Prevalence and Associated Risk Factors for Hypertension among HIV Positive Patients Attending Comprehensive Care Centre at Thika District Hospital, Kenya, 2008

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University

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DEDICATION

This thesis is dedicated to my former teacher and mentor, the late Dr Geoffrey Griffin, from whom I learnt that hard work and honesty is the key to glory.

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LIST OF ABBREVIATIONS

ACEI	Angiotensin Converting Enzyme Inhibitor
ARB	Angiotensin Receptor Blocker
ARVs	Antiretroviral Drugs
BB	Beta Blocker
BMI	Body Mass Index
BP	Blood Pressure
CCB	Calcium Channel Blocker
CCC	Comprehensive Care Centre
CI	Confidence Interval
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic Blood Pressure
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
NNRTI	Non Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NS	Not Significant
PI	Protease Inhibitor
OR	Odds Ratio
SBP	Systolic Blood Pressure
WHO	World Health Organization

ABSTRACT

Hypertension is one of the major risk factors for stroke, heart failure, kidney failure, eye disease and premature death. With the advent of Human Immunodeficiency Virus (HIV) infection and antiretroviral drugs, there has been conflicting reports on their effect on hypertension with some studies associating the two with hypertension. However, data is still scanty especially in Africa as few studies have been done. This study aimed at evaluating the prevalence of hypertension among HIV positive patients and associated risk factors.

A cross-sectional study was carried out over 2 months (between 15th September and 10th November, 2008) at the out-patient based Comprehensive Care Centre, Thika District Hospital. A total of 200 HIV positive patients were selected through systematic random sampling. Blood pressure was measured in all selected participants in order to assess the prevalence of hypertension. A detailed semi-structured questionnaire was also administered to determine the risk factors for hypertension.

Prevalence of hypertension among HIV positive patients was 18% (95% Confidence Interval [CI]:12.5-23.5%). The hypertensive and the normotensive groups were comparable in terms of duration of HIV infection and use of antiretroviral drugs. The hypertensive group was older by six years (43.3±10.4 vs 37.4±9.3; p-value=0.001) with an age of ≥35 years being independently and significantly associated with hypertension at logistical regression analysis (Odds Ratio [OR]:4.55; 95% CI: 1.72-12.03; p-

value=0.002). The hypertensive group had a higher body mass index (BMI) (23.53±3.4 vs 21.96±3.9; p-value= 0.03) with a BMI of ≥25 being significantly associated with hypertension (OR: 3.01; 95% CI: 1.32-6.85; p-value=0.009). Having had kidney disease was also significantly associated with hypertension (OR: 13.38; 95% CI: 1.81-98.73; p-value=0.01).

Hypertension is not uncommon in HIV positive patients and better prevention, detection, control and treatment policies should be formulated. An age of ≥35 years, being overweight and having kidney disease were the risk factors identified in this study.

CHAPTER ONE: INTRODUCTION

1.1 Background

Hypertension is the intermittent or sustained elevation in diastolic or systolic blood pressure above the normal. It is defined as having a systolic blood pressure (SBP) of ≥140 and/or a diastolic blood pressure (DBP) of ≥90 mm Hg. (WHO, 2003)

Blood pressure rises through childhood and adolescence and reaches the plateau of normal adult levels in the third decade. However, blood pressure continues to rise with age but with considerable individual variations (Macsween *et al.*, 1992). Since the advent Human Immunodeficiency Virus (HIV) infection in the early 1980s, there has been considerable debate regarding HIV infection as a possible cause of hypertension. However, what is clear is that HIV infection has been shown to cause blood vessel changes which can predispose to high blood pressure at an earlier age (Aoun and Ramos, 2000).

In the management of HIV infection, the highly active antiretroviral therapy (HAART) has resulted in decreased morbidity and mortality from HIV and hence improved long term survival of these patients (Palella *et al.*, 1998). This has made it necessary for clinicians to focus on other chronic illnesses such as hypertension that usually affect older people as these patients are now able to live longer.

Additionally, these drugs have been associated with metabolic disorders such as hyperlipidemia, impaired glucose tolerance and lipodystrophy that can cause hypertension (Gazzaruso *et al.*, 2002). This study aimed at assessing the burden of hypertension among HIV positive patients and determining the risk factors associated with it.

