PREVALENCE OF IMPAIRED FASTING GLUCOSE AND DIABETES MELLITUS AMONG HIV INFECTED INDIVIDUALS ON ANTI-RETROVIRAL THERAPY AT THE ADULT INFECTIOUS DISEASE CENTRE, LUSAKA

By

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A dissertation submitted in Partial Fulfilment of the Requirements for the Degree of Master in Public Health- Population Studies

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DECLARATION

I hereby declare that this dissertation is my original work and has not been presented either wholly or in part for a degree at the University of Zambia or any other University.

Signed……

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I have read this dissertation and recommend it for examination

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ABSTRACT

Background: Traditional host factors and treatment related metabolic changes are implicated in the increase of impaired glucose levels and Type 2 diabetes mellitus in HIV patients. Diabetes mellitus has specific morbidity and mortality consequences. It also contributes to the burden of other non-communicable and communicable diseases. In HIV patients it could further contribute to ill health and present new challenges for therapeutic management of HIV/AIDS. As new HIV guidelines are implemented and scale up of ART programs takes effect, the number of individuals on lifelong therapy is bound to increase and potentially the incidence of impaired glucose levels and Type 2 diabetes mellitus in this population.

Objective: To determine the prevalence and risk factors associated with impaired fasting glucose and Type 2 diabetes mellitus amongst HIV infected individuals on antiretroviral drugs at the Adult Infectious Disease Centre, Lusaka.

Methods: A cross sectional study included HIV infected individuals accessing care and receiving antiretroviral therapy at the Adult Infectious Disease Centre (AIDC), University Teaching Hospital in Lusaka. Eligible participants presenting to facility for scheduled follow up visits were consecutively enrolled. A modified WHO global surveillance initiative NCD-STEP 3 method was adapted for data collection to determine point prevalence of impaired fasting glucose and Type 2 diabetes mellitus. Diabetes mellitus and impaired fasting glucose were defined per WHO 2006 diagnostic criteria as fasting blood sugar concentration of $\geq$ 7.0 mmol/L and $\geq$ 6.1 to $\leq$6.9 mmol/L respectively. Data was analysed using STATA version 12 and cross tabulations utilized to assess relationship between impaired fasting glucose, diabetes mellitus and explanatory variables. Categorical data were compared using chi-square test and expressed as proportion with a 95% confidence interval.

Results: Of the 224 participants in the survey, 56.7% were females. 71% of the participants were of age 20-45 years. Twenty 20 (8.9%) participants (12 females and 8 males) had impaired fasting glucose, while 4 (1.8%) participants (all males) had diabetes mellitus, giving an overall prevalence of impaired glucose level of 10.7%. It was also found that 28.1 % of the participants were overweight while 15.2% were obese. Body Mass Index and age were associated with Impaired Fasting Glucose and Type 2 Diabetes Mellitus.

Conclusion: There is a significant prevalence of dysglycemia among HIV infected patients on ART accessing care at AIDC in UTH, Lusaka. Dysglycemia is a potential threat to HIV infected persons and likely influenced by a host of factors. Regular monitoring and screening for hyperglycemia is imperative for early diagnosis, prevention and treatment of impaired glucose levels/ Type 2 diabetes mellitus to minimize incidence and severity of acute and long term complications and avert premature mortality.

Dedicated to mum, Freda Chalwe Mapulanga for her unwavering love and support.

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Table of Contents

LIST OF TABLES

LIST OF FIGURES

Appendices

LIST OF ABBREVIATIONS

AIDC – Adult Infectious Disease Centre

AIDS – Acquired Immune Deficiency Syndrome

ART- Antiretroviral Therapy

ARV- Antiretroviral

BMI- Body Mass Index

FBS- Fasting Blood Sugar

HAART - Highly Active Antiretroviral Therapy

HIV- Human Immunodeficiency Virus

IFG – Impaired Fasting Glucose

MOH – Ministry of Health

NCD- Non Communicable Disease

PLHIV- People Living with HIV/AIDS

RAPIA- Rapid Assessment Protocol on Insulin Access

SSA- Sub-Saharan Africa

T2DM – Type 2 Diabetes Mellitus

UNFPA- United Nations Population Fund

UTH – University Teaching Hospital

WHO- World Health Organization

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

There is said to be an increased prevalence of diabetes mellitus among infected HIV individuals particularly with the use of antiretroviral drugs. In general, cases of Type 2 diabetes mellitus are escalating globally with latest estimates revealing 382 million people living with the disease worldwide with a predicted 55% increase by the year 2035 (IDF 2013). The greatest increases which were anticipated in some of the world's poorest regions, with Sub-Saharan Africa being impacted the most, are already being observed. Identified as one of Africa's new silent killers, T2DM is largely being propelled by urbanization and epidemiological transition (Cohen et al., 2010). Accompanying lifestyle changes including widespread tobacco use, substance and alcohol use/abuse, reduced physical activity and consumption of diets rich in saturated fats and refined sugars are major contributing factors (Azevedo and Alla, 2008). Traditional risk factors associated with T2DM in the general population apply to HIV infected individuals. Further, the iatrogenic effects of antiretroviral therapy (ART) and the HIV infection itself are thought to increase risk for impaired blood glucose levels and T2DM. In Zambia research on diabetes mellitus is limited. However, previous estimates from a 2011 comprehensive general population based survey on the prevalence rate of impaired glucose or diabetes mellitus and its correlates among persons 25 years or more in Lusaka Urban District provide some baseline information. The study of 1928 respondents, found a combined prevalence for impaired glucose level or diabetes mellitus of 4%. Age and mild hypertension were significantly associated with impaired glucose level or diabetes mellitus (Nsakashalo et al., 2011).

1.2 Diabetes Mellitus and intermediate states of hyperglycemia

Diabetes mellitus, Impaired Fasting Glucose and Impaired glucose tolerance, are seen as progressive stages of the same disease process. The term diabetes mellitus describes a metabolic disorder with heterogeneous etiologies. It is characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Individuals with diabetes mellitus are also at increased risk of cardiac, peripheral arterial and cerebrovascular disease (WHO 2014). Type 2 diabetes mellitus accounts for 90% of diabetes cases globally (WHO 2014) and is also the most predominant form of the disease in the region (Levitt, 2008). T2DM etiology is associated with obesity, decreased physical activity and unhealthy diets. It occurs more frequently in individuals with hypertension, dyslipidemia (abnormal cholesterol profile), and central obesity and is a component of "metabolic syndrome". Individuals with a family history of diabetes mellitus have an increased risk of occurrence however, it is a complex disease caused by mutations in more than one gene, as well as by environmental factors. Impaired fasting glucose (IFG) is a state of higher than normal fasting blood glucose concentration, but lower than the diagnostic cut-off for diabetes mellitus. It is an intermediate condition in the transition between normality and diabetes mellitus. It is considered pre-diabetic or a risk category for progression to T2DM although this is not inevitable. IFG is linked to a greater risk for vascular problems, kidney disease, nerve and retinal damage. Moreover 5-10% of pre-diabetics transition to diabetes mellitus each year (Mainous et al., 2014). Impaired Glucose Tolerance (IGT) is a state of higher than normal blood glucose concentration 2 hours after 75 gram oral glucose load but less than the diagnostic cut-off for diabetes mellitus. Impaired Fasting Glucose and Impaired Glucose Tolerance are predictors of incident T2DM. Thus, a high IGT prevalence alongside a low

T2DM prevalence may indicate the early stage of a diabetes epidemic (Hall et al., 2011). WHO (2006) recommends that glucose levels associated with low risk of developing diabetes mellitus or cardiovascular disease, that is levels below those used to define intermediate hyperglycemia be considered normal glycemic since there are insufficient data to accurately define normal glucose.

1.3 Diabetes Mellitus in HIV patients

Clinical presentation of diabetes mellitus in HIV patients is consistent with that of T2DM and evidence of islet autoimmunity suggestive of Type 1 diabetes mellitus is distinctly uncommon (De Wit, 2008). Chronic infection with HIV is associated with impaired glucose levels and T2DM in patients. Several factors partly explain the pathogenesis of diabetes mellitus detected during the natural history of HIV infection. The chronic inflammatory nature of the infection affects different body organs including the pancreas. Damage to the pancreas can result in inadequate insulin secretion and consequently insulin resistance or diabetes mellitus. A study found inflammatory markers, particularly those associated with TNF-α activity, 48 weeks after ART initiation were associated with incident diabetes in all groups of HIV-infected men compared with HIV-uninfected control subjects. This was consistent even among those who were not receiving ART, suggesting an effect of HIV infection itself (Brown et al., 2010). HIV is also associated with various endocrine abnormalities, including those of the growth hormone axis. These include deficiency of growth hormone, as well as growth hormone resistance. Growth hormone deficiency may contribute to insulin resistance in HIV-infected patients. The increased accumulation of visceral fat, with wasting of subcutaneous fat, noted in these patients, creates higher levels of inflammatory cytokines such as TNFα. This in turn leads to diabetes mellitus or impaired glucose tolerance by increasing insulin resistance. Viral factors which contribute to risk of

diabetes mellitus or accelerate the pathogenesis of the disease are high pre-ART viral loads/increase in viral burden, low baseline CD4+ counts, and longer duration of HIV infection. In general, people with severe, long-standing HIV infection are more prone to developing diabetes mellitus (Kalra et al., 2011; Moyo et al., 2014).

Diagnostic testing for diabetes mellitus in HIV patients is similar to non-HIV infected persons, with the exception of glycated hemoglobin (HbA1c). HbA1c appears to underestimate exposure by 10% to 15% in HIV-infected patients, hence not recommended. Although the precise mechanism is unclear it is partially explained by the effects of the virus on hemoglobin, and the effects of some antiretroviral drugs, such as Zidovudine (Diop et al., 2006).

1.4 ART and Diabetes Mellitus

Though its occurrence is thought to be multifactorial, several studies have established a strong association between use of antiretroviral therapy and impaired glucose tolerance, diabetes mellitus and lipid disorders leading to an increase in cardiovascular diseases (De Wit et al., 2008; Hall et al., 2011; Maher and Sekajugo, 2011; Samaras, 2009). Up to a fourfold increase in diabetes mellitus risk has been associated with ART exposure. Incidence of diabetes mellitus has been reported to be between 1-10% in HIV-infected adults receiving ART in high income countries (Yoon et al., 2004) while another study has found a prevalence of 14% (Brown et al., 2005). There are several thoughts on the mechanism of ART induced diabetes mellitus including class-specific and drug-specific adverse metabolic effects (Samaras, 2009). Protease inhibitor drugs, Nucleoside Reverse Transcriptase Inhibitors (NRTI's) such as Stavudine and Zidovudine are implicated to have a direct effect on glucose metabolism. They may also induce insulin resistance indirectly, through changes in body

composition that include the loss of beneficial subcutaneous fat and gain of harmful visceral fat (Brown et al., 2010). While Stavudine has shown the strongest relationship with new-onset diabetes mellitus, exposure to Zidovudine and Didanosine has also been linked (De Wit et al., 2008).

According to De Wit and others (2008) the ART regime itself might confer individual or additive risks that could trigger cumulative diabetes mellitus events in the genetically disposed. The efficacy of combined ART and improved nutritional status may result in significant weight gain in many HIV-infected patients which may result in additional risk factors such as insulin resistance. Antiretroviral drugs have also been implicated with lipodystrophy – an abnormality in the metabolism or deposition of body fat distribution in HIV positive patients. This has been strongly associated with insulin resistance and/or glucose intolerance, with excess trunk or visceral fat being, as in the general population, a risk factor for insulin resistance among those with HIV. Moreover, effective treatment with ART significantly reduces morbidity and mortality; this means an increase in life expectancy for HIV infected individuals and consequent susceptibility to age-related comorbidities such as diabetes mellitus.

The commonly used antiretroviral drugs in Zambia are listed in Table 1 with the diabetogenic/lipogenic drugs highlighted. The drugs appear to work well among conventional patients diagnosed to be HIV positive and treated accordingly. However, therapeutic management of patients is potentially compromised when polypharmacy, diet modifications and related expenses that accompany co-infections such as Diabetes mellitus Tuberculosis and Hypertension occur.

1.5 Challenges of diabetes mellitus as a comorbidity in HIV/AIDS patients in Zambia

Zambia like many African countries will be contending with the dual disease burden of infectious diseases and emerging non-communicable diseases. HIV/AIDS continues to be a major public health issue with a prevalence rate of 14.3% (ZDHS, 2007). Rapid scale up of ART services is one of the most significant responses in the fight against HIV/AIDS. According to the 2010 Annual Health Statistical Bulletin, the total number of adults and children receiving ART in accordance with the nationally approved treatment protocol increased from 283863(2009) to 344407(2010), representing a 21% increase. ART services including prescription and or provision of clinical follow up are available in 454 healthcare facilities (2010), a 22% increase from 373 healthcare facilities in 2009. The ultimate objective is to attain 100% coverage and ensure zero infections to mothers and their newborns. Zambia intends to achieve this through new guidelines including Treatment as prevention TasP, the most recent eMTCT-option B+ among others.

Laboratory evaluations are a significant component of HIV/AIDS therapy. Patients in industrialized countries are routinely monitored for asymptomatic laboratory abnormalities as a result of potentially life threatening toxicities associated with some antiretroviral medications (Koenig et al., 2010). Moreover, these countries also have established guidelines for management of diabetes mellitus. Majority of the health sectors in the region are financially burdened by infectious diseases and emerging non-communicable diseases. These constraints in most countries limit laboratory monitoring in patients on ART. As a result often focus scarce resources on tests that will have the most impact on care and clinical benefits. The country national guidelines for HIV/AIDS management are based on WHO recommendations. Similar to other countries within the region Zambia lacks adequate

resources to conduct all recommended laboratory investigations in patients on ART. Currently glucose testing is not part of routine laboratory tests conducted in HIV patients (see Appendix 1).

1.6 Impact of dual disease burden

In Zambia the prevalence of diabetes mellitus in HIV patients is yet to be established. The burden of infectious diseases and limited resources has meant less priority given to non communicable diseases. However, diabetes mellitus not only has specific morbidity and mortality consequences, it also contributes to the burden of other non-communicable diseases such as renal and cardiovascular disease as well as communicable diseases such as pneumonia and tuberculosis, further increasing its impact on public health (Rabkin et al., 2012). Diabetes mellitus also requires substantial amounts of money as revealed by a study of the economic burden of diabetes mellitus in the WHO African region. The estimated total economic loss due to the disease was US$41.76 billion, with US$37.54 billion towards direct cost, of which 98.80% was spent solely on Insulin and devices for administration (African Health Monitor, 2008). Therefore the emergence of impaired glucose levels and T2DM in HIV patients has implications for our patients and the healthcare system hence the need for a proactive approach.

Table 1: ART drugs used in Zambia 2013 (Those associated with dysglycemia are in bold)

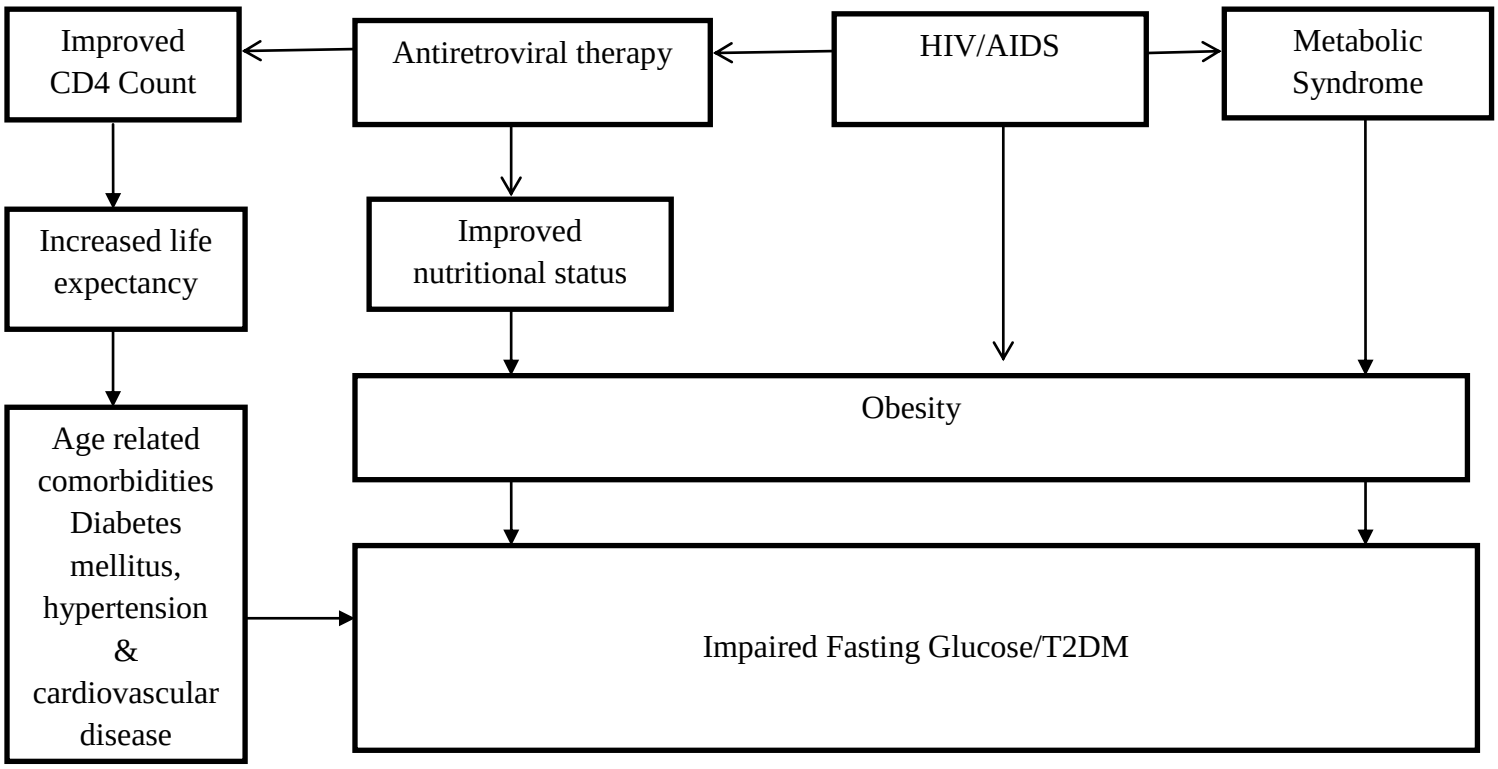
Nucleoside Reverse Transcriptase Inhibitors (NRTI's)
Abacavir (ABC)
Lamivudine (3TC)
Emtricitabine (FTC)
Zidovudine (AZT)
Stavudine (d4T)
Tenofovir Disoproxil Fumarate (TDF)
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI's)
Nevirapine (NVP)
Efavirenz (EFV)
Etravirine (ETR)
Protease Inhibitors (PI)
Lopinavir/ritonavir (LPV/r)*
Darunavir (DRV)
Atazanavir (ATV)
Ritonavir (r)
Integrase Strand Transfer Inhibitors (INSTI)
Raltegravir (RAL)

Source-www.aidsinfo.nih.gov/drugs

1.7 STATEMENT OF THE PROBLEM

Conventional diabetes mellitus risk factors, antiretroviral drugs used in the treatment of patients and the HIV infection itself are said to potentiate dysglycemia and consequently diabetes mellitus in HIV-infected individuals. Emergence of diabetes mellitus and its associated complications is a threat to patient health and could present new challenges for management of HIV/AIDS. Currently screening for impaired glucose levels and Type 2 diabetes mellitus is not a component of routine laboratory investigations under the national HIV guidelines in Zambia. Further, there is no focused assessment for diabetes mellitus in patients. In the absence of routine monitoring, impaired glucose levels and diabetes mellitus are likely to remain undiagnosed. Diagnosis when made is usually a consequence of related complications. This has an impact on treatment outcomes and contributes to increased morbidity and premature mortality in HIV patients. This study is elucidating impaired glucose levels and Type 2 diabetes mellitus in HIV patients on antiretroviral therapy and the associated risk factors.

FIGURE 1: PROBLEM ANALYSIS DIAGRAM FOR PREVALENCE OF IMPAIRED FASTING GLUCOSE AND T2DM IN HIV POSITIVE PERSONS ON ART



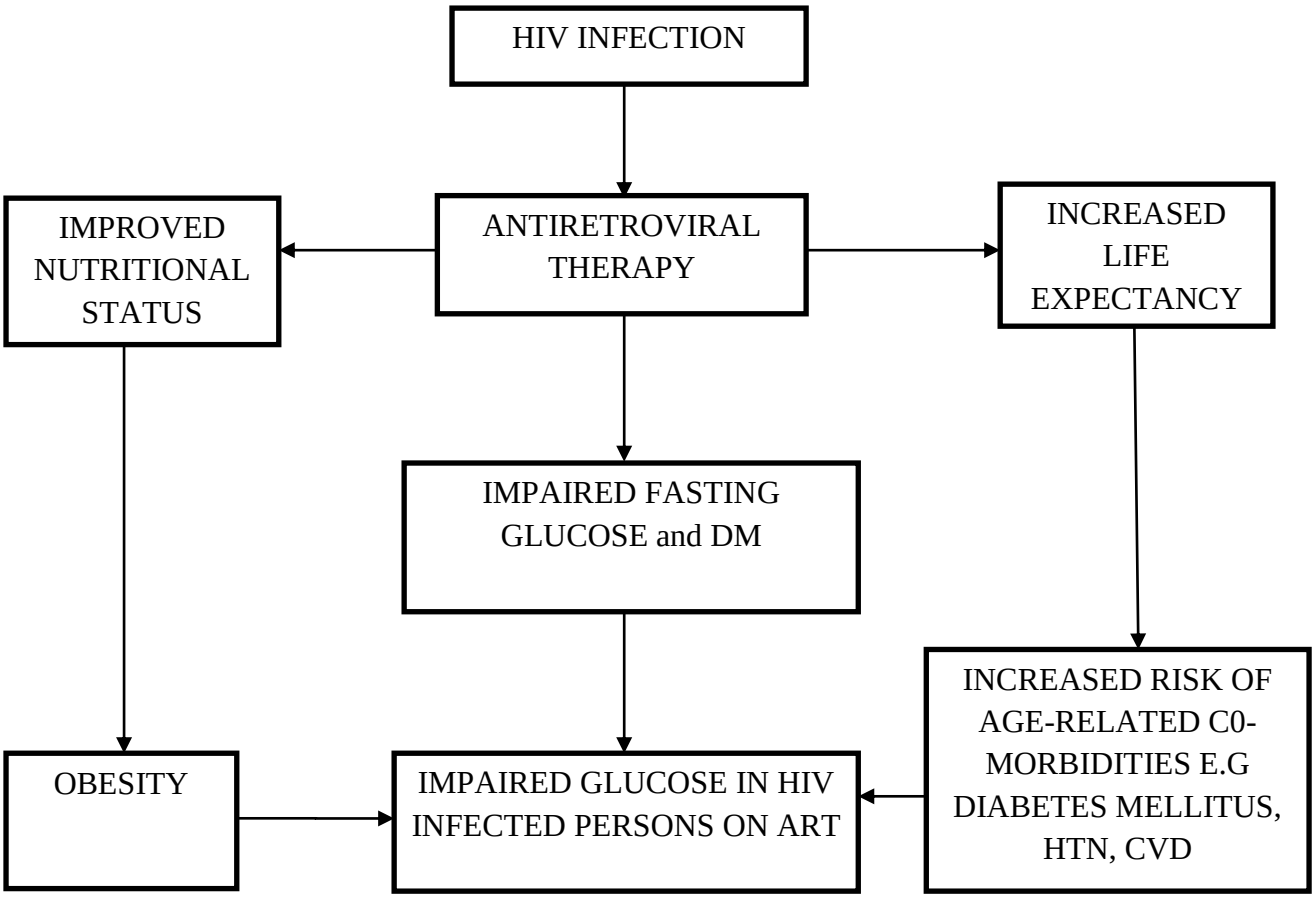
1.8 JUSTIFICATION OF STUDY

Reports of increasing incidence of impaired glucose levels and T2DM in HIV patients in other countries may also be true for Zambia. The adverse effects of antiretroviral drugs may be unavoidable in lieu of the life saving function. However, the associated risk to metabolic derangements cannot be overlooked. With the success of integrated HIV programs including ART services, less consideration may be given to impaired glucose levels and T2DM as a threat at this time. However glucose levels can increase unknowingly over time. Impaired fasting glucose also known as pre-diabetes is linked to a greater risk for vascular problems, kidney disease, nerve and retinal damage. Moreover 5-10% of pre-diabetics transition to diabetes mellitus each year (Mainous et al., 2014). HIV specialists or endocrinologists may be well aware of such conditions and evaluate and treat a patient accordingly. However, inadequate human resource means most of our facilities do not have a specialist on staff leaving frontline health care personnel to manage patients. Inadequate or wrong management of conditions at health centres mean delayed diagnosis and treatment. This results in challenges in managing the disease adequately especially in the presence of immunosuppression and predisposes individual to premature mortality. Moreover, this has cost and social implications for patients, their families, communities and the healthcare system. As reported the African diabetic patient is characterized by high mortality, death either before developing complications or prematurely as a result of complications. A majority of the cases of diabetes mellitus go undetected and undiagnosed with estimation as high as 60-80% in Cameroon, Ghana and Tanzania (Jamison et al., 2006). Therefore, assessment that relies solely on a clinician cannot be sufficient. Additional tools such as routine screening focused diabetic assessment, awareness among healthcare staff, sensitization among patients and communities are indicated. The numerous advances being made in diabetic education, prevention and treatment make it a chronic condition that can be

managed successfully, provided key early intervention. To date a policy framework that incorporates clear defined guidelines for prevention, treatment and organization of care for diabetes mellitus in Zambia is yet to be implemented. Researching the subject in local context helps to identify the problem and its magnitude and facilitates public health responses that match our needs and resources.

CONCEPTUAL FRAMEWORK

Figure 2: Conceptual framework for prevalence of Impaired Fasting Glucose and T2DM in HIV infected individuals on ART



The figure illustrates the main determinants of impaired fasting glucose and diabetes mellitus. These are some of the factors contributing to the prevalence of diabetes mellitus in HIV positive individuals. Other factors that could be taken into consideration are the HIV infection itself, age, sex, family history and traditional risk factors of diabetes mellitus such as obesity and physical inactivity. For the purpose of this study the main variable explored was fasting blood sugar. Age, sex, BMI, ART regimen, family history of diabetes mellitus and residence were considered as correlates.

1.9 RESEARCH QUESTION

Is Impaired Fasting Glucose and Type 2 diabetes mellitus more prevalent in HIV patients on Antiretroviral Therapy?

1.9.1 GENERAL OBJECTIVE

- To determine the prevalence and risk factors associated with impaired glucose levels and Type 2 diabetes mellitus amongst HIV infected individuals on antiretroviral drugs at the Adult Infectious Disease Centre, Lusaka.

1.9.2 SPECIFIC OBJECTIVES

- Determine the prevalence of impaired glucose levels and Type 2 diabetes mellitus amongst HIV infected individuals receiving antiretroviral drugs at the Adult Infectious Disease Centre
- Examine association between determinants of impaired glucose levels and Type 2 diabetes mellitus and occurrence of the disease amongst HIV infected individuals receiving antiretroviral drugs at the Adult Infectious Disease Centre

1.10 VARIABLES AND INDICATORS OF MEASUREMENTS

The 2006 WHO Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia were used to define the following per fasting blood sugar concentration; Diabetes mellitus $\geq$ 7.0 mmol/L (126mg/dl) and Impaired Fasting Glucose $\geq$ 6.1 and $\leq$ 6.9 mmol/L (110mg/dl to 125mg/dl). Capillary and venous glucose samples being identical in a fasting state.

Table 2: STUDY VARIABLES, CUT – OFF POINTS & INDICATORS

Variables	**Cut-off point**	**Indicator**
Independent variables		
Age	≥ 18 years	
Sex	Male Female	
Residence	Low density area Medium density area High density area	
Body Mass Index	≤ 18.5 kg/m^2 18.5-24.9 kg/m^2 25 - 29.9 kg/m^2 ≥30 kg/m^2	Underweight Normal Overweight Obese
ART regimen	Antiretroviral drugs prescribed	
Family History of diabetes mellitus	Yes No	
Dependent Variable		
Fasting Blood sugar concentration	≥ 7.0 mmol/L ≥ 6.1 mmol/L- ≤ 6.9 mmol/L < 6.1 mmol/L	Diabetes mellitus Impaired Fasting Glucose (IFG) Normal

CHAPTER TWO

2.0 LITERATURE REVIEW

The potential interaction between HIV and diabetes mellitus has been researched in industrialized countries. A 1% - 10% incidence of the disease has been reported in HIV-infected adults receiving ART (Yoon et al., 2004). In another study a prevalence of diabetes mellitus of up to 14% was reported by Brown et al., (2005). Globally cases of diabetes mellitus are escalating with latest estimates revealing 382 million people living with diabetes worldwide. This figure is predicted to increase by 55% by the year 2035 (IDF 2013). The prevalence is expected to increase in some of the world's poorest region with Sub-Saharan Africa affected the most. The thought is that this will change some important infections in the region, such as TB and particularly HIV as a result of life long ART used in treatment. The risk factors for diabetes mellitus in the region are no different from the global attributes. However, rapid urbanization and globalization has caused a health transition and change in lifestyles as many adopt western dietary practices, consume and abuse alcohol, develop smoking habits and adopt sedentary lifestyles (Lekoubou, 2010). Traditional diabetes risk factors apply to HIV infected individuals as in the general population. Further, HIV- specific risk factors have been implicated in the occurrence of the disease in HIV patients. The clinical presentation of diabetes mellitus in HIV infected individuals is consistent with that of Type 2 diabetes mellitus. Previous literature reveals no evidence of autoimmunity suggestive of Type 1 Diabetes Mellitus. Whilst epidemiological studies outside sub-Saharan Africa (SSA) have associated diabetes mellitus with infectious diseases of great importance in this region, the literature review identified little epidemiological data on this association in SSA (Hall et al., 2011). The effect of HIV on insulin resistance and diabetes mellitus in patients in Africa is largely unknown with the exception of studies in South Africa and Botswana.

2.1 Epidemiology of Diabetes mellitus in HIV infected individuals

The epidemiology of diabetes mellitus in HIV infected individuals includes traditional risk factors of diabetes mellitus and HIV-specific risk factors. Traditional risk factors some modifiable and others non-modifiable, include age, sex, obesity, physical inactivity and family history of diabetes mellitus. The HIV-specific risk factors include the HIV infection, CD4 count, and antiretroviral therapy.

2.2 Traditional risk factors

2.2.1 Age

Regardless of HIV status, age is a consistent risk factor for impaired glucose levels and T2DM. Studies examining the association between HIV and diabetes mellitus found older age was a risk factor for dysglycemia in HIV patients (Butt et al., 2009; Dave et al., 2011). In a related Swiss HIV cohort study , older people (>65 years) with HIV were up to four times more likely to develop diabetes mellitus compared with those under the age of 50 years (Hasse et al., 2011). The advent of effective antiretroviral therapy also means HIV infected individuals live longer and consequently susceptible to aging-related comorbidities, such as diabetes mellitus.

Impaired glucose levels in SSA, as in other regions of the world, increase with age. In Zambia, Nsakashalo et al., (2011) reported that impaired glucose levels and diabetes mellitus were associated with older participants' compared to those in the age group 25-34 years. While the prevalence varied with age, the highest prevalence was in the age group 45+ years, with a rate of 1.2% in those 54-55 years of age. While diabetes mellitus has previously been observed in the elderly, literature reveals the trend is changing as much younger people are affected. Further, the burden of T2DM is disproportionately borne by individuals in the

reproductive and economic stage of life, which is also the age-group most profoundly affected by HIV in this region.

2.2.2 Sex

Males have typically been known to have an increased risk for impaired glucose levels and T2DM. A large multinational cohort analysis on the incidence and risk factors for new-onset diabetes mellitus in HIV-infected patients, found that male sex was associated with a 60% higher risk of diabetes mellitus (De Wit et al., 2008). This is consistent with a study in Cape Town, South Africa that reported being male as a risk factor for impaired glucose levels in HIV patients (Dave et al., 2011).

Sub-Saharan Africa is home to about 76% of all HIV- positive women with 13 women in the region infected with HIV for every 10 men (UNAIDS global report fact sheet on SSA, 2011). In nearly all countries in the region, majority of people living with HIV are women, especially girls and women aged 15-24. In Zambia, more women than men are HIV infected accounting for 16.1% and 12.3% respectively (ZDHS 2007). While in South Africa, HIV prevalence among women aged 20-24 is approximately 21%, compared to about 7% among men in the same age range. In Lesotho, nearly 8% of young women aged 15-19 are living with HIV, compared to about 3% of their male counterparts.

Unlike other studies, in Zambia, prevalence of impaired glucose levels and diabetes mellitus was found to be higher in women compared to men. Nsakashalo et al., (2011) reported a total of 24 (1.3%) participants with impaired glucose levels (8 (33.3%) males and 16 (66.7%) females. Fifty one (2.7%) participants had diabetes mellitus (13 (25.5%) males and 38 (74.5%) females)

2.2.3 Obesity

Worldwide obesity is reported as a significant risk factor for Type 2 diabetes mellitus leading to the use of the word "diabesity" both in rural and urban areas. Once prevalent in high income countries obesity is now common in low-middle income countries. Increasing prevalence has been attributed to changes in lifestyle that reduce physical activity, increase caloric intake and subsequent weight gain. According to WHO, in 2008, more than 1.4 billion adults were overweight and more than half a billion were obese (WHO's Action Plan for the Global Strategy for the Prevention and Control of Non communicable Diseases). At least 2.8 million people each year die as a result of being overweight or obese. In Africa, in general, WHO estimates that more than one-third of the women are obese compared to one-fourth of the men, with the poor being as vulnerable as the rich (Azevedo and Alla, 2008). In some cultures particularly in Africa larger body sizes are perceived as signs of good health and affluence thus may not necessarily be considered a health risk. In HIV patients, 'Return to health' phenomenon (Reid et al., 2012) may increase risk as a result of improved nutritional status that often accompanies effective ART. This predisposes patients to obesity and consequently impaired glucose levels and diabetes mellitus. Specific drugs and metabolic syndrome have also been known to induce obesity in patients. In their study Butt et al., (2009) concluded that BMI in addition to other factors had a more profound effect upon the risk of diabetes mellitus among HIV infected persons. Samaras, (2012) reported diabetes rates in HIV-infected individuals, were two-fold higher in obese participants, compared with those with normal body mass index. In a related study Botswana researchers assessing the characteristics of HIV and diabetes mellitus in patients receiving antiretroviral therapy (ART) found notably, pre-ART weight, particularly if >70 kg, was associated with the diagnosis of diabetes mellitus in HIV-infected patients (Moyo et al., 2014). Similarly in Zambia obesity is a growing public health concern. A prevalence and correlates study of

obesity among Lusaka residents, found 14.2% of the participants (5.1% of males, and 18.6% of females) were obese (Rudatsikira et al., 2012). In a separate study on prevalence and correlates of diabetes mellitus Nsakashalo et al., (2011) reported the highest rates among participants who were obese. In general nutritional status and management in HIV/AIDS is aligned more with weight gain and maintenance. This might be in line with the stigma that accompanies weight loss and wasting in some HIV infected individuals.

2.2.4 Family History

A positive family history of diabetes mellitus seems to be an independent risk factor of occurrence of the disease.

2.2.5 Urbanization

According to UNFPA (2014), the world is undergoing the largest wave of urban growth in history with more than half of the world's population now living in towns and cities. This number is expected to increase to about 5 billion by the year 2030. Much of the urbanization is expected to unfold in Africa and Asia, bringing huge social, economic and environmental transformations. Urbanization has been cited as a contributing factor in the increasing prevalence of Type 2 diabetes mellitus in the region. It is often accompanied by improvement in socio-economic status that brings about life style changes that include unhealthy diets and decreased physical activity. In comparison to rural areas, urban settings present an increased prevalence of obesity. Projections that by 2025 70% of Africans will live in cities, with a regional annual urban growth rate of 4.5% suggest that levels of obesity and T2DM diabetes will continue to rise in the region (Jamison et al., 2006).

2.3 HIV-specific risk factors

2.3.1 HIV infection

Chronic infection with HIV is associated with impaired glucose levels and T2DM in patients. Several factors partly explain the pathogenesis of diabetes mellitus detected during the natural history of HIV infection. The chronic inflammatory nature of the infection affects different body organs including the pancreas. Damage to the pancreas can result in inadequate insulin secretion and consequently insulin resistance or diabetes mellitus. HIV is also associated with various endocrine abnormalities, including those of the growth hormone axis. These include deficiency of growth hormone, as well as growth hormone resistance. Growth hormone deficiency may contribute to insulin resistance in HIV-infected patients. The increased accumulation of visceral fat, with wasting of subcutaneous fat, noted in these patients, creates higher levels of inflammatory cytokines such as TNFα. This in turn leads to diabetes mellitus or impaired glucose tolerance by increasing insulin resistance. A study found higher insulin resistance markers of TNF-α activation 48 weeks after initiation of ART were associated with incident diabetes in all groups of HIV-infected men. This was comparable in HIV-uninfected control subjects, even among those who were not receiving ART, suggesting an effect of HIV infection itself (Brown et al., 2010). HIV infection is associated with the development of the metabolic syndrome found in 18% to 33% of HIV infected individuals (Hall et al., 2011). Metabolic syndrome refers to the constellation of phenotypes of abdominal obesity, hyperlipidemia, elevated fasting glucose and hypertension. These can result in several conditions including new onset diabetes mellitus or decrease in glycemic control in existing diabetic patients (Cohen et al., 2010; Hall et al., 2011). A study by Samaras et al., (2007) found metabolic syndrome was more common in those receiving protease inhibitors (PIs; P = 0.04). Further, Type 2 diabetes prevalence was fivefold to nine

fold higher in those with metabolic syndrome. Viral factors which contribute to risk of diabetes mellitus or accelerate the pathogenesis of the disease are high pre-ART viral loads/increase in viral burden, low baseline CD4+ counts, and longer duration of HIV infection. In general, people with severe, long-standing HIV infection are more prone to developing diabetes mellitus (Kalra et al., 2011; Moyo et al., 2014).

2.3.2 CD4 count

There have been conflicting results regarding the role of CD4 count and risk of developing diabetes mellitus. In one study, HIV-infected men with a lower nadir CD4 count had an increased risk of incident glucose abnormalities compared with those with higher nadir CD4 counts (Brown et al., 2005; Kantor et al., 2005). However, in another French cohort study of HIV-infected patients followed for 10 years, there was no association between CD4 nadir and the onset of diabetes mellitus (Capeau et al., 2012).

2.3.3 Antiretroviral therapy

Current evidence suggests combinations of medications used in the management of HIV/AIDS are associated with glucose abnormalities that consequently lead to diabetes mellitus. Most importantly, the association remained significant after adjusting for potential risk factors for diabetes mellitus. The thought is that the drugs exert their effect by a number of mechanisms and action can be class or drug specific. Certain ARV drugs more than others may directly or indirectly predispose patients to metabolic derangements.

Despite its benefits ART has been implicated in increased risk of insulin resistance in 25%-30% of HIV–infected patients (Adeyemi et al., 2009), diabetes mellitus, lipoatrophy and dyslipidemia. A Multicenter AIDS Cohort Study determining the prevalence and incidence of diabetes mellitus in a cohort of HIV-infected and HIV-seronegative men revealed the

following; incidence of diabetes mellitus in HIV-infected men with HAART exposure was greater than 4 times that of HIV-seronegative men, representing a risk that was higher than previous estimates. Out of the 411 HIV-infected men using HAART at the baseline visit, fifty-seven (14%) had prevalent DM compared with 33 (5%) of the 711 HIV-seronegative men (Brown et al., 2005). Exposure to Zidovudine and Didanosine also increased the risk. In another study, Stavudine, Zidovudine and Didanosine were shown to have a stronger relationship with diabetes mellitus and implicated to have a direct effect on glucose metabolism. The (D: A: D) study reported a 19% relative risk of developing diabetes mellitus with exposure to Stavudine (De Wit et al., 2008). The drugs may also induce insulin resistance indirectly, through effects on body composition. According to De Wit et al., (2008) the association between diabetes/insulin resistance and Stavudine/Zidovudine through indirect mechanism i.e. lipodystrophy, is a state associated with accelerated onset and increased prevalence of diabetes mellitus. This is consistent with a study examining the case definition of lipodystrophy in HIV-infected adults that found a 7% prevalence of diabetes mellitus in those with lipodystrophy compared to 3% in those without lipodystrophy (Carr et al., 2003). Protease Inhibitors (PIs) such as Ritonavir and Lopinavir were the first HIV medications to be implicated in the pathogenesis of glucose abnormalities among HIV-infected patients (Samaras, 2009). Research has shown that individual PIs have different mechanisms of inducing insulin resistance and that risk for diabetes mellitus is dose (Taylor et al., 2010) and duration dependent (Capeau et al., 2012). In almost all patients where PIs were discontinued hyperglycemia resolved (Lee et al., 2004). The use of antiretroviral drugs in combination and varying individual treatment regimens have made it difficult to completely isolate which class of drugs may be solely responsible for the risk of diabetes mellitus. Instead it is thought risk of diabetes mellitus may be attributed to a cumulative dose effect. In their study Butt et al., (2009) concluded that increasing age, HCV co-infection and

BMI had a more profound effect upon the risk of diabetes among HIV infected persons, with long term ART increasing the risk. The Women's Interagency HIV Study reported similar findings of a relative hazard of 2.64 [95% CI: 1.11-6.32] for the risk of diabetes mellitus among PLHIV who were exposed to Nucleoside reverse transcriptase inhibitors for more than three years suggesting that longer exposure to NRTI's may increase risk of diabetes (Tien et al., 2007). It has been suggested that the ART regimen itself might confer individual or additive risks that could trigger acute or cumulative diabetes mellitus events in the genetically predisposed (De wit et al., 2008). In South Africa an estimated 5-6 million people are infected with HIV. HAART which is widely available in the public sector has been immensely beneficial. However, several metabolic problems associated with long-term use, including diabetes mellitus and impaired glucose tolerance (IGT) a condition of elevated levels of blood glucose and a significant risk factor for development of diabetes mellitus have also been observed. A study by Dave and others (2011) determining the prevalence and associated risk factors of dysglycemia and insulin sensitivity in HIV-infected South Africans revealed a low prevalence of diabetes mellitus. However, there was a high prevalence of pre-diabetes among people with HIV. The prevalence of dysglycemia in 406 ART-naive patients and 443 patients on ART was 25.7% and 21.9% respectively. Older age, male gender, higher CD4 count and use of Efavirenz were associated with dysglycemia, with no difference between those on therapy and the ART naive. The risk of diabetes mellitus increased with patients' age and years of exposure to ART. Participants receiving Efavirenz or protease inhibitor therapy were more likely to have Diabetes mellitus. Neither mean pre-ART CD4 cell count nor pre-ART viral load >100 000 copies/ml were associated with a significant risk of diabetes. This suggests a complex interrelation among traditional host factors and treatment-related metabolic changes in the pathogenesis of diabetes mellitus in patients

receiving ART. The study concluded that all patients with HIV were at risk of developing dysglycemia and the risk increased with age. The upscale of ART programs and their impact is anticipated to continue reducing mortality from HIV/AIDS. On the other hand it is likely to increase the number of people in Africa at risk of possible metabolic side effects such as diabetes mellitus resulting from life-long ART.

It has been documented that impaired glucose levels and diabetes mellitus is a potential problem in HIV patients. Several factors are associated with increased risk. Studies have been conducted globally and a few at the regional level. However, a lot remains to be investigated locally.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study setting

Lusaka province was purposively selected, having the highest HIV prevalence in the country at 20.8% (ZDHS 2007). Of the four districts, Lusaka was conveniently selected the other three being Chongwe, Kafue and Luangwa district. UTH being the country's main referral hospital, with the AIDC housing the longest established ART clinic was conveniently selected on this basis. The clinic also utilizes Smart Care for management of patient health information and serves a large volume of clients.

3.2 Study population

Study participants were HIV infected adults aged 18 years and above, receiving antiretroviral drugs and selected from the AIDC situated at UTH.

3.3 Sampling

Over a 3-month period, consecutive HIV patients presenting for scheduled follow up clinic visits were recruited. Those who accepted the invitation and met the inclusion criteria were enrolled following informed consent. A registry entry was made using client assigned study number and clinic ART number to avoid multiple enrollments. Enrollment was continuous till sample size was met. Shown is the formula used to calculate sample size.

Formula $n = \frac{(Z)^2 \text{ X } P\ (1\text{-}P)}{e^2}$

P = proportion

n = Sample size.

e = Design effect.

Z = Z score at 95% Confidence interval

14% sample mean (Brown et al, 2005)

$$\frac{1.96^2 \text{ x } 0.14\ (1\text{-}0.14)}{0.05^2}$$

n = **185**

20% adjustment for non-response

0.2 x 185 = 37

185 + 37 =**222 Total sample size**

3.4 Study design

A cross sectional survey of HIV infected individuals accessing care and receiving antiretroviral therapy (ART) at AIDC, University Teaching Hospital in Lusaka was conducted to obtain point prevalence of impaired fasting glucose and Type 2 diabetes mellitus. This was a low risk study performing what would be routine procedure in a regular clinic set up. Study enrollment was a onetime encounter, as individuals came to the clinic for routine review. The study was introduced to the client by a nurse with an invitation to enroll. The general and specific objectives of the study were explained to participants. Participation was voluntary and study eligibility was based on the following inclusion criteria; HIV infected adult aged 18 and above, and giving consent. Only individuals on ART for a

minimum of 1 year without any modification to their ART regimen since initiation were enrolled. Participants were required to be in a fasting state prior to FBS testing. Fasting was defined as no caloric intake for a minimum of 8 hours. Written informed consent was obtained and enrollment completed before nurse proceeded with anthropometric measures. The study was approved by University of Zambia (UNZA) Research Ethics Committee (REC) and written permission was obtained from study site administrator. All entry forms were stored in a lockable cabinet and completed questionnaires accessible only to approved study personnel.

3.5 Data collection

A modified WHO global surveillance initiative NCD-STEP 3 method was adapted for data collection. Step 1 consisted of a questionnaire, Step 2 physical examinations, and Step 3 biochemical examinations. The questionnaire was interviewer-administered and interviewers included AIDC nurses responsible for conducting routine clinic visits. These had undergone a 2 day training in administering the questionnaire and piloting the tools on selected respondents.

3.5.1 Interviews

An interview schedule was used to obtain responses from the interviewees. Data collected included among others: Socio-demographic information (age, gender, education level, occupation and residency), clinical data (HIV diagnosis, CD4 count, ARV treatment regimen, previous diabetes diagnosis/family history of diabetes mellitus, comorbid diseases, and concurrent medications), anthropometric measurements (Height and Weight), and biochemical measurement (fasting blood sugar).

Height

A Stadiometer was used to measure the height of the participant. Height was measured without the participant wearing foot or head gear. Before the reading was taken, the participant was requested to have feet together, heels against the back board, knees straight, and look straight ahead. Height was recorded in centimeters.

Weight

Weight was measured using an adult Seca Brand scale. Participants were asked to stand still, face forward, and place arms on the sides of the body. Weight was recorded in kilograms.

Weight and height were measured for computation of Body Mass Index (BMI). BMI is a statistical measure of body weight based on a person's weight and height and used to estimate a healthy body weight.

Body mass index (BMI), calculated as weight in kilograms divided by the square of the height in meters, was stratified as <18.5 (underweight), 18.5–24.9 (normal), 25–29.9 (overweight), and 30+ (obese).

Fasting Blood Sugar

Fingertip capillary whole blood samples were collected for determination of impaired fasting glucose and diabetes mellitus. Samples were analyzed using Accu-check Active, Roche diagnostic (model GC) instrument. Calibration of the instrument was performed each morning using the test kit glucose control solution. Nurses were responsible for obtaining all blood samples and performing the glucose test. Testing was done provided 8 hours had lapsed since participants' last reported meal. Participants reporting caloric intake prior to testing were requested to return to the clinic the following morning in a fasting state for

glucose testing. Results of fasting blood sugar testing were categorized per WHO 2006 diagnostic criteria. Diabetes mellitus was defined as fasting blood sugar concentration of ≥ 7.0 mmol/L and impaired fasting glucose as fasting blood sugar ≥ 6.1 mmol/L ≤ 6.9 mmol/L. Normoglycemia was defined by levels below those used to define intermediate hyperglycemia as fasting blood sugar of ≤ 6.0 mmol/L. Participants requiring further evaluation where referred to site physician per standard site regulations by study nurses.

3.6 Data management and analysis

Questionnaires were reviewed for errors and completeness by study nurses and double checked by researcher. Data was coded and entered into Microsoft excel, exported and analyzed using Stata® version 12 (Stata Corporation, College Station, Texas). The dependent variable was Fasting Blood Sugar and independent variables included socio-demographic characteristics, Body Mass Index and family history of diabetes mellitus. Demographic, health and treatment characteristics were summarized and compared between those with impaired and normal glucose levels. Chi square was used to determine the association between impaired glucose levels and each of the associated factors. Significance (P-value) was set at 5% with a confidence interval at 95%. Fasting Blood Sugar and Body Mass Index were our main indicators for risk measurable. Risk was defined as elevated fasting blood sugar above normal or/and BMI above normal (overweight & obese) to include diabetics and those at high risk of diabetes mellitus. To determine the risk factors two categories of FBS were combined to form one category i.e FBS of 6.1 to 6.9 and FBS of ≥ 7 (diabetics and those at high risk of diabetes).

Univariate logistic regression analysis was employed to estimate odds ratios (ORs) for each characteristic. Multivariate logistic regression analysis was conducted to assess the influence

of variables in predicting diabetes while adjusting for each other to control for confounding. All independent variables were included in the multivariate logistic regression regardless of significance.

CHAPTER FOUR

4.0 RESULTS

4.1 Demographic characteristics for the sampled population

The study enrolled a total of 224 participants, of which 56.7% were females. The mean age of the sample was 41.3 ± 9 years. 48.2% of the respondents had attained secondary level of education. Further description of the sample is presented in Table 3.

Table 3: Demographic characteristics for the sampled population

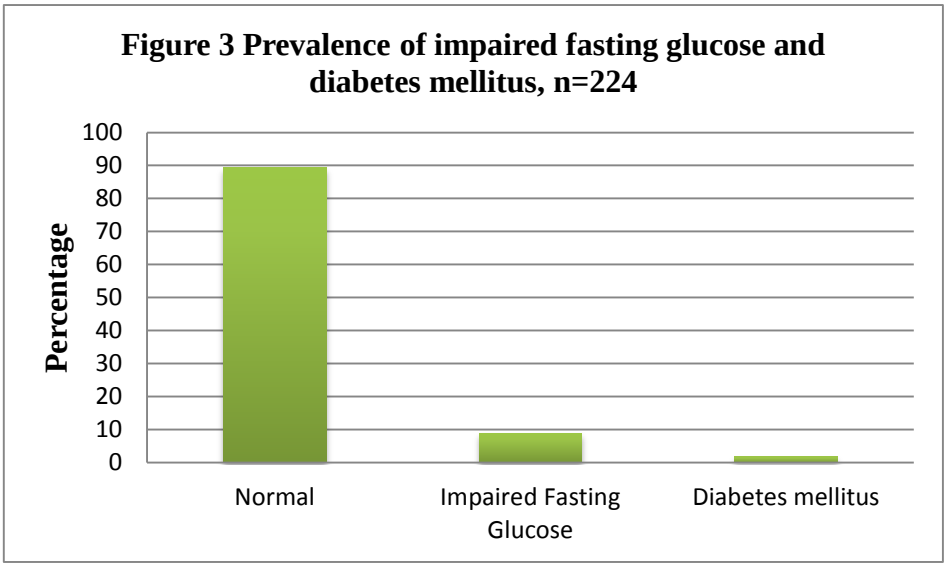
Characteristic		**Number of respondents % *(n)**
Sex	Male	43.3(97)
	Female	56.7(127)
Age (years)	20-45	71.0(159)
	46-55	21.9(49)
	56-65	7.1 (16)
Marital Status	Single	13.8(31)
	Married	63.4(142)
	Divorced/Widowed	22.8(51)
Education Level	No education	1.8(4)
	Primary	22.3(50)
	Secondary	48.2(108)
	Higher	27.7(62)
Residence (density)	Low	24.1(54)
	Medium	29.9(67)
	High	46.0(103)

***n = 224**

4.2 Prevalence of impaired fasting glucose and diabetes mellitus

The range for fasting blood sugar results observed was 2.7 mmol/L to 13.0mmol/L (see appendix 11). Twenty 20 (8.9%) participants (12 females and 8 males) had impaired fasting glucose, while 4 (1.8%) participants (all males) had diabetes mellitus, giving an overall prevalence of impaired glucose level of 10.7%. Of the four diabetics, two had a pre-existing diagnosis of diabetes mellitus made 6-7 years post ART initiation. At study enrollment/clinic visit FBS results obtained for the known diabetics were 7.5mmol/L and 13.0mmol/L. Both were receiving anti-diabetic treatment, Daonil 5mg daily. Prevalence of impaired glucose levels was highest among those aged 45-65 years compared to those in the younger age group 20-45 years (16.9% Vs 8.2%). 200 (89.3%) participants in the sample had normal fasting blood sugar concentrations i.e. below cut off for impaired glucose levels. Figure 3 shows prevalence of impaired fasting glucose and diabetes mellitus.

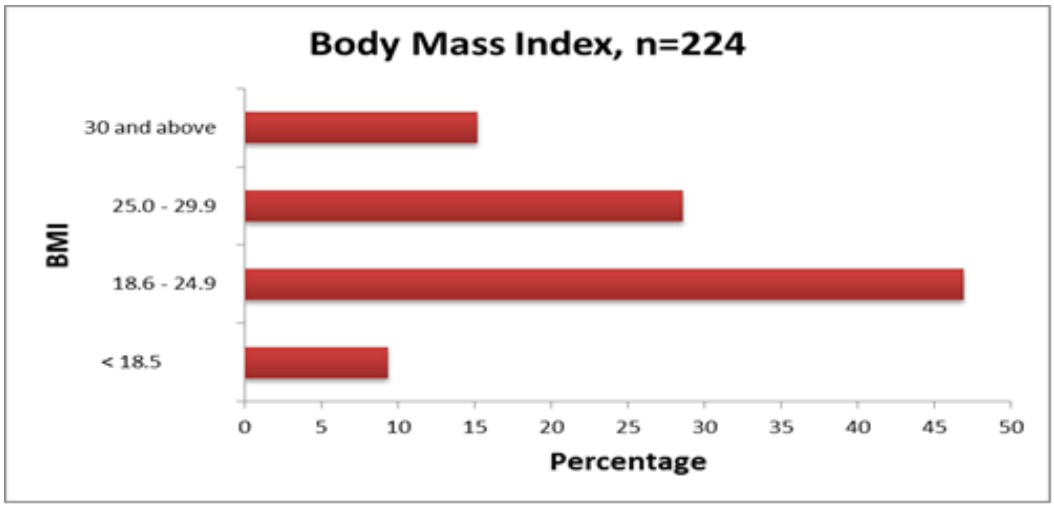
Figure 3 Prevalence of impaired fasting glucose and diabetes mellitus, n=224



4.3 Risk factors associated with impaired fasting glucose levels in HIV infected persons on ART

Table 4 shows the association of risk factors with impaired glucose levels considered in the current study using Pearson's Chi square test. Comparison between sexes showed more males than females (12.4% versus 9.4%) with a higher proportion of impaired glucose levels however there was no significant association (P=0.484). Prevalence was highest among those aged 45-65 years, with older age being significantly associated with impaired glucose levels (p=0.055). There was a significant relationship between marital status and impaired glucose levels (p=0.034). Those with at least a secondary level of education were the largest group with impaired glucose levels 10 (41.7%), though nonsignificant. Impaired glucose levels were not observed in participants who had no formal education. The mean BMI was 24.2±4.7. A combined 43.8% had an abnormal BMI, including 28.6% who were overweight and 15.2 % who were obese (figure 4).

Figure 4 Distribution of Body Mass Index



Respondents with BMI levels above normal (overweight and obese) had higher levels of impaired glucose compared to those with normal BMI (66.7% Vs 41%), though relationship

was not significant (P=0.107). However, further analysis of BMI by sex showed females had a higher proportion (50.3%) of abnormal body weight (combined overweight and obese) compared to males (35.1%) and was statistically significant (P= 0.009). When analyzed against age, BMI was found to increase with age. The elderly had higher BMI readings compared to those in the younger age group (20-45 years) with age being significantly associated with BMI (P=0.029) .

A total 30 (13.4%) respondents reported an existing medical diagnosis of hypertension and 24 of these were receiving antihypertensive medications. Impaired glucose levels were observed in 4 out of the 30 hypertensive individuals. There was no relationship between Hypertension and impaired glucose levels (P= 0.618).

16.1% of our sample population reported a family history of diabetes, with family defined as a first degree relative, a parent or sibling. However, there was no association between family history of diabetes mellitus and impaired glucose levels.

Almost half, 46% (103) of the participants recruited in the study resided in high density areas while 24.1% (54) resided in low density areas. There was no significant association between area of residence and impaired fasting glucose and diabetes mellitus (P=0.370).

Table 4: Factors associated with impaired fasting glucose levels in HIV infected individuals on ART

	Fasting Glucose Level Proportion n (%)		
Characteristic	**Impaired**	**Normal**	***P-value**
Sex			
Male	12(12.4%)	85(87.6%)	0.484
Female	12(9.45%)	115(90.6%)	
Age			
20-45 years	13(54.2%)	146(73%)	0.055*
46-55 years	11(45.8%)	54(27%)	
Marital Status			
Single	6(25%)	25(12.5%)	0.034*
Married	17(70.8%)	125(62.5%)	
Divorced/Widowed	1(4.17%)	50(25%)	
Education Level			
No education	0(0%)	4(2%)	0.728
Primary	7(29.2%)	43(21.5%)	
Secondary	10(41.7%)	98(49%)	
Higher	7(29.2%)	55(27.5%)	
Residence			
Low	8(33.3%)	46(23%)	0.370
Medium	8(33.3%)	59(30%)	
High	8(33.3%)	95(47%)	
BMI (kg/m$^{2)}$			
≤ 18.5	2(8.3%)	19(9.50%)	0.107
18.6-24.9	6(25%)	99(49.5%)	
25-29.9	10(41.7%)	54(27%)	
30 and above	6(25%)	28(14%)	
****BMI (kg/m$^{2)}$**			
Mean (Sd)	25.9(5.2)	24.0(4.7)	0.070
Existing hypertension			
No	20(83.3%)	174(87%)	0.618
Yes	4(16.7%)	26(13%)	
Family History of T2DM			
No	19(79.2%)	169(84.5%)	0.501
Yes	5(20.8%)	31(15.5%)	

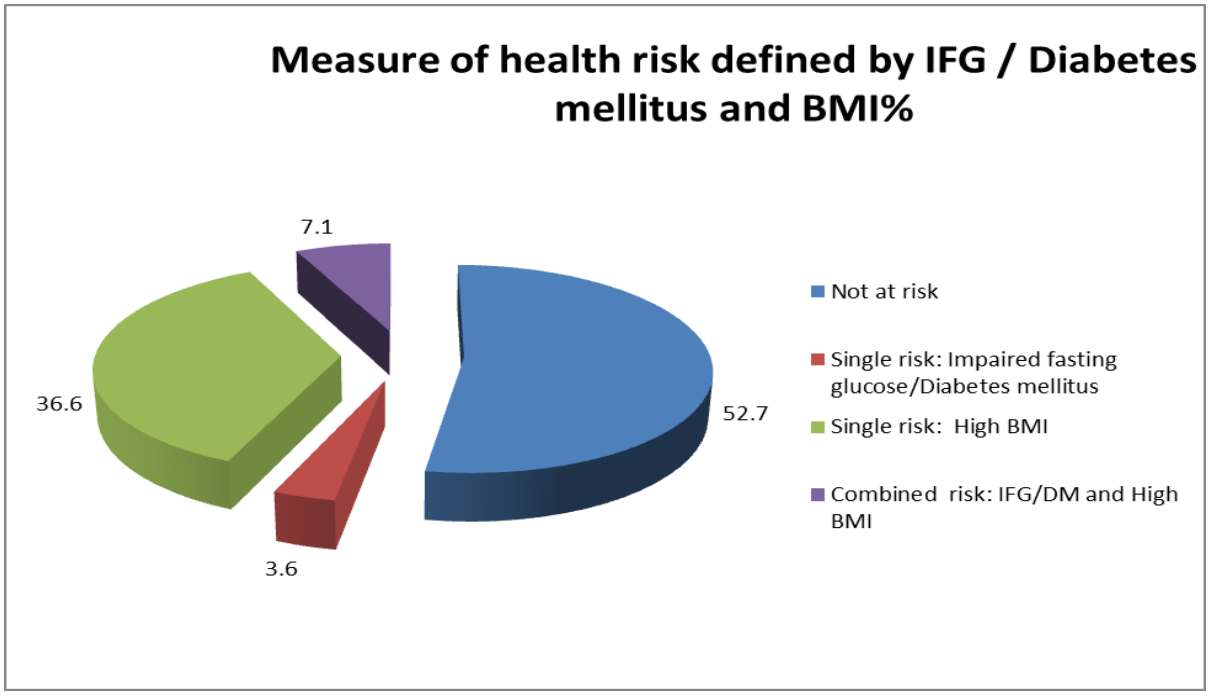
*P- values tested by Chi square** BMI as continuous variable

4.4 Measure of health risk defined by IFG / diabetes mellitus and Body Mass Index

The overall health risk of participants in the sample was measured and defined by abnormal fasting blood sugar concentration (IFG and diabetes mellitus) and high Body Mass Index. High BMI was defined as body weight above normal (overweight and obese). Single risk

was considered as either above normal fasting blood sugar concentration or high BMI. Combined risk was considered as having both above normal fasting blood sugar concentration and high BMI. Not at risk was defined as neither abnormal glucose concentration nor high BMI. Out of our total sample population, 106 (47.3%) were considered to have a health risk based on their fasting blood sugar level or BMI. When analysis was limited to individuals with both an impaired glucose level and high BMI, 16 (7.1%) of our sampled population had a combined health risk (Figure 5).

Figure 5 Measure of health risk defined by IFG / Diabetes mellitus and BMI



4.5 Predictors of impaired glucose levels in HIV infected individuals on ART

All independent variables regardless of statistical significance were used in the univariate logistic regression model. This was to determine the association of each risk factor and impaired glucose levels to obtain odds ratios, p-values and CI. In table 5 of the univariate logistic regression analysis, age was found to be significantly associated with impaired glucose levels. Being older than 45 years of age increased the likelihood of impaired glucose level (OR=2.53, (95%CI [1.00-6.33]); P=0.048. Marriage or previous marriage (divorced/widowed) was associated with a lower risk of impaired glucose levels (OR=0.56 (95%CI [0.20, 1.58]); P=0.27, (OR=0.08 (95%CI [0.00, 0.73]); P=0.025 respectively. Increasing BMI (overweight and obese) increased likelihood of impaired glucose, (OR= 1.76 (0.35, 8.76); P=0.490 and OR 2.04 (0.37, 11.2); P=0.413 respectively compared to participants with normal BMI.

Table 5: Predictors of impaired glucose levels in HIV infected individuals on ART

Variables	OR** (95% CI***)	P-Value*
Sex		
Male	1	1
Female	0.74 (0.31, 1.73)	0.485
Age		
20-45 years	1	1
46-55 years	2.53 (1.00, 6.33)	0.048*
56-65 years	1.60 (0.33, 7.84)	0.559
Marital Status		
Single	1	1
Married	0.56 (0.20, 1.58)	0.277
Divorced/Widowed	0.08 (0.00, 0.73)	0.025*
Education Level		
None/Primary	1	1
Secondary	0.69 (0.25, 1.91)	0.470
Higher	0.85 (0.28, 2.61)	0.783
Residence		
Low	1	1
Medium	0.78 (0.27, 2.23)	0.643
High	0.48 (0.17, 1.37)	0.172

Body Mass Index		
≤ 18.5	1	
18.6-24.9	0.58 (0.11, 3.07)	0.518
25-29.9	1.76 (0.35, 8.76)	0.490
30 and above	2.04 (0.37, 11.2)	0.413
Existing Hypertension		
No	1	
Yes	0.75 (0.24, 2.36)	0.619
Family history of T2DM		
No	1	
Yes	0.70 (0.24, 2.01)	0.503
*** P-value = statistically significant**	**OR**: Odds ratio**	**CI***: Confidence interval**

Table 6 shows multivariate logistic regression of factors associated with IFG. On multivariate logistic regression, age remained significantly associated with impaired glucose levels. Compared to participants in the age group 20-45 years, older participants were at three times greater risk for impaired glucose levels (AOR = 3.07 (95% CI [1.04, 9.11]) for 46-55 years age group. With increasing age there was a twofold increase in risk for those in the 56-65 years age group (AOR =7.57 (95% CI [0.69, 83.5]). Lower risk of impaired glucose levels was more pronounced in the divorced/widowed group. Participants with BMI above normal were more likely to have impaired glucose levels (AOR =2.34 (95% CI [0.39, 14.01]) for overweight, and (AOR=3.91(95%CI [0.55, 27.8]) for the obese.

Table 6: Predictors of impaired glucose levels in HIV infected individuals on ART

Variables	AOR**(95% CI***)	P-Value*
Sex		
Male	1	
Female	0.45 (0.14, 1.39)	0.164
Age		
20-45 years	1	
46-55 years	3.07 (1.04, 9.11)	0.043*
56-65 years	7.57 (0.69, 83.5)	0.098
Marital Status		
Single	1	
Married	0.25 (0.69, 0.91)	0.036*
Divorced/Widowed	0.02 (0.01, 0.23)	0.002*

Education Level		
None - Primary	1	
Secondary	0.34 (0.09, 1.21)	0.096
Higher	0.27(0.06, 1.14)	0.075
Residence		
Low	1	
Medium	0.95 (0.28, 3.24)	0.936
High	0.44 (0.12, 1.57)	0.206
Body Mass Index		
≤ 18.5	1	
18.6-24.9	0.69 (0.11, 4.17)	0.687
25-29.9	2.34(0.39, 14.01)	0.352
30 and above	3.91 (0.55, 27.8)	0.173
Existing hypertension		
No	1	
Yes	1.44 (0.33, 6.18)	0.627
Family History of T2DM		
No	1	
Yes	0.89 (0.26, 3.12)	0.858

* P-value = statistically significant **AOR; Adjusted odds ratio *** CI; Confidence interval

CHAPTER FIVE

5.0 DISCUSSION

Multiple studies (Brown et al., 2005, Butt et al., 2009, Dave et al., 2011) have reported an increasing prevalence of impaired glucose and diabetes mellitus in HIV infected individuals receiving Anti-retroviral drugs. However, none of them has reported such for the Lusaka population. This could be the first study to report prevalence rates of impaired glucose levels and associated factors in HIV infected persons on ART in Lusaka. This knowledge will serve as a basis for future research and aid in planning effective prevention and control measures for diabetes mellitus.

In 224 HIV infected adults on ART at the Adult Infectious Disease Centre, UTH, Lusaka, there was a combined prevalence of dysglycemia of 10.7% (8.9% impaired fasting glucose and 1.8 % diabetes mellitus). The study further identified increasing Body Mass Index (overweight and obese) and age above 45 years as factors associated with impaired fasting glucose and diabetes mellitus, among the HIV infected individuals on ART.

Our estimates for impaired fasting glucose and diabetes mellitus in HIV patients was higher than previous rates obtained in a general population study on combined prevalence of impaired glucose level or diabetes and its correlates in Lusaka urban district at 4% in 1,928 participants. Other studies have reported prevalence rates between 1-25% (Yoon et al., 2004, Brown et al., 2005, Butt et al., 2009, Dave et al., 2011). The proportion for impaired fasting glucose in this study was higher than diabetes mellitus (8.9% versus 1.8%). Similarly, a study conducted in Cape Town, South Africa reported low prevalence of diabetes mellitus; however, there was a high prevalence of pre-diabetes (impaired glucose) among people with HIV. It has been documented that impaired fasting glucose levels are a precursor for Type 2

diabetes mellitus. Individuals with impaired fasting glucose levels are not only at risk for long term complications, but also between 5 and 10% cases of impaired fasting glucose (pre-diabetics) transition to diabetes each year (Mainous et al., 2014). Further, thought is that low diabetes mellitus prevalence with a high prevalence of impaired glucose levels could be indicative of a pending epidemic. Therefore the reported 8.9% prevalence rate of impaired fasting glucose should not be ignored, as in the absence of intervention has potential to progress to Type 2 diabetes mellitus.

Only two out of the total study population had an existing diagnosis of diabetes mellitus and were on treatment. Diagnosis of the disease was made six and seven years post ART initiation. However, it could not be established if this was a pre-existing condition prior to ART initiation due to lack of baseline screening. Currently, screening for impaired glucose levels is not part of routine laboratory tests conducted in HIV patients. It is therefore plausible that there are other undiagnosed cases of impaired fasting glucose and diabetes mellitus.

Study results showed that participants with BMI above normal (overweight or obese) had higher odds [2.34(0.39, 14.01)] and [3.91 (0.55, 27.8)] of having impaired glucose levels, compared to those with normal BMI [0.69 (0.11, 4.17)]. In this sample almost half (43.8%) of the participants had BMI above normal. This included 28.6% who were overweight and 15.2% who were obese. BMI was significantly associated with older age (P=0.029) and females (P= 0.009). This is essentially confirmation of multiple studies that have demonstrated correlation of impaired glucose levels/diabetes mellitus with excess weight and obesity. The combined prevalence study in Lusaka also reported the highest prevalence of impaired glucose among participants who were obese (Nsakashalo et al., 2011). In Botswana, researchers assessing the characteristics of HIV and diabetes mellitus in patients

receiving ART found that, pre-ART weight, particularly if >70 kg, was associated with the diagnosis of diabetes mellitus in HIV-infected patients (Moyo et al., 2014). Samaras, (2012) reported diabetes rates in HIV-infected individuals, were two-fold higher in obese participants, compared with those with normal body mass index. BMI was also noted as one of the factors that had a profound effect on increased risk of diabetes mellitus even after adjusting for age and sex (De wit et al., 2008 and Butt et al., 2009).

In HIV patients, weight gain has been attributed to several factors including improved nutritional status, result of ART efficacy, and/or metabolic syndrome. Additionally cultural beliefs have been cited to have an influence on weight. This is particularly in Africa where larger body sizes are perceived as a sign of good health and affluence thus may not necessarily be considered a health risk. Obesity in this sample is parallel to growing health concerns in the general population. Rudatsikira et al., (2012) in their obesity prevalence study among 1,915 Lusaka residents, found 14.2% of the participants (5.1% of males, and 18.6% of females) were obese. Our findings and previously observed data, suggest there is considerable risk in this population

Importance of balanced diet in management of HIV patients is similar to non HIV infected persons for maintenance of general health. However, the stigma attached to the syndrome of weight loss and wasting associated with HIV/AIDS may have an impact on weight maintenance. Nonetheless, the fact remains that obesity is a modifiable risk factor with evidence based interventions, and therefore can be the tool for targeted risk reduction.

Older age, has been cited as an important determinant of diabetes mellitus in HIV patients. Participants who were in the 20-45 years age group were less likely to have impaired glucose levels compared to older participants aged 45 years or older [2.53 (1.00, 6.33)]. Similar to our study results Nsakashalo et al., (2011) also found that impaired glucose level/diabetes

mellitus was associated with older age. While the prevalence varied with age, the highest prevalence was reported in the age group 45+ years. In their studies, Butt et al., 2009 and Dave et al., 2011 reported similar findings of increased risk for diabetes mellitus with increasing patient age. The life expectancy of HIV infected individuals has increased as a result of ART efficacy. Typically, as individuals' age, their physical activities decreases and weight gain is likely for most. The resultant weight gain predisposes individuals to increased risk for impaired glucose levels and diabetes mellitus. The aging process is also accompanied by distortion or loss of an effective immune system (immune senescence) and increases in irritating proteins in the blood, such as interleukin-6 and tumor necrosis factor (Bhatia, Ryscavage & Taiwo, 2011). This process of immune dysregulation and chronic inflammation increases susceptible to aging-related comorbidities, such as diabetes mellitus and is true even for non-HIV populations. While prevalence has previously been associated with increasing age, the trend is changing as much younger individuals are affected as a result of life style changes. Moreover, the burden of T2DM is disproportionately borne by people of working age, which is also the age-group most profoundly affected by HIV in this region including Zambia.

Significant associations were observed between marital status and impaired glucose levels (P = 0.034). Individuals reported to have been married had the highest proportion of impaired glucose levels compared to those who were single or previously married combined (70.8% Vs 29.17%). This could be attributed to several factors including socio-economic, cultural or reflect confounding.

Cumulative exposure to ART has been shown to play a major causative role in metabolic glucose disorders in HIV patients. In this population ten different drugs are used in combination of three. Most commonly prescribed drugs in this sample were Efavirenz,

Tenofovir and Emtricitabine (see Annex 13 for complete list). In our analysis we examined association of antiretroviral drugs and were unable to isolate a specific drug that could potentiate impaired glucose levels and found no relationship with combined ART regimen. However, in contrast to our study Moyo et al., (2014) reported a positive correlation between Efavirenz and dysglycemia. Participants receiving Efavirenz or protease inhibitor therapy were more likely to have diabetes mellitus, a finding consistent with that of Dave and others (2011). Notably Efavirenz is part of first-line ART regimens across SSA because of its perceived lower toxicity compared with Nevirapine. It is also widely prescribed in Zambia with 82.4% of our respondents using Efavirenz as part of their ART regimen. Therefore it could be of clinical significance and have implications for our patients and requires further investigations. A possible explanation for our finding could be the sample size and cross sectional study design. Cumulative exposure to ART in most studies remained a significant association even after adjustment for potential risk factors for diabetes mellitus. Previous studies (Tien et al., 2007, Brown et al., 2005) indicated that impaired glucose levels could be observed a minimum of a year post ART initiation. In our sample 56% of the patients had already been on treatment for at least 5 years and as such had some cumulative exposure (see Appendix 14). It would be expected that individuals in our cohort would yield similar results. Therefore with time it is possible that we could see more metabolic derangements in HIV infected individuals, as government continues scale up efforts and individuals initiate ART early.

Family history of diabetes mellitus has been implicated in the development of impaired glucose in HIV patients (De Wit et al., 2008). 16% of our study participants reported a family history of diabetes mellitus, with family defined as a first degree parent or sibling. Five 5 (20.8%) of these participants had impaired fasting glucose levels. However, there seemed to be no relationship between family history and impaired glucose levels (P=0.501).

This suggests a combination of traditional risk factors; HIV related factors and genetic disposition could be responsible for inducing dysglycemia in these individuals. According to De Wit and others (2008) the ART regime itself might confer individual or additive risks that could trigger cumulative diabetes mellitus events in the genetically disposed.

Rapid globalization has contributed to health transition and changes in lifestyles. Residency in low density areas has been associated with affluence and high income which improves livelihood and provides access to lifestyles that can increase risk for impaired glucose levels and diabetes mellitus. Many have adopted western dietary practices that involve increase in consumption of refined sugars, saturated fats and reduced fiber intake, consumption and abuse alcohol, development of smoking habits and adoption of sedentary lifestyles (Azevedo and Alla, 2008; Cohen et al., 2010; Lekoubou, 2010) thereby increasing risk for impaired glucose levels and diabetes mellitus. Zambia is no exception to this transition as eating habits transform and work and living situations become more sedentary. In this study, almost half (46%) of the participants in the study reported living in a high density area. There was representation of impaired glucose levels in each residential area. Although low density areas have been associated with affluence and consequent risk for impaired blood glucose level there was little or no correlation between the two. Literature suggests an inverse relationship between socioeconomic status and the prevalence of diabetes mellitus. Individuals with low disposable incomes are likely to purchase and consume foods that are sold cheaply and in bulk. These are usually high in saturated fats and refined sugars with little or no nutritional value, thereby increasing their risk for Type 2 diabetes mellitus. Therefore, it is possible that all individuals are at risk regardless of their area of residence. As such in planning and implementing preventive and control measures it should be kept in mind that diabetes mellitus is no longer a disease of the affluent as publications have alluded.

Evidence suggests increasing linkages between HIV/AIDS and Non-communicable diseases. Cardiovascular diseases, cancer, chronic respiratory diseases and diabetes mellitus are the most prevalent NCDs emerging alongside HIV/AIDS. In those sampled we found that the other most common diagnosed medical condition was Tuberculosis. This study found no evidence of hyperglycemia in participants with a diagnosis of TB. Thirty 30 (13%) of the respondents reported an existing medical diagnosis of hypertension and 24 of these were receiving antihypertensive medications. Hypertension was significantly associated with older age 46-65 years (p-value 0.000). However, there was no relationship between impaired glucose levels and hypertension. Similarly, researchers in Botswana found no significant association between co-morbid diseases, tuberculosis, hypertension or cancer and risk of diabetes mellitus. Other findings in this study were a 25% use of alcohol among participants. Only 2.7 % reported use of tobacco specifically smoking.

5.1 STUDY LIMITATIONS

The nature of our study design meant we were only able to evaluate association between the examined variables and impaired glucose levels. Hence we could neither fully demonstrate correlation between HIV specific factors and impaired glucose levels nor account for all confounders. This was a rather low powered study compared to similar studies with a larger sample size. Study setting was selected conveniently and may not be representative to generalize findings to other parts of the country.

5.2 CONCLUSION

Based on these study results dysglycemia is a potential threat to HIV infected persons on ART and likely influenced by a host of factors. Excessive weight has been identified as a significant risk factor for impaired glucose levels and diabetes mellitus. This component that

is part of current assessments in HIV patients when observed should be investigated. Abnormality in weight needs to be mitigated and normality can only be maintained with adequate advice. Having recognized the impact of modifiable risk factors such as BMI, nutritional counseling should be expanded to include weight maintenance, healthy diet and physical activity. BMI and family history of diabetes mellitus can serve as indicators for monitoring risk for diabetes mellitus.

In industrialized countries incidence of diabetes mellitus in HIV-infected adults receiving ART has been reported to be between 1% and 10% (Yoon et al., 2004). Moreover, western countries also have established guidelines for non-communicable diseases like diabetes mellitus. Few studies have been conducted on diabetes mellitus to influence the formulation of policies that could guide prevention and treatment in most parts of the region, including Zambia. Knowledge is a key feature in control and management of diabetes mellitus. It requires health personnel to be trained in screening, prevention and adequate management of complications of diabetes mellitus in order to sensitize patients and communities appropriately. Lack of information in turn promotes community reliance on traditional beliefs and traditional healers. This results in delayed medical diagnosis and treatment and ultimately increases morbidity and mortality.

5.3 RECOMMENDATIONS

Prospective cohort studies should be considered to include a larger sample, comparison groups and continuous collection of data at baseline and over an individual's life time. This can help provide pertinent information in understanding the etiology, course, and outcome of diabetes mellitus in HIV patients. Additional indicators that have not been considered in the current study can be included and explored extensively to provide information for evidence

based practice and policy framework. In South Africa, guidelines recommend screening HIV-positive patients with risk factors every 6 months (SEMDSA, 2009). It is recommended that countries without current guidelines for screening HIV-infected patients for diabetes mellitus perform annual fasting blood glucose for all patients on HAART, where resources are available. Moreover, frequent monitoring may be reasonable for patients who are at highest risk due to family history, and/or lipodystrophy (Reid et al., 2012). Similarly we need to undertake such measures before the problem escalates as numerous challenges accompany diabetes mellitus care; high cost of drugs and supplies, inaccessibility to health facilities (Levitt, 2008).

Nutritional counseling, education on exercise and sensitization among health care workers and patients can raise awareness of risk factors. Western countries are already a step ahead in the fight against obesity and its related risk factors such as Type 2 diabetes mellitus. However, within the region, Malawi recently included non-communicable diseases (such as stroke, and diabetes mellitus) in its Essential Health Programme (Ministry of Health [Malawi], 2011). This upgrade means that primary care and prevention should be available to all people with these conditions in Malawi (Rudatsikira et al., 2012).

The current clinical picture and prognosis for diabetic patients in Africa is grim. They have worse diabetic outcomes and progression of complications such as retinopathy, nephropathy, foot ulcerations, and cardiovascular diseases. These complications are debilitating and in some instances fatal (Addoor, 2011). Majority of the cases of diabetes mellitus in the region go undetected and the undiagnosed cases are estimated to be as high as 60-80% in Cameroon, Ghana and Tanzania (Jamison et al., 2006). The Rapid Assessment Protocol on Insulin Access (RAPIA) highlighted several challenges affecting diabetic care in Zambia. This included the medical and nursing students curriculum not adapted to treating diabetes

mellitus and other non-communicable diseases. There was also lack of tools and infrastructure for diagnosis and follow-up. Further, low levels of health care worker training resulted in a substantial risk of misdiagnosis or failure to detect diabetes mellitus. This indicates a need to raise the diabetic profile in the country.

The HIV epidemic has affected those in the productive age group that ultimately contribute to the country economic development. Over time we could see an increase in impaired glucose levels and diabetes mellitus as HIV recommendations are continually updated and new guidelines for early initiation of ART take effect and more individuals are on life-long treatment. Their poor health or premature death impacts not only their families negatively but also the economy. Treatment of diabetes mellitus at earlier stages has been shown to prevent progression to later stages by diet, exercise and lifestyle management. Therefore deliberate effort is required to engage individuals to exercise or participate in other physical activities. Further, routine glycemic monitoring is imperative and should be all inclusive in this population regardless of age.

Continued lack of awareness and monitoring could potentially increase the incidence of impaired glucose levels and diabetes mellitus in this population in the absence of an intervention.

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APPENDICES

APPENDIX 1: Zambian National Guideline Recommendations for Baseline, Routine/Follow up Testing.

Zambian National Guideline Recommendations for Baseline Testing:

HIV Serology: See HIV Diagnosis.

CD4 count

Creatinine (preferable for all cases but required if to start TDF)

ALT and/or AST (required if to start NVP)

Hgb, WBC (required if to start AZT)

If available, chemistry panel to include glucose, cholesterol, triglycerides.

If unable to perform Creatinine, ALT, or other essential laboratories, then specimen should be sent to nearest facility where test can be performed.

RPR (repeat yearly)

PAP smear (if unavailable, then visualization with acetic acid screening)

HBsAg if available

Pregnancy testing in women of reproductive age

Urinalysis for urine protein

Additional considerations for baseline testing include the need for sputum sampling and/or chest x-ray in patients with suspected TB .

Zambian National Guideline Recommendations for Routine/Follow-up Testing:

Week 2: If on NVP and CD4 >250 or pregnant or rash check ALT and/or AST.

Week 4: If on NVP check ALT and/or AST. If on AZT , check Hgb.

Month 2: If on NVP check ALT and/or AST.

Month 3: If on NVP check ALT and/or AST.

Every 3 months: If on NVP check ALT and/or AST. If on AZT , check Hgb. If on TDF, check creatinine. If available, check VL.

Every 6 months: WBC, Hgb, ALT, CD4. If on TDF, check creatinine. If available, check VL

Repeat PAP at 6 months and if normal, every 12 months. If visual screen only with acetic acid, repeat as with Pap smear if normal; if abnormal, refer for treatment.

If on PI-containing regimen, consider chemistry profile (including LFTs, glucose, cholesterol, and triglycerides) on a yearly basis if normal.

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Zambia Information Author: Larry William Chang, MD, MPH

APPENDIX 2 INFORMATION SHEET

PREVALENCE OF DIABETES IN HIV-INFECTED ADULTS ON ART AT UTH COE ART CLINIC

INTRODUCTION

I am Chama Mapulanga a student in the Masters in Public Health program at the University of Zambia. I am conducting a study to determine the presence of Diabetes in HIV patients receiving ART at the UTH COE ART clinic. Prior to your participation, the purpose of the study including benefits or risks will be explained. You will be given an opportunity to ask questions and you have the right to seek clarification. Please note that participation in the study is completely voluntary and you are free to withdraw at any point in time. You will be required to sign or thumb print a consent form in the presence of a witness should you agree to participate in this study. Refusal to enroll in the study will not affect any part of your current or future care.

PURPOSE OF STUDY

The study is designed to assess whether patients on ART are developing diabetes and if it is a consequence of therapy. The results obtained will facilitate policy measures on early detection, diagnosis and treatment of diabetes. It will also help raise awareness among healthcare practitioners and aid sensitization of patients on signs and symptoms, complications and management of diabetes.

PROCEDURES

As part of the study we will first ask you a couple of questions related to your health. This may take approximately 15-30 minutes to complete. Height and weight will be measured. A blood sample will be collected by finger prick for the rapid glucose test. A qualified health worker will be responsible for obtaining all blood samples.

RISKS/DISCOMFORT

Study risk is minimal and may include slight discomfort from finger prick during blood collection.

BENEFITS

This study has no immediate benefits. However, your participation will help provide information that may guide decision makers in formulating measures that can be used for the early detection, diagnosis and treatment of diabetes in HIV patients receiving antiretroviral drugs. No compensation (monetary/gift) will be offered in exchange for your participation in this study. Twenty kwacha (Kr 20) will be provided as transport reimbursement for study purposes.

CONFIDENTIALITY

No personal identifiers will be used; instead a unique code will be assigned to each participant. Responses provided will be kept strictly confidential and data access restricted to authorized study personal.

APPENDIX 3

CONSENT FORM

The purpose of the study has been explained to me. I understand the objective, benefits and risks of the study. I have been given the opportunity to ask questions.

I am under no obligation to enroll in the study, my participation is voluntary and I am free to withdraw at any time without penalty.

I _____ (last – first name) agree to participate in this study.

Signed: _____ Date: _____ (Participant)

Participant's signature/thumb print

Signed: _____ Date: _____ (Witness)

Signed: _____ Date: _____ (Investigator)

PROBLEMS OR QUERIES CONTACT:

1. Research student

   Chama Mapulanga

   P.O Box 310143

   Lusaka

   Phone: 0964038384

2. The Chairperson

   Dr. J. C Munthali

   UNZA Biomedical Research Ethics Committee

   Ridgeway Campus

   P.O. Box 50110

   Lusaka

   Phone: 260-1-256067

   E-mail: unzarec@unza.zm

APPENDIX 4

INFORMATION SHEET (NYANJA TRANSLATION)

PREVALENCE OF DIABETES AMONG HIV INFECTED INDIVIDUALS ON ART AT UTH ART CLINIC

CHIYAMBI

Ene dzina langa ndine Chama Mapulanga. Ndine mwana wa sikulu mumapunzidziro ya za umoyo pa sikulu ya University of Zambia. Ndifufuza kuona angti autu omwe alandira maukwala ku UTH a kalombo ka HIV anga pezeke ndimatenda a shuga (Diabetes). Mukalibe kutengako mbali ti za longosola pa ma phunziro aya., ti za longosola ubweno ndi ziopyezo. Muza pa sidwa mupata kufunsa ma funso. Kutengako mbali mu maphunziro aya ndi saukho lanu. Munga sankhe kutengako mbali mumu phunziro aya, kapena ai. Muzapempdwa ku sian kapena kufwatika chi pepala cha chivomerezo pa maso pamboni mukatengako mbali. Kusatengako mbali muma phunziro aya muzapilidza ku landira kasamalidwe kamasiku onse komwe iye ayenera kulandira monga mwa nthawi zonse.

LINGO LA MAPHUNZIRO

Kufufuza uku ndi kuonagati odwala alipa mankwala ya kalombo ka HIV apezeka ndimatenda ya shuga (Diabetes) ndipo angti ngati yachokela kumankwala ya kalombo ka HIV. Zotulukamo zizatandizira kuona kapena kupeza mankwala o chilisa matenda ya shuga, pomwepo kutandizira ya nchito a muszi patala ku chengeza antu pazi zendi kero ndi ze sonyezo ndi mavuto omwe anaga pezeke ndika samalidwe ka matenda ya shuga.

ZOMWE ZI ZA CHITIDWA

Monga mbali yama phundziro tiza kufunsani mafunso yokuuza umoyo wanu. Tiza tenga ma miniti 15-30. Tiza pema utali, sikelo, ndi ma gazi kuchusa kukakumo ku pema Shuga. A nchito achipatala azankala omwe otenga magazi.

KODI NDI ZIYOPEZO/KUSANVERA BWINO KOTANI

Ziyopezo ndi zo chepela potenga magazi ku ka kumo

ZABWINO

Zabwino paku fufuza uku si kwa sopano. Koma kutengoko mbali kwanu kuzatandizira amaphunziro ku peza matenda a shuga musunga ndi ku chiritsa shuga muli antu a ndi kalombo ka HIV alipa makwala. Palibe malipilo omwe muza tengapo pama phunziro aya.

CHISINSI

Zina lanu sili zalembedwa pama pepala, muzapasidwa nambala. Zonse zomwe tizamva ku chokela kwainu ziz sungidwa mu office. Ndipo akulu oyanganila pakufufuza uku akhala ndi ma keyi.

APPENDIX 5

CONSENT FORM (NYANJA TRANSLATION)

CHIPEPALA CHA CHIVOMEREZDTSO

Lingo lamaphunziro aya nda uzidwa, zochitika, maphindu yangapezekemo ndi ziyopezo ndauzidwa. Nda pasidwa mpata o funsa mafunso.

Kutenga ko mabali mumaphunziro aya ndiku zi funira neka, niga choke ntawe ili yonse kopanda ku taya kasamalidwe.

Zina laotenga mbali _____

Kusaina/kufwatika kwa wotenga mbali _____ Siku_____

Zina lamboni_____

Kusaina kwa mboni_____ Siku_____

Zina la otenga chivomekezano_____

Kusaina kwa wotenga chivomekezano_____Siku_____

APPENDIX 6

PREVALENCE OF DIABETES AMONG HIV-INFECTED ADULTS ON ART AT UTH ART CLINIC

SECTION A

DEMOGRAPHIC CHARACTERISTICS

INSTRUCTIONS

- Introduce self to client
- Fill out form completely in appropriate spaces provided

INTERVIEWER INITIALS

DATE OF INTERVIEW

(ddmmyy)

1. Respondent's identification number : _____
2. Sex: M-1 F-2
3. In what month and year were you born?

   (Month) (Year)
4. How old are you?

   (Years)
5. Marital Status
   Single -1 Married- 2 Divorced-3 Widowed-4
6. What is your highest level of education?
   None -1 Primary-2 Secondary-3 College/University-4
7. What do you do for living (Occupation)? _____
8. Where do you live?_____ (No physical address i.e. street name/house #)

SECTION B
DIABETIC AND HIV ASSESSMENT

1. Weight (kg)

   Height (cm)

   BMI

2. Do you have High blood pressure?

   Yes-1 No-2

   Have you been diagnosed with High blood pressure by a physician?

   Yes-1 No-2

   Are you currently taking any medication to control your blood pressure?

   Yes-1 No-2

3. Date of HIV diagnosis:

4. Current/Last CD4 count: _____

5. Is client on ART?
   Yes -1 No-2

   If YES, ART start date:

6. List prescribed ARV drugs

_____

_____

_____

7. List any other drugs you are currently taking

_____

_____

_____

8. Do you

	Yes-1	No-2
Drink alcohol		
Smoke/chew tobacco		

9. Have you been experiencing any of the following?

Polyuria (excessive urination)	
Polydipsia (excessive thirst)	
Polyphagia (excessive hunger)	
Unexplainable weight loss	

10. Do you have sugar disease?

Yes-1 No-2

6

7

Has diagnosis been confirmed by a physician?

Yes -1 No-2

Year of Diabetes diagnosis

Are you currently taking any medications or injections to control your sugar levels?

Yes-1 No-2

Do you have a family history of Diabetes i.e. a parent/brother/sister?

Yes-1 No-2

11. FBS result:_____

    FBS result: _____ (*On subsequent day ONLY for initial FBS> 7mmol)

12. List any other diagnosed medical conditions

    _____

    _____

    _____

    _____

Appendix 7
Ethical clearance (To be inserted at printing)

Appendix 8
Board of graduate approval (To be inserted at printing)

Appendix 9
Project management

S/N	ACTIVITY/DECRIPTION OF TASKS TO BE PERFORMED	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR
1	Presentation of the proposal to the university of Zambia post Graduate forum							X				
2	Approval of the proposal by the dean-UNZA-SOM and seeking authority from relevant authorities								X	X		
3	Organizing resources for the project										X	
4	Selection of research assistants										X	
5	Training of administrators and two research assistants										X	
6	Conducting pretesting and analyzing pretest. Making corrections on the data collection tools based on results										X	
7	Data collection by research team										X	X
8	Data processing and editing/cleaning										X	X
9	Analyzing data										X	X
10	Report writing										X	X
11	Presentation of report draft to the supervisors										X	X
12	Scrutiny of draft by the supervisors										X	X
13	Revise draft report											X
14	Presentation of final report											X
15	Printing final report											X

Appendix 10

THE UNIVERSITY OF ZAMBIA

SCHOOL OF MEDIINE

MASTER OF SCIENCE IN PUBLIC HEALTH – POPULATION STUDIES

PREVALENCE OF DIABETES IN HIV INFECTED INDIVIDUALS ON ART

ESTIMATED RESEARCH BUDGET

ITEM	QUANTITY	UNIT COST KR	TOTAL COST KR
STATIONARY			
Reams of Paper	5	25	125
Pens	10	2.50	25
Eraser	5	0.50	2 .50
Pencils	5	1.50	7 .50
Stapler	1	45	45
Staples	2	20	40
Perforator	1	50	50
Highlighters	5	5	25
Notebooks	2	15	30
File Folders	5	2	10
Memory Stick 2G	1	200	200
Lockable Storage containers	1	80	80
SUBTOTAL			**640**
TESTING SERVICES			
Sharps container	2	75	150
Glucometer	2	280	560
Testing strips	6	140	840
Lancets	5	50	250
Methylated spirit 2.5L	2	21.50	43
Cotton wool	5	27.50	137.50
Gloves	5	35	175
SUBTOTAL			**2 155. 50**
SECRETARIAL SERVICES			
Typing and printing participant data collection sheet	250	1.50	375
Typing and printing draft reports Binding	3	1.50*50pages	225
Typing and printing dissertation final report	3	1.50*50pages	225

Binding final dissertation	3	85	255
SUBTOTAL			**1 080**
PERSONEL			
(R.A) Lunch allowance (orientation)	1	50*2 days	100
(R.A) Allowance	1	25*60days	1 500
Nurse allowance	2	35*60days	4 200
SUBTOTAL			**5 800**
FIELD EXPENSES			
Transport reimbursement(clients)	222	10	2 220
Transport allowance	2	15*60days	1 800
Statistician consultation	1	150*2 days	300
SUBTOTAL			**4 320**
TOTAL			**13 995.50**
CONTIGENCY 10%			**1 399.55**

GRAND TOTAL: KR 15 395.05

Budget Justification

A total sum of KR15 395.5 was required to conduct the study. Nurses working in the clinic were incorporated as study nurses to assist with introducing the study to patients and performing blood glucose testing. Testing kits and supplies were needed to facilitate this process safely. Study participants were reimbursed for transportation. A fee was paid to the nurses for their assistance. Stationary was utilized for the purposes of recording information, compiling, typing, photocopying, printing, filing and storage of materials.

Appendix 11: Distribution of Fasting Blood Sugar (FBS) results

Fasting Blood Sugar (mmol/L)	Frequency	Percent	Cumulative Percent
2.7	1	.4	.4
3.5	2	.9	1.3
3.6	1	.4	1.8
3.8	3	1.3	3.1
4.1	2	.9	4.0
4.2	1	.4	4.5
4.4	2	.9	5.4
4.5	4	1.8	7.1
4.6	6	2.7	9.8
4.7	5	2.2	12.1
4.8	14	6.2	18.3
4.9	14	6.2	24.6
5	15	6.7	31.2
5.1	9	4.0	35.3
5.2	22	9.8	45.1
5.3	14	6.2	51.3
5.4	22	9.8	61.2
5.5	10	4.5	65.6
5.6	4	1.8	67.4
5.7	18	8.0	75.4
5.8	12	5.4	80.8
5.9	7	3.1	83.9
6	12	5.4	89.3
6.1	4	1.8	91.1
6.2	4	1.8	92.9
6.3	3	1.3	94.2
6.4	4	1.8	96.0
6.5	2	.9	96.9
6.6	1	.4	97.3
6.8	1	.4	97.8
6.9	1	.4	98.2
7.2	1	.4	98.7
7.3	1	.4	99.1
8.4	1	.4	99.6
13	1	.4	100.0
Total	224	100.0	

Appendix 12

Distribution of Body Mass Index

Body Mass Index kgs/m^2	Frequency	Percent	Cumulative Percent
15	2	.9	.9
16	3	1.3	2.2
17	3	1.3	3.6
18	13	5.8	9.4
19	18	8.0	17.4
20	15	6.7	24.1
21	15	6.7	30.8
22	19	8.5	39.3
23	20	8.9	48.2
24	18	8.0	56.2
25	19	8.5	64.7
26	14	6.2	71.0
27	17	7.6	78.6
28	10	4.5	83.0
29	4	1.8	84.8
30	8	3.6	88.4
31	8	3.6	92.0
32	6	2.7	94.6
33	2	.9	95.5

34	3	1.3	96.9
35	3	1.3	98.2
36	1	.4	98.7
37	2	.9	99.6
40	1	.4	100.0
Total	224	100.0	

Appendix 13

Antiretroviral drugs prescribed

Lamivudine (3TC)
Abacavir (ABC)
Alluvia (ALV)
Zidovudine (AZT)
Stavudine (D4T)
Efavirenz (EFV)
Emtricitabine (FTC)
Nevirapine (NVP)
Tenofovir Disoproxil Fumarate (TDF)
Truvada (TVD)

Appendix 14

Year of HIV diagnosis against ART initiation date (year)

		ART initiation date (Year)											
		2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
Year of HIV diagnosis	1992	0	0	0	0	0	0	1	0	0	0	0	1
	1999	0	0	0	0	0	0	0	0	0	1	0	1
	2001	0	0	0	0	0	0	0	0	2	1	0	3
	2002	0	2	0	0	0	0	0	0	1	0	0	3
	2003	3	1	0	0	1	0	1	0	0	0	0	6
	2004	0	7	0	0	1	0	0	0	0	0	0	8
	2005	0	0	3	0	0	1	0	0	0	0	0	4
	2006	0	0	0	4	2	2	0	4	1	0	0	13
	2007	0	0	0	0	8	4	1	1	3	0	0	17
	2008	0	0	0	0	0	19	3	0	1	2	0	25
	2009	0	0	0	0	0	0	20	4	3	0	0	27
	2010	0	0	0	0	0	0	0	35	10	2	0	47
	2011	0	0	0	0	0	0	0	0	25	9	1	35
	2012	0	0	0	0	0	0	0	0	0	31	3	34
Total		3	10	3	4	12	26	26	44	46	46	4	224

Appendix 15

Concomitant medications

	Frequency	Percent
None	123	54.9
ATT	2	.9
Daonil	2	.9
Dapsone	1	.4
Enalapril	1	.4
Fluconazole	1	.4
Folic Acid	1	.4
Losartan	1	.4
Moduretic	4	1.8
Nifedipine	5	2.2
Septrin	83	37.1
Total	224	100.0