Baseline	-	-	-	-	0.498
	6	referent	-	-	-	
	12	3.1	1.299, 7.352	0.011	S	
	>12	9.6	3.205, 28.57	0.001	S	
Obesity						
	Baseline	-	-	-	-	0.868
	6	referent	-	-	-	
	12	1.71	0.590, 4.950	0.322	NS	
	>12	5.95	1.284, 18.770	0.023	S	
Hyperglycemia						
	Baseline	-	-	-	-	0.816
	6	referent	-	-	-	
	12	2.23	0.910, 5.681	0.079	NS	
	>12	8.33	2.283, 30.303	0.001	S	

Note. *Hypertension* and *hyperglycemia* were defined according to ATP III criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). S= Significant, NS= Not significant. OR=Odds ratio, CI= Confidence interval, Sig=Significance

ORs and corresponding confidence interval (CI) for obesity at 12 months and >12 months were 1.71(95% CI, 0.590, 4.950) and 5.95 (95% CI, 1.284, 27.77) respectively (Table 12). These ORs show that obesity is 5.95 times more likely to develop when on HAART for >12 months and 1.71 times more likely to develop when on HAART for 12 months. However, after controlling for gender, age, and CD4+ cell count, the OR for obesity increased to AOR= 1.82 when on HAART for 12 months and increased to AOR 5.44 when on HAART for >12 months (Table 13). Statistically, HAART regimen for >12 months was significantly related to obesity ($p = .023 < .05$), whereas, HAART regimen for 12 months only was statistically not significantly related to obesity ($p = 0.322 > .05$) (Table 12). However, after adjustment for covariates, it resulted in statistical significance at 12 months duration ($p < .001$). R^2 was 0.868, showing that 86.8% of the variance could be explained.

Hyperglycemia was 2.23 times odds of developing in patients on HAART for12 months (OR= 2.23, 95% CI, 0.910, 5.681) (Table 12) and 8.33 times odds of developing in patients on HAART for >12 months (OR= 8.33, 95% CI, 2.283, 30.303) (Table 12). However, after controlling for all the covariates, OR was nearly doubled (AOR= 3.91) when on HAART for 12 months. Similarly, OR was nearly doubled (AOR= 14.71) when on HAART for >12 months (Table 13). There was no prediction at baseline and 6 months. The results showed that gender, age, and CD4+ cell count have an influence on the dependent variables. R^2 of 0.816 showed that 81.6% of the variance could be explained. Statistically, unadjusted OR of the group on HAART for 12 months was not significant ($p = .079$), while the group on HAART for >12 months was statistically

significantly related to hyperglycemia ($p = .001 < .05$). Furthermore, after adjusting for covariates, statistical significance was achieved for both groups. Consequently, I rejected the null hypothesis and accepted the alternative hypothesis that duration of HAART regimen increases the odds of hyperglycemia.

Table 13
Adjusted Odds Ratio for Metabolic Syndrome Components by Duration of HAART Regimen

Variable	Duration on HAART	AOR	(95% CI)	*p*- value	Sig	R^2
Hypertension						
	Baseline	-	-	-	-	0.793
	6	referent	-	-	-	
	12	4.15	1.949, 8.849	< .001	S	
	>12	18.52	5.464, 42.50	< .001	S	
Obesity						
	Baseline	-	-	-	-	0.835
	6	referent	-	-	-	
	12	1.82	4.349, 26.92	< .001	S	
	>12	5.43	2.227, 13.158	< .001	S	
Hyperglycemia						
	Baseline	-	-	-	-	0.800
	6	referent	-	-	-	
	12	3.91	1.942, 9.259	< .001	S	
	>12	14.71	4.425, 27.619	< .001	S	

Note. *Hypertension* and *hyperglycemia* were defined according to ATP III criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). S = Significant, NS = Not significant. AOR= Adjusted odds ratio, CI= Confidence interval, Sig = Significance.

The relationship between immune statuses of patients measured by CD4+ T lymphocyte and metabolic syndrome components is presented in Table 14. The $\chi 2$ test for hypertension was 45.140 and its corresponding $p < .001$. This showed that CD4+ cell count was statistically significantly related to hypertension. The effect size for the association was large (0.396). Chi-square for obesity was 19.780, p-value = .003 < .05 indicated that CD4+ cell count was statistically significantly related to obesity. The association also had a medium effect size (0.262). Similarly, $\chi 2$ for hyperglycemia was 27.327, p-value < .001. This $\chi 2$ result implies that CD4+ cell count is statistically significantly related to hyperglycemia. The effect size was 0.308 (Table 14). The results justified the inclusion of CD4+ T-lymphocyte count as a covariate in the final model.

Table 14
Relationship Between Metabolic Syndrome Components and Immune Status of Patients on HAART

Variable	Chi-square ($\chi 2$)/ Likelihood ratio	*p*-value	Effect size	Significance
Hypertension	45.140	< .001	0.396	S
Obesity	19.780	.003	0.262	S
Hyperglycemia	27.327	< .001	0.308	S

Note. *Hypertension* and *hyperglycemia* were defined according to ATP III criteria (NCEP, 2002). *Obesity* was defined according to WHO criteria (WHO, 2015). S = Significant, NS = Not significant.

Summary

The characteristics of the population studied include gender, age, WHO HIV disease staging, CD4+ T lymphocyte cell count, blood pressure measurement, body mass index, and fasting blood sugar level in the pre-HAART control group and HAART group. The variables were assessed at baseline and thereafter as recorded in their treatment records. All the participants in the HAART group adhered to their regimen. Most of the participants in the HAART group were in WHO disease stage < 3 at enrolment and a few in WHO stages 3. Unlike the HAART group, all the participants in the pre-HAART group at enrolment were in WHO disease stage 1. There were 59 males and 85 females in the HAART group, whereas the pre-HAART group had 18 males and 30 females. The mean value for age in the pre-HAART group was 35.25 years, and that of the HAART group was 38.7 years. The average values for CD4+ cell count in the pre-HAART group and HAART group were 707cells/mL and 281.6cells/mL respectively. I stratified the HAART group into three according to the duration of HAART regimen. Each stratum had 48 participants each at six months, 12 months, and >12 months. The HAART group also had 82 participants on the Lamivudine, Stavudine, and Nevirapine regimen, 158 on the Combivir and Nevirapine regimen, 24 participants each on Combivir and Efavirenz regimen and Truvada and Efavirenz regimen.

In the determination of the prevalence of the metabolic syndrome components, I found that 18 (12.5%) participants in the pre-HAART group were obese at baseline. However, there were no cases of hypertension and hyperglycemia at baseline. The

prevalence of systolic and diastolic hypertension was 73.4% and 26.6% respectively, and the overall prevalence of hypertension was 16.7%.

I stratified the independent variables by types of HAART regimen and duration of HAART regimen. I used the χ^2 test for independence to examine the relationships between the nonparametric variables. I also analyzed the bivariate odds of covariates (age, gender, and CD4+ cell count); I then included only statistically significant variables in the final model. The results showed that ORs differed by duration of HAART for all components, but differed less for the types of HAART regimen. To control for the potential influence of covariates on metabolic syndrome components, I included covariates to the multiple logistic regression models that served as the final model. I used multiple logistic regression analysis to assess odds ratios of types of HAART regimen and duration of HAART regimen after controlling for all covariates. This was done to determine whether these variables increased the odds of hypertension, obesity, and hyperglycemia.

In this study, the odds of hypertension, obesity, and hyperglycemia increased with duration of HAART, and I recorded statistical significance with hypertension in the group on HAART for 12 months and the group on HAART for >12 months ($p < .05$). I also recorded statistical significance with obesity and hyperglycemia in the group on HAART for >12 months only ($p < .05$). However, there was no statistical significance with obesity and hyperglycemia in the group on HAART for 12 months ($p > .05$). The OR for hypertension at 12 months was 3.1 (95% CI, 1.299, 7.352, $p < .05$), at >12 months OR was 9.6 (95% CI, 3.205, 28.57, $p < .05$). The OR for obesity at 12 months was 1.71

(95% CI, 0.590, 4.950, $p > .05$), at >12 months OR was 5.95 (95% CI, 1.284, 18.770). The OR for hyperglycemia at 12 months was 2.23 (95% CI, 0.910, 5.681, $p > .05$), at >12 months OR was 8.33 (95% CI, 2.283, 30.303, $p < .05$). Conversely, types of HAART regimen did not increase odds of hyperglycemia. The OR for hyperglycemia with the COMB, NVP regimen was 1.14 (95% CI, 0.526, 2.463), with the COMB, EFV regimen OR was 3.11 (95% CI, 1.393, 6.944, $p = .006$), with the TRUV, EFV regimen OR was 1.13 (CI, 0.257, 5.000, $p = .867$). OR with HAART regimen was not done for hypertension and obesity because of the no significant association results obtained with the $\chi 2$ test.

The odds of hyperglycemia did not increase with the Combivir and Nevirapine regimen (OR=1.14, 95% CI, 0.526, 2.463, $p > .05$) and the Truvada and Efavirenz regimen (OR=1.13, 95% CI, 0.257, 5.000, $p = .867$). Only the Combivir and Efavirenz regimen (OR=3.11, 95% CI, 1.393, 6.944, $p = .006$) achieved statistical significance and increased the odds of hypertension, obesity, and hyperglycemia.

I accepted the null hypothesis (H_0) for research question 1A that stated that HAART regimen does not increase the odds of hypertension and rejected the alternative hypothesis because of lack of statistical significance. Similarly, due to no statistically significant relationship between types of HAART regimen and obesity, I accepted the null hypothesis for research question 1B that stated that HAART regimen does not increase the odds of obesity and rejected the alternative hypothesis. Furthermore, due to no statistically significant relationship, I accepted the null hypothesis for research

question 1C that stated that types of HAART regimen does not increase the odds of hyperglycemia and rejected the alternative hypothesis.

For research question 2A, the results generated produced statistically significant relationship to reject the null hypothesis in favor of the alternative hypothesis that stated that duration of HAART regimen increases the odds of hypertension (AOR = 4.15, 95% CI, 1.949, 8.849, $p < .001$) with the group on HAART for 12 months and AOR = 18.52 (95% CI, 5.464, 42.50) with the group on HAART for >12 months. I also rejected the null hypothesis for research question 2B and accepted the alternative hypothesis that stated that duration of HAART regimen increases the odds of obesity with respect to duration of HAART for 12 months AOR=1.82 (95% CI, 4.349, 26.92, $p < .001$) and HAART for >12 months (AOR= 5.43 (CI, 2.227, 13.158, $p < .001$). Furthermore, for research question 2C, I accepted the alternative hypothesis that stated that duration of HAART increases the odds of hyperglycemia and rejected the null because the result was statistically significant (AOR =3.91, 95% CI, 1.942, 9.259, $p < .001$) at 12 months and AOR = 14.71 (95% CI, 4.425, 27.619, $p < .001$) at >12 months.

In chapter 5, I interpret and discuss the results presented in this chapter. I interpreted the results based on the metabolic theory and literature reviewed. I also discuss the strengths and limitations of this study in Chapter 5. In addition, I present the importance of the findings of this study to the population and recommend further in-depth studies with primary data to validate the results of this study. I also discuss recommendations for possible future intervention programs in chapter 5.

Chapter 5: Discussion, Conclusions, and Recommendations

Discussion

The purpose of this study was to quantitatively analyze data from the treatment records of HIV-positive individuals accessing treatment in the ART clinic in FMC, Umuahia. I also determined whether HAART regimen and duration of HAART regimen increased the odds of developing hypertension, obesity, and hyperglycemia in HIV-positive individuals. The aim of this study was to answer two research questions: (a) what is the relationship among types of HAART regimen and hypertension, obesity, and hyperglycemia as metabolic syndrome components in HIV-infected individuals?; (b) what is the relationship among duration of HAART regimen and hypertension, obesity, hyperglycemia as metabolic syndrome components in HIV-infected individuals? In addition, I determined the prevalence of hypertension, obesity, and hyperglycemia among HIV-positive individuals 18 years or older receiving treatment in the ART clinic in FMC Umuahia.

In this study, I found a significantly high burden of hypertension (33.3%) and hyperglycemia (10.8%) of the diabetic range among HIV-positive patients accessing treatment in the ART clinic in FMC Umuahia. But obesity prevalence (5.6%) was not as high. Hypertension, obesity, and hyperglycemia constitute major risk factors for CVD in these groups of population (Chow et al., 2012; Guaraldi, et al., 2010; Palios, Kadoglou, and Lampropoulos, 2012; Malangu, 2014; Muhammad et al., 2013; Zhou et al., 2014). These risk factors, however, vary by population and racial differences (Ngatchou et al., 2013).

Metabolic syndrome components prevalence in HIV-infected individuals associated with HAART regimen has been observed in cross-sectional observational studies (Durang et al., 2011; Guaraldi, et al., 2010; Palios, Kadoglou, and Lampropoulos, 2012; Ngatchou et al., 2013). Before my study, there had been no report on the analysis of the relationship between HAART regimen and metabolic syndrome components in Umuahia metropolis. In this chapter, I interpret and discuss the findings presented in Chapter 4. I also discuss the study limitations, the strength of the study, and recommendations for further study based on the findings of this study. I also discuss the implications for positive social change and public health practice, and the summary of the key results of this study.

Interpretation of Findings

In this study, I used data from HIV- positive patients accessing treatment in FMC Umuahia to provide information about the relationship among types of HAART regimen and hypertension, obesity, and hyperglycemia; and the relationship among the duration of HAART regimen and hypertension, obesity, and hyperglycemia. Information on the prevalence of hypertension, obesity, and hyperglycemia among HIV-positive patients 18 years and older that were managed for HIV infection was also provided. The results of this study showed that duration of HAART regimen is strongly related to hypertension and hyperglycemia; less so with obesity and that hypertension tends to develop in patients on HAART regimen for more than 12 months (OR = 9.6). Key findings of this study confirmed suspicions that duration of HAART regimen increased the odds of developing hypertension and hyperglycemia in HIV patients, and that the factors

associated with statistical significance were taking HAART regimen for more than 12 months.

Prevalence of Metabolic Syndrome Components

Hypertension and *diabetes* were defined according to the ATP III criteria (NCEP, 2002), while *obesity* was defined according to WHO criteria (WHO, 2015). The overall prevalence of hypertension was 33.3%; that of hyperglycemia was 10.5%, and only 5.6% obesity prevalence was recorded in this study. The results of this study are consistent with previous prevalence reports on metabolic syndrome components (Berhane et al., 2012; Denue et al., 2012; Dimodi et al., 2014). Similar to my study results, are the results obtained by Gazzaruso et al. (2003) was 34.2% hypertension in patients on HAART.

Though the overall study population was relatively young (average age was 34.5 years in the pre-HAART group and 38.7 years average age in the HAART group), hypertension, obesity, and hyperglycemia were more prevalent in the older age groups than in the younger age groups. This result is consistent with the results of Muhammad et al. (2013) who reported a mean age of 32.5 years in their study.

Metabolic syndrome components were more prevalent in males than in females in this study, and prevalence also increased with age. This result is consistent with the reports of Malangu (2014) that male patients were 2-fold more likely to have metabolic syndrome compared to females.

Muhammad et al. (2013) evaluated the cardiovascular risks among patients on HAART in a cross-sectional study amongst HIV patients placed on HAART for at least six months, and HAART- naïve group in Aminu Kano Teaching Hospital, Nigeria. They

compared the prevalence of metabolic syndrome components in the pre- HAART group and the HAART group. Their result showed that the incidence of hypertension in patients exposed to HAART regimen was approximately eight times higher than the non-exposed, 17% and 2% respectively ($p < .001$). Obesity prevalence of 2% and 11% was recorded in the HAART naïve and HAART groups respectively and diabetes prevalence of 3% in each of the two groups.

The study established significant correlations in cardiovascular risk factors such as hypertension, obesity, diabetes, and hypercholesterolemia in patients treated with HAART. But their results are not totally consistent with the results of this study. In my study, I found higher obesity prevalence in the pre- HAART group (12.5%). However, results obtained in this study are consistent to that obtained in the Data Collection on Adverse Events of Anti-HIV Drugs (D. A. D) study where HAART naïve subjects were more obese than the subjects on HAART. Akinboro, Onayemi, Ayodele, Mejiuni, and Atiba (2013) also reported the presence of obesity 33.97±1.06 in the pre-HAART group and no obesity in the HAART group. The recorded higher obesity prevalence in the pre-HAART group may have stemmed from the fact that patients in the pre- HAART group had higher mean CD4+ cell count (707cells/ml), and were all at WHO HIV disease stage 1. At this stage, weight loss and other opportunistic infections had not set in compared to the HAART group with mean CD4+ value of 281cells/ml. In contrast, our study did not observe any hypertension and hyperglycemia prevalence in the pre- HAART group. However, there was no statistically significant association between HAART regimen and hypertension ($\chi^2 = 3.108$, $p = 0.375$). Denue et al. (2012) and Muhammed et al. (2013) in

their studies also reported a non-statistically significant relationship between HAART and hypertension ($p > 0.05$).

All participants in the HAART group were on the 2NRTI plus 1 NNRTI regimen. The regimens were in a cocktail of four different combinations as follows: (a) Lamivudine, Stavudine, and Nevirapine (b) Combivir and Nevirapine (c) Combivir and Efavirenz (d) Truvada and Efavirenz. None of the patients were on a PI containing regimen. The pre- HAART control group had no patient on HAART. The development of metabolic syndrome component is likely to be as a result of the exposure to HAART. But the relationship that exist between the individual antiretroviral agent and metabolic syndrome components is not clear.

In this study, the prevalence of hypertension was higher in patients on the Truvada and Efavirenz regimen (20.8%), while obesity and hyperglycemia were observed more in patients on the Lamivudine, Stavudine, and Nevirapine regimen (20.7%) and (8.5%) respectively. However, there was no statistically significant association ($p > .05$) between types of HAART regimen and metabolic syndrome components. This finding of a non-statistically significant relationship between types of HAART regimen and metabolic syndrome components is similar to the previous findings of Denue et al. (2012). They found no statistical significance between classes of HAART and hypertension.

In this study, the prevalence of the three metabolic syndrome components increased with duration of HAART regimen. This result agrees with the report of Berhane et al. (2012), where they found the duration of HAART to be independently

associated with metabolic syndrome components. In their study, they found factors associated with metabolic syndrome to be taking HAART for over twelve months. Similarly, the effect of duration of HAART regimen was also reported by Malangu (2014). Malangu indicated that prevalence of metabolic syndrome components was higher as the length of treatment increased. This suggests that the use of HAART for more than 12 months predisposes patients to develop metabolic syndrome.

Relationship Among Types of HAART Regimen, Duration of HAART Regimen and Hypertension

Based on the total medical records of HIV-positive patients 18 years or older that met the eligibility criteria, more than 30% of patients were hypertensive by ATP III criteria that specified hypertension as systolic blood pressure measurement ≥130 and a diastolic blood pressure measurement ≥85mm Hg (NCEP, 2002). The ≥130/85 mm Hg range implies an increasing blood pressure that can reach the categorical level for hypertension since hypertension is a progressive condition. The 33.3% recorded in this study was higher than the 15.9% reported by Sachithananthan et al. (2012) in Ethiopia. Prevalence was higher among males (56.3%) and the group older than 50 years (58.3%). This result is consistent with previous research results by Malangu (2014) and Denue et al. (2012). To determine if the relationship between HAART regimen and hypertension and the relationship between duration of HAART regimen and hypertension are statistically significant, I used the χ^2 test of independence. The χ^2 for types of HAART regimen and hypertension (3.108, $p = 0.375$) suggested that there was no association between HAART regimen and hypertension. Muhammed et al. (2013) reported similar

findings in a previous study that HAART was not statistically significantly associated with hypertension. However, χ^2 (20.813, $p < .001$) for duration of HAART and hypertension showed that there is an association. The effect size (0.380) signifies a large effect size. Further bivariate logistic regression analysis revealed that hypertension was more than 3 times (OR= 3.10, 95% CI, 1.299, 7.352) likely to develop in patients on HAART for 12 months, and more than 9 times (OR 9.62, 95% CI, 3.205, 28.57) as likely for patients on HAART for more than 12 months, compared with patients on HAART regimen for less than 12 months.

Despite the increase in ORs by more than one fold and more than 8-fold after controlling for covariates, statistical significance for hypertension was still maintained for the duration of HAART for 12 months and >12 months respectively. As a result, the null hypothesis that duration of HAART does not increase the odds of hypertension was rejected. Denue et al. (2012) reported similar results. Their study examined the impact of HAART on blood pressure after two years of commencement of HAART in a cohort of 227 HIV patients. Their results showed a rise in blood pressure with time. The study by Arruda Junior et al. (2010) also is consistent with our results. Furthermore, this study demonstrated that the significant increase in OR for hypertension when all covariates were controlled, indicated that the actual independent effect of duration of HAART on hypertension was not confounded by age, gender, and CD4+ cell count.

Relationship Among HAART regimen, Duration of HAART Regimen and Obesity

Using the WHO definition of *obesity*, I considered BMI ≥30 kg/m^2 obese, and regarded BMI ≤ 30 kg/m^2 as not obese. The literature reviewed showed that exposure to

HAART affects body fat distribution in HIV-infected patients and also increases the risk of CVD (Brown et al., 2009). Based on the above definition of obesity, this study showed overall obesity of 5.6% and χ^2 for HAART regimen and obesity was 2.761, $p = .430$. This result implies that the association between obesity and HAART regimen is not statistically significant.

Due to the inability to observe a significant association between HAART regimen and obesity, HAART regimen was excluded from the subsequent logistics regression models. As a result of the insufficient evidence to accept the alternative hypothesis, the null hypothesis that HAART regimen does not increase the odds of obesity was accepted. Muhammed et al. (2013) reported similar findings of no association between obesity and HAART regimen. While this study was unable to establish that HAART regimen statistically significantly increased odds of obesity, several other studies did observe statistical significance (Dimodi et al., 2014; Jacobson, Tang, Spiegelman, Thomas, Skinner, Gorbach, et al., 2006; and Wu et al., 2012). Conversely, there was a statistically significant association between obesity and duration of HAART ($\chi^2 = 24.354$, $p < .001$).

Further bivariate logistic regressions analysis produced results that supported the association between duration of HAART and obesity. ORs indicated that obesity is nearly 2 folds (OR= 1.71, 95% CI= 0.590, 4.950) more likely in patients on HAART regimen for 12 and more than 5 folds (OR= 5.95, 95% CI= 1.284, 27.77) more likely in patients on HAART regimen for >12 months, respectively. This result is consistent with the findings of Sharma et al. (2014) where they reported statistical significance $p < .05$ between duration of HAART and obesity. However, adjusting for covariates increased

the ORs by more than a fold for patients on HAART for 12 months (AOR= 4.15, 95% CI, 1.949, 8.849), and increased the OR by more than 8 fold for patients on HAART for >12 months (AOR = 18.52, 95% CI, 5.464, 42.50) on HAART, respectively.

Relationship Among HAART Regimen, Duration of HAART Regimen and Hyperglycemia

Diabetes was defined according to the ATP III definition of fasting blood glucose >100mg/dl (NCEP, 2002). However, due to the absence of other diabetes mellitus indices such as Hb A1C test results in patients' records, I chose to use the term hyperglycemia instead. Like hypertension, type 2 diabetes mellitus is a progressive condition. Elevated blood glucose (hyperglycemia) is a marker for insulin resistance, which together with glucose intolerance lead to chronically high circulating blood sugars which subsequently results in diabetes mellitus (Reaven, 1988; Schneider, 2014). Based on the definition, overall hyperglycemia in this study was 10.5%. This result is similar to the 8% reported by Sachithananthan et al. (2012) in Ethiopia. In examining the relationship between HAART and hyperglycemia and the relationship between duration of HAART and hyperglycemia, $\chi^2 = 0.167$, $p = .045$ and $\chi^2 = 63.08$, $p < .001$ were obtained for HAART regimen and duration of HAART regimen, respectively. These associations were statistically significant with medium (0.167 for HAART) to large (0.468 for the duration on HAART) effect size, respectively.

Further bivariate logistic regressions showed odds of hyperglycemia was more than two folds at 12 months (OR= 2.23, 95% CI= 0.910, 5.681) and more than 8-fold at >12 months (OR= 8.33, 95% CI= 2.283, 30.303). There was no statistical significance at

12 months before adjustment. However, adjusting for covariates increased OR by nearly 2-fold (AOR= 4.15) and statistical significance at 12 months ($p < .001$). Also, after taking age, gender, and CD4+ cell count into account in subsequent analyses to control for their influence, HAART regimen at >12 months OR dropped by more than 6-fold (AOR= 1.82), but maintained statistical significance ($p < .001$). Thus, there was sufficient evidence to reject the null hypothesis and accept the alternative hypothesis that duration of HAART regimen increases the odds of hyperglycemia. Abebe et al. (2014) reported a similar result in their study conducted in Ethiopia, where they examined the association between antiretroviral treatment and hyperglycemia and dyslipidemia. Diouf et al. (2012) in Senegal also reported associations between prolonged exposure to HAART and diabetes. However, Hansen et al. (2009) had a different report of no association between presence of metabolic syndrome and HAART duration in Denmark.

The reference point for significance in this study was $p < .05$ and the decision to accept the null hypotheses for each sub-question were based on this reference point, while failure to reach statistical significance was set at the 95% confidence interval (CI). The 95% CI in all the models used implied that the odds in those with hypertension, obesity, and hyperglycemia fell within the ranges of the confidence interval 95% of the time.

To minimize the possibility of a type II error, I interpreted the p-values taking into consideration the confidence intervals (CI). I also interpreted practical significance based on the effect sizes. It is noteworthy to say that the effect sizes obtained in this study were moderate to large. The medium to large effect size implied that the effect sizes are

sufficient to be of practical significance. The statistical and practical significance in the models supports the application of metabolic syndrome theory to the prevalence of hypertension, obesity, and hyperglycemia in this population. Lack of statistical significance in some cases may be that sample size was not big enough and did not necessarily mean that there was no association.

Regarding practical significance of the findings, the effect of duration of HAART on obesity, hypertension, and hyperglycemia was moderate to large (effect size for obesity = 0.291, for hypertension = 0.380, and for hyperglycemia = 0.468). This result showed that duration of HAART supports the metabolic syndrome theory with the covariates adjusted. Thus, going by the metabolic syndrome theory, development of hypertension, obesity, and type 2 diabetes mellitus is an integrated and multi-staged process that involves several metabolic processes.

Also, the inability to establish an association between HAART regimen and the metabolic syndrome components and failure to link NRTIs and NNRTI to the metabolic syndrome components could be due to the reason that only NRTIs and NNRTIs and no PIs drug combinations were used. This is supported by reports of other researchers that metabolic abnormalities are less likely to occur with NNRTI drug combinations (Hansen et al., 2009; Muhammed et al., 2013; Wu et al., 2012).

Although causal relationships between HAART and hyperglycemia, obesity, and hyperglycemia could not be established in this study due to the nature of study design, information on the temporal associations upon which other studies can build was provided. This study also increases the body of knowledge. Results are pointers to the

fact that the length of time a patient is on HAART affect the metabolism of lipid and glucose, as well as the functions of adipose tissue. This effect on metabolism significantly influences metabolic syndrome in HIV patients on HAART regimen. Thus, in this study, HAART regimen for more than 12 months increased the odds of hypertension more than 9-fold; increased the odds of obesity more than 5-fold, and increased the odds of hyperglycemia more than 8-fold before adjustment. However, after adjusting for covariates, HAART regimen for more than 12 months increased the odds of hypertension more than 8-fold; decreased the odds of obesity one- fold, and increased the odds of hyperglycemia by more than six-fold.

The confidence intervals obtained were fairly wide, but most of the results have intervals higher than 1.0. The high interval indicates the observed associations are truly significant, and, with a larger sample size, the interval would be narrowed.

Association Between Immune Status and Metabolic Syndrome Components

CD4+ cells are white blood cells that are vital and play significant role in the immune system (AIDS.gov, 2015). The CD4+ cell counts are used to monitor the immune status and disease progression in HIV patients. CD4+ cell count is a significant indicator of how well the immune system is (AIDS.gov, 2015). The normal CD4+ cell count for healthy adults and adolescents is between 500 cells/ml and 1,200 cells/ml. HIV-infected individuals are usually initiated to commence HAART treatment when the count is < 350 cells/ml. There are conflicting reports on the association between CD4+ cell count and metabolic syndrome. While some previous studies found no association (Worm et al., 2009), other cross-sectional studies found that higher CD4 + cell count increased

the risk for metabolic syndrome (Alvarez, Salazar, & Galindez, 2010). Another cross-sectional study found a different result of low CD4+cell count < 100 cells/ml to be associated with higher risk of metabolic syndrome (Bonfanti, De Socio, Marconi, et al., 2010). This study however found statistically significant associations between CD4+ cell count and hypertension ($\chi^2 = 45.140$, $p < .001$), obesity ($\chi^2 = 14.117$, $p < .05$), and hyperglycemia ($\chi^2 = 25.702$, $p < .001$). Their effect sizes were moderate to large. This result thus justified my inclusion of CD4+ as a covariate in the final model.

In this study, being male, older age, and duration of HAART regimen were factors associated with developing hypertension, obesity, and hyperglycemia. Though not all the findings were statistically significant, this study is consistent with findings from previous similar studies. Comparing results of this study with results obtained in other populations regarding metabolic syndrome is a bit difficult. It is difficult because there are differences in methods, study designs, and data collection, as discussed in Chapter 2. There are no other similar studies that used secondary data, same methods, and design within this population with which to compare findings. Similar studies in other parts of Nigeria (northeast and the southwest) differed in study design and methods (Denue et al., 2012; Muhammed et al., 2013). They used primary data for their studies so did Berhane's et al study in Ethiopia.

In summary, this study is the first study to examine the relationship among HAART regimen and hypertension, obesity, and hyperglycemia; duration of HAART regimen and hypertension, obesity, and hyperglycemia in HIV patients in Umuahia metropolis. The odds of hypertension were more than 4-fold when on HAART for 12

months and more than 18-fold when on HAART for >12 months, compared to HIV patients on HAART for less than 12 months, after adjusting for covariates. Similarly, odds of obesity were nearly 2-fold when on HAART for 12 months and more than 5-fold when on HAART for >12 months. Similarly, odds of hyperglycemia were more than 3-fold when on HAART for 12 months and more than 14-fold when on HAART for >12 months. Statistical significance was achieved in the analyses of HAART duration on hypertension, obesity, and hyperglycemia after controlling for covariates. Regardless of the significant findings, this study has some limitations that are worthy of mention. I discuss these limitations in the following section.

Limitations

The first limitation of this study was the incomplete capture of patient's data in the treatment care cards. Information such as family history of diabetes and hypertension were not recorded. Also not recorded was information on cigarette smoking, alcohol use, and socioeconomic status. These are possible confounders shown by other studies to be associated with metabolic syndrome (Alvarez, Salazar, Galindez et al., 2010). A second limitation was that the hemoglobin A1C (HbA1C) test which is a more reliable method of diagnosing diabetes was not recorded; similarly, there was no information on the use of anti-hypertensive and anti-diabetic medications.

Since there were no sufficient indices for diabetes mellitus diagnosis, I decided to use only the fasting blood sugar (FBS) test report. Hence, I used the term *hyperglycemia* instead of diabetes mellitus where FBS was ≥100mg/dL. The third limitation was that there was no information on lipid profile in patients' records. As a result, low-density

cholesterol and triglycerides assessment which are known risk factors from literature could not be assessed. The fourth limitation was that only NRTI and NNRTI-based regimens were used, and no PI-based regimens were used.

Despite the strength of this study in the stratified method of sampling that should minimize bias and promote generalizability, the study results may not be generalizable beyond the study population because metabolic syndrome components differ by race, ethnicity, and region (Narayanan et al., 2010). Also, because of the limitations detailed above, the internal validity of my study results may be influenced. However, despite these limitations, some significant findings that are consistent with other cross-sectional and association studies were recorded. The validity of the metabolic syndrome components was supported by the ATP III criteria used to define hypertension and hyperglycemia and WHO criteria used to define obesity. Hypertension, obesity, and hyperglycemia were measured laboratory values that used gold standards and were recorded on the individual patients' treatment care cards. The values were continuous and later dichotomized to reflect the presence or absence of each of the component.

Conclusion

The length of time an HIV-infected patient is on the HAART regimen significantly increased the odds of hypertension, obesity, and hyperglycemia. The odds are further increased when patients are older and are males. On the other hand, being on NNRTIs and NRTIs-based regimen alone did not increase the odds of hypertension, obesity, and hyperglycemia. In this study, prevalence of hypertension was higher than

prevalence rates recorded for obesity and hyperglycemia. Prevalence also increased with age, length of time on HAART, and higher in males.

This study showed that while the immune statuses of patients were being improved through HAART regimen, patients were being predisposed to developing hypertension, obesity, and hyperglycemia. As a result, there is a need to assess HIV patients periodically for cardiovascular risk factors while on the regimen. Periodic assessment will ensure early detection and proper management of the risk factors and prevent the additional burden of heart disease. Thus, there is a need to create population awareness of the risks posed by being exposed to HAART regimen for a longer duration. There is also need to develop and implement lifestyle intervention programs for the HIV-positive population undergoing anti-retroviral therapy in Umuahia metropolis.

Recommendations

Given the limitations of this study, and being the first study of this nature in Umuahia metropolis, a prospective study with primary data should be conducted to confirm these results. Data should include all the possible known confounders such as cigarette smoking, alcohol use, type of diet, physical activities, the use of anti-hypertensive and anti-diabetic that were not recorded in patients' medical records. Furthermore, because of the findings of this study that hypertension, obesity, and hyperglycemia increased with age, being male, and duration of treatment, I at this moment recommend that HIV patients on HAART regimen be monitored periodically for high blood pressure, obesity, and hyperglycemia. The periodic monitoring will make room for necessary control and management of the metabolic syndrome components,

especially in the older males. It is pertinent to note that metabolic syndrome components and the risk factors for metabolic syndrome are modifiable. As a result, lifestyle/behavior change intervention programs are advisable for HIV patients on HAART regimen.

My findings provide population-based evidence that can be used by decision makers such as WHO, United States Agency for International Development (USAID), National Agency for the Control of AIDS (NACA), State Agency for the Control of AIDS (SACA), and the management of the Federal Medical Centre, Umuahia for policy making. Also, publishing findings will contribute to the wealth of scientific knowledge. There is the need for more studies to confirm the effects of specific risk factors and covariates such as length of time on HAART regimen, CD4+ cell count, age and sex that appeared to confer risk differently in HIV-infected patients.

Implications

In this study, the length of time a patient was placed on the HAART regimen played a significant contributory role in the prevalence of hypertension, obesity, and hyperglycemia. This has important implications for, metabolic syndrome theory, health care practice, and positive social change in this population.

Implications for Metabolic Syndrome Theory

Despite differences in study aims, design, and methods, results of this study are consistent with previous studies in similar populations, as well as other populations. The results also strengthened the general concept of the metabolic syndrome theory. Thus, metabolic syndrome components not only occur together, but their co-occurrence while

on HAART for more than 12 months was statistically significant as measured after adjusting for gender, age, and CD4+ cell count.

Findings of this study showed that being on HAART regimen for more than 12 months conferred the most risk for hypertension, obesity, and hyperglycemia; and the risks increased with older age, being male and lower CD4+ cell count. This expansion of the metabolic syndrome theory is supported by other studies (Alvarez, Salazar, Galindez et al., 2010; Bonfanti et al., 2010; Dimodi et al., 2014; Malangu, 2013).

Implications for Health Care Practice

In this study, the population-based evidence of risk factors that contribute to hypertension, obesity, and hyperglycemia were shown. These evidence-based risk factors can be taken into consideration by health care providers while caring for patients in this population. Findings in this study support the initiation of and periodic screening for hypertension, obesity, and hyperglycemia in HIV patients on HAART especially when they are older. The periodic screening will help to prevent occurrence of metabolic syndrome components. Also, efforts geared towards disease prevention should focus more attention on blood pressure, BMI, lipids, and fasting blood glucose measurements. This is because early detection and management can go a long way in preventing CVD, thereby preventing additional disease and financial burden on this population group.

Though weight is routinely checked during clinic visits and height taken only at enrolment, the BMI was not calculated to screen for obesity. Thus, this should be addressed by health care providers. Also to be addressed by health care providers is the

inclusion of lipid profile tests as part of the routine tests conducted to enable assessment of the lipid profile of HIV patients while on HAART regimen.

Implications for Positive Social Change

Access to the findings of this study by HIV-infected patients through health talks or population-based intervention programs will equip them with knowledge of the risk factors for hypertension, obesity, and diabetes. By reducing the prevalence of metabolic syndrome components, the risk for CVD, diabetic complications such as blindness and amputation of the lower limbs, and kidney failure will be significantly reduced. Knowledge of study findings will also reduce or eliminate additional medical expenses caused by hospitalization as a result of chronic diseases, thereby improving the overall health and quality of life of this population. Furthermore, loss of income through reduced productivity as a result of ill health will also be minimized.

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Appendix A: Data Abstraction Form

Data abstraction form

Participants Serial Number	Enrolment/ Clinic visits/HAART Initiation Dates	Duration on HAART	Age	Sex	Type of HAART	Weight (Kg)	Height (M)	Blood Pressure Measurement (mm Hg)	Fasting Blood Glucose (mg/dl)	CD4+ Cell Count (cell/ml)
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