1.2 Statement of the problem

In the year 2000, it was estimated that 26.4% (about 1 in 4 people) of the general adult population aged 20 years and above in the world was hypertensive and the percentage is expected to rise to 29.2 % in 2025 (Kearney *et al.*, 2005). However, the prevalence of hypertension varied from country to country with the lowest having been reported in rural India (3.4% in men, 6.8% in women) and the highest in Poland (68.9% in men and 72.5% in women) (Kearney *et al.*, 2004).

Hypertension is a chronic condition that often leads to end-organ damage if not well managed. It is a major and independent risk factor for cerebrovascular, cardiovascular, renal and eye complications (Jung *et al.*, 2004; Gu *et al.*, 2008; Qureshi *et al.*, 2005) as well as a major cause of death in the world (Norman *et al.*, 2007; Sai *et al.*, 2007). It causes over 7 million premature deaths each year worldwide and about 13% of global fatalities (WHO, 2002).

Furthermore, hypertension is the 2nd commonest cause of kidney failure after diabetes and it increases the risk of end-stage renal disease by more than four fold (Klag *et al.*,

1996). Besides increasing the risk of stroke by 4-6 times, hypertension is also the most common risk factor for congestive heart failure and it increases its risk by more than two fold (Levy *et al.*, 1996).

The burden of hypertension in HIV has not been well documented but it varies from country to country. In some of the studies that have been published, the prevalence has ranged from as low as 13.1 % in Spain (Jerico *et al.*, 2005) to as high as 34.2% in Italy (Gazzaruso *et al.*, 2002).

1.3 Justification for the study

The burden of hypertension and HIV co-morbidity has not been well documented in Africa although several studies have been done in other parts of the world with conflicting findings. For better management of hypertension among HIV positive patients, it is important to have locally available data, yet this is lacking in Kenya.

This study aimed at estimating the burden of hypertension in HIV positive patients in a sub-urban town of Kenya. This was intended to provide local data on the problem that will assist in formulating better management practices that would eventually lead to improvement in the lives of these patients

1.4. Hypotheses

1.4.1 Null hypothesis

There are no specific risk factors associated with Hypertension among HIV positive patients attending the Comprehensive Care Centre at Thika District Hospital.

1.4.2 Alternative hypothesis

There are specific risk factors associated with Hypertension among HIV positive patients attending the Comprehensive Care Centre at Thika District Hospital

1.5 Objectives

1.5.1 General objective

To determine the prevalence and associated risk factors for hypertension among the HIV positive patients attending the Comprehensive Care Centre at Thika District Hospital, Kenya.

1.5.2 Specific objectives

1.5.2.1 To determine the prevalence of hypertension among HIV positive patients attending the Comprehensive Care Centre at Thika District Hospital, Kenya.

1.5.2.2 To determine the risk factors for hypertension among HIV positive patients attending the Comprehensive Care Centre at Thika District Hospital, Kenya.

CHAPTER TWO: LITERATURE REVIEW

2.1 Global burden of hypertension

2.1.1 Prevalence of hypertension in the general population

The estimated prevalence of hypertension in the world for adults (20 years and above) in the year 2000 was 26.4% (972 million people) (Kearney *et al.*, 2005). However, this prevalence was found to vary from region to region with the highest prevalence being estimated in Europe and America and lowest being estimated in India, China and Sub-Saharan Africa

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Wolf-Maier *et al.* (2003) estimated the prevalence of hypertension for North America and Europe by analyzing several surveys that had been done in USA, Canada and 6 European countries (Italy, Sweden, England, Spain, Finland and Germany). The estimated age- and sex-adjusted prevalence of hypertension was 44% in Europe and 28% in North America (USA and Canada). However, this varied from country to country with the prevalence being highest in Germany (55%) and lowest in Canada (27.4%). The prevalence was estimated to be 27.7% in United States, 41% in England and 48.7% in Finland. The prevalence of hypertension was higher in males for all the countries studied.

In another study done to compare the prevalence of hypertension in West Africa (Cameroon and Nigeria), the Caribbean (Jamaica, St. Lucia and Barbados) and the United States, the age-adjusted prevalence of hypertension was 32.6% in USA, 25.5%

in the Caribbean and 15.6% in West Africa (Cooper *et al.*, 1997). The lowest prevalence was found in the rural areas of Cameroon (15.4%) and the highest was among the females in USA (33.6%).

A study done in Tanzania to compare the prevalence of hypertension in the urban and rural areas found the prevalence to be quite high in both rural and urban Tanzania (Edwards *et al.,* 2000). The crude prevalence of hypertension in the urban area was 30% and 28.6% among the males and females, respectively while it was 32.2% and 31.4% in the rural area among males and females, respectively. However, when the prevalence was age-standardized, the prevalence in the urban area was 37.3% and 39.1% among males and females, respectively, while it was 26.3% and 27.4% in the rural area among males and females, respectively.

Data on prevalence of hypertension in Kenya is very scanty. However, a study done in Kitui District in 1986 sampled 360 people in the community and found a prevalence of 6.4%. There was no difference in prevalence between the urban and rural areas (Katsivo *et al.*, 1991)

2.1.2 Prevalence of Hypertension in HIV positive patients

There is no consensus as to whether the prevalence of hypertension is higher among the HIV positive people than in the general population. However, it is generally agreed that HIV infected patients are at a higher risk of developing hypertension at a younger age than in the general population (Aoun and Ramos, 2000). While some

researchers have found the prevalence to be higher in HIV positive people, others have found it to be the same or even lower than in the general population.

One study done in Spain found the prevalence of hypertension among HIV-infected patients to be 13.1%, which was similar to the prevalence among the HIV negative group (Jerico *et al.*, 2005). In Norway, a study conducted by Bergersen *et al.* (2003) found no significant difference in the prevalence between the HIV-positive and the HIV-negative groups. In this study, the prevalence was 24% in the HIV-negative group and 21% for those who were on highly active antiretroviral therapy (HAART). In addition, a lower prevalence of 13% was found among HIV positive patients who were not on HAART.

More recently in a study done in America, Khalsa *et al.* (2007) found the prevalence of hypertension to be 26% among the HIV positive patients and 28% in the HIV negative groups. Another study done in Italy found the prevalence to be 34% in patients on HAART, as compared to 11.9% for HIV negative controls. However, there was no comparison done with HIV patients who were not on HAART (Gazzaruso *et al.,* 2002). Other studies done in Germany and Switzerland found the prevalence of hypertension in the HIV to be 29% (Jung *et al.*, 2004) and 26% (Glass *et al.,* 2006), respectively. However, both studies did not compare the prevalence to that of HIV negative groups.

2.2 Classification of hypertension

The 2003 Joint National Committee on Prevention, Detection, Evaluation and the Treatment of High blood pressure guidelines classify blood pressure by stages and provide recommendations for treatment and follow-up (Chobanian *et al.*, 2003). It classifies blood pressure into 3 stages; Normal, Pre-hypertension and Hypertension. The hypertension stage is further subdivided into stage I and II (Table 2.1).

Table 2.1: Standard Blood Pressure Classification for Adults (18 years and above)

Blood pressure classification	**SBP, mm Hg**	**DBP, mm Hg**
Normal	<120	And <80
Prehypertension	120-139	Or 80-89
Stage I Hypertension	140-159	Or 90-99
Stage II Hypertension	≥160	Or ≥100

SBP -Systolic Blood Pressure DBP- Diastolic Blood Pressure
Source: Chobanian *et al.* (2003)

2.3 Causes and risk factors for hypertension

2.3.1 Causes of hypertension

In about 95% of the cases of hypertension, the cause is not clear and is, therefore, termed as primary/essential/idiopathic hypertension. In the remaining 5%, hypertension is secondary to other known disease processes and is, therefore, referred to as secondary hypertension (Macsween *et al.*, 1992). Although the exact cause in

primary/essential/idiopathic hypertension is not known, many factors have been identified as risk factors.

Among the causes of secondary hypertension, renal diseases account for 90% of the cases. Other causes include pregnancy, adrenal diseases, hyperparathyroidism, acromegaly, thyrotoxicosis, coarctation of the aorta and drugs such as oral contraceptive drugs (Macsween *et al.*, 1992).

2.3.2 Risk factors for hypertension

2.3.2.1 Antiretroviral drugs and HIV infection

There are contrasting reports on antiretroviral drugs as causes of hypertension. While some studies have shown an association between antiretroviral drugs and hypertension (Chow *et al.*, 2003; Gazzaruso *et al.*, 2002; Crane *et al.*, 2006; Cattelan *et al.*, 2001), many other studies have not demonstrated any relationship between the two (Jerico *et al.*, 2005; Jung *et al.*, 2004; Khalsa *et al.*, 2007; Bergersen *et al.,* 2003).

Chow *et al.* (2003) conducted a retrospective study in America and examined blood pressure changes for patients who were on antiretroviral drugs between 1995 and 2001. They found that Protease Inhibitors (PIs) and Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) were independently associated with hypertension with the former having a bigger effect on hypertension. There was no significant blood pressure change for patients who were on Nucleoside Reverse Transcriptase

Inhibitors (NRTIs). In an observational cohort study PIs were significantly associated with hypertension with Lopinavir/Ritonavir drug having the most effect on hypertension (Crane *et al.,* 2006). In their study, Cattelan *et al.* (2001) also found Indinavir, which is a PI, to be significantly associated with hypertension.

Antiretroviral drugs have been reported to cause metabolic syndrome (dyslipidemia and insulin resistance) which is significantly associated with hypertension (Gazzaruso *et al.,* 2002). Friis-Moller *et al.* (2003) showed that antiretroviral drugs cause dyslipidemia (changes in lipid profile) by elevating the total cholesterol levels. They observed that PIs caused the highest elevation of total cholesterol, followed by NNRTIs and NRTIs. According to Fontas *et al.* (2004), PIs and NNRTIs cause dyslipidemia with PIs having the largest effect on lipid profile as compared to NNRTIs. They further demonstrated that even within the different classes of antiretroviral drugs, there existed differences in individual drugs.

Chronic HIV infection has been associated with hypertension in some studies. This has been attributed to the fact that HIV infection has been found to cause vasculitis, aneurysms and a syndrome of acquired glucocorticoid resistance, all of which can cause hypertension (Aoun and Ramos, 2000). However, reports by other researchers (Khalsa *et al.*, 2007; Jung *et al.*, 2004) have not found any association between chronic HIV infection and hypertension.

2.3.2.2 Age

Several studies have shown that growing old is associated with increased risk for hypertension (Poulter *et al.* 1984, Cooper *et al.* 1997, Edwards *et al.*, 2000). Wolf-Maier *et al.* (2003) and Cappuccio *et al.* (2004) showed that blood pressure rises with age with significant rise from the age of 35. They showed that both age-specific systolic blood pressure and diastolic blood pressure rises with age but that the former rises more steadily and steeply than the latter. However, unlike systolic blood pressure, diastolic blood pressure stabilizes or takes a U-shape after the age of 55. Some of the studies conducted among HIV positive patients that have indicated that hypertension increases with advancing age include Thiebaut *et al.* (2005), Jung *et al.* (2004), and Jerico *et al.* (2005).

2.3.2.3 Overweight and Obesity

Overweight and obesity has been reported in several studies to be a risk factor for hypertension. Thiebaut *et al.* (2005) in a study done in France among HIV positive patients showed that a high body mass index increased the risk of hypertension. Similar findings were reported in similar studies conducted in Germany and Spain (Jung *et al.*, 2004 and Jerico *et al.,* 2005, respectively). In particular, these studies found a BMI of 25kg/m^2 or more to be significantly associated with hypertension.

Other studies that have found a positive association between a high BMI and hypertension include Poulter *et al.* (1984), Savitha *et al.* (2007) and Edwards *et al.*

(2000). More recently, Khalsa *et al.* (2007) found a BMI of more than 30kg/m^2 to be a risk factor for hypertension.

2.3.2.4 Race

Race has been reported in several studies to have a significant relationship with hypertension. The National Health and Nutritional Survey (NHANES) in America showed that hypertension was more prevalent in black Americans (32%) than in white Americans (23%) (Burt *et al.*, 1995). In another study conducted in South Africa in 1983, the age adjusted prevalence showed that hypertension (using WHO classification, ≥160/95) was highest in urban blacks of the Zulu tribe (25%), intermediate in whites (17%), lower in Indians (14%) and lowest in rural blacks (9%), (Seedat, 1983).

Numerous potential explanations for the higher prevalence of hypertension in blacks have been proposed with majority of the people agreeing that it is a combination of both genetics and environment (Tomson and Lip, 2005). Even within blacks, blood pressure has been noted to rise significantly with change of environment from rural to urban areas. In the Luo migration study that was conducted in Kenya in 1980s, Poulter *et al.* (1984) showed that blood pressure did not rise significantly with age in the rural villages. However, blood pressure rose significantly with age for those who had migrated to urban Nairobi.

Although most studies in America show that blacks migrating there have higher prevalence of hypertension than the whites, other studies done in Europe have not shown any differences in blood pressure between the black population migrating there and the white population (Cruickshank *et al.,* 1985). Therefore, the difference in blood pressure between blacks in America and Europe could to be a factor of the environment.

Some of the suggested genetic explanations for the higher prevalence of blood pressure in blacks in USA include low rennin levels, increased sodium sensitivity, abnormalities in sodium transport and increased vascular responsiveness to pressor stimuli. Others include insulin resistance and stresses attributed to low socio-economic status (Tomson et al., 2005).

2.3.2.5 Reduced physical activity

Reduced physical activity has also been associated with hypertension. It has been shown that among people who have regular physical exercises, the risk of developing hypertension is much lower. In patients who are already hypertensive, regular exercise has been shown to reduce their blood pressure significantly. Vriz *et al.* (2002) studied 572 male subjects with borderline and mild hypertension and found that blood pressure decreased significantly with increased physical activity. Kokkinos *et al.* (1995) also showed that regular exercises reduce blood pressure significantly in people with severe hypertension.

In a meta- analysis of 72 randomized control trials, Cornelissen *et al.* (2005) observed that regular physical exercises reduces blood pressure. However, the reduction in blood pressure was more marked in hypertensive subjects as compared to normotensive subjects. He noted that several mechanisms are responsible for the reduction in blood pressure including reduction in systematic vascular resistance, plasma norepinephrine, plasma rennin activity and body weight.

2.3.2.6 Diet

Poor dietary habits have been shown to be a risk factor for hypertension. Excessive consumption of dietary sodium chloride (salt), coupled with diminished dietary potassium, induces an increase in fluid volume and an impairment of blood pressure regulating mechanisms resulting to hypertension. A high sugar (sucrose) intake also elevates blood pressure possibly through an increase in the production of adrenaline which in turn causes vasoconstriction. A diet that has a high fat content may also lead to hypertension by causing arterial narrowing that may cause increased vascular resistance (Macsween *et al.,* 1992)

Savitha *et al.* (2007) demonstrated that decreased consumption of vegetable and fruits was a significant risk factor for hypertension. Fruits and vegetables have high levels of potassium, magnesium and fiber which have been found to protect people from hypertension. In a study called Dietary Approaches to Stop Hypertension (DASH), Appel *et al.* (1997) demonstrated that hypertension can be prevented or lowered by

eating foods low in sodium but rich in potassium, calcium, magnesium, Vitamin C, Vitamin A, complex carbohydrates, polysaturated fat and fiber.

The DASH diet encourages use of fruits and vegetables (high in Potassium, magnesium and fiber), low- fat dairy foods (high in calcium and magnesium) and food that is low in saturated fat, total fat and cholesterol. In addition it encourages whole grains, poultry, fish, and nuts. It also advocates for reduced fats, red meats, salt, sweets and sugared beverages which can cause hypertension. Other studies that have found similar findings on DASH diet include Svetkey *et al.* (1999) and Plaisted *et al.* (1999).

2.3.2.7 Alcohol

Alcohol has been associated with hypertension for a long time. Klatsky *et al.* (1977) studied 83,947 men and women from 3 races and demonstrated that taking more than two drinks of alcohol per day (>30mls of ethanol) was a significant risk factor for hypertension. These findings have been replicated by many other researchers including Dyer *et al.* (1977), Grogan *et al.* (1994) and Gillman *et al.* (1995).

2.3.2.8 Smoking

The association of smoking and hypertension has been controversial. Although some researchers have found smoking to be a risk factor for hypertension (Tuomilehto *et al.,* 1982; Mann *et al.,* 1991), other researchers have not found any association

between smoking and hypertension. In fact some of the researchers have reported lower blood pressure levels in smokers than in non smokers (Berglund *et al.,* 1975; Seltzer, 1974). In a nationwide survey involving 33,860 people in England, Primatesta *et al.* (2001) were able to show a positive association between smoking and hypertension. However, this association was only observed in older men aged 45 years and above and not in younger men or women. They therefore concluded that independent chronic effect of smoking on blood pressure is small.

2.3.2.9 Male Sex

Significant differences have been reported between sexes and hypertension with males being found to be at a higher risk of hypertension. Even in some of the studies conducted on HIV positive patients, male sex has been shown to be associated with hypertension (Gazzaruso *et al.*, 2002; Thiebaut *et al.*, 2005).

2.3.2.10 Family history of hypertension

Another risk factor that has significantly been associated with hypertension in HIV infected patients is a family history of hypertension from a first degree relative. This implies that in some cases of hypertension, there is genetic inheritance from first degree relatives. Researchers that have found an association between family history of hypertension and hypertension include Gazzaruso *et al.* (2002) and Kuschnir *et al.* (2007).

2.4 Clinical presentation of hypertension

Unless there are complications, hypertension is mostly asymptomatic although it may present with occasional headache, fatigue and palpitations. Many people, therefore, do not know that they are hypertensive and are only diagnosed when they present to hospital for routine examination or for other ailments including hypertension complications (Haslett *et al.*, 1999). It is estimated that only about half of the people who are hypertensive in the United Kingdom are actually diagnosed, only half of those diagnosed are on treatment, and only half of those who are on treatment are well controlled (Smith *et al.*, 1990).

2.5 Complications of hypertension

Hypertension can present with several complications that mostly affect central nervous system, heart, kidney and the retina (Haslett *et al.*, 1999). Complications of the Central Nervous System include stroke and hypertensive encephalopathy with the former being caused by either cerebral hemorrhage or cerebral infarction. It is estimated that hypertension increases the risk of stroke by 4-6 times. Hypertensive encephalopathy is a rare condition characterized by high blood pressure and neurological symptoms such as transient disturbances of speech or vision, paraesthesiae, disorientation, fits and loss of consciousness (Haslett *et al.*, 1999).

Complications of the heart include coronary artery disease, left ventricular hypertrophy and left ventricular failure. Hypertension is the most common risk factor for congestive heart failure and it increases its risk by more than two fold (Levy *et al.*,

1996). Hypertension can also cause complications of the kidney that mostly involve damage to renal vasculature leading to renal failure. Hypertension is the second commonest cause of kidney failure after diabetes and it increases the risk of end-stage renal disease by more than four fold (Klag *et al.*, 1996). Other complications of hypertension include arteriolar damage in the retina that may lead to retina ischemia, infarction, retinal hemorrhages, papilloedema and central retinal vein thrombosis (Haslett *et al.*, 1999).

2.6 Management of hypertension

The 7th edition of the Joint National Committee on Prevention, Detection, Evaluation and the Treatment of High blood pressure gives the latest international guidelines on how hypertension should be managed (Chobanian *et al.,* 2003). According to the guidelines, there is no specific difference in the treatment of hypertension whether one is HIV positive or not. The target blood pressure for patients with stage I or II uncomplicated hypertension is <140/90 mm Hg. However, for patients with co-morbidities such as diabetes or chronic kidney disease the target is <130/80 mm Hg (Chobanian *et al.*, 2003).

Two methods are commonly employed in the management of hypertension. These include:

i) Lifestyle modifications (non pharmacologic method) and

ii) Pharmacologic/drug treatment.

Lifestyle modification is the preferred initial therapy for stage I hypertension and should be tried for up to 1 year unless there are other risk factors or complications. For those with other risk factors or complications, lifestyle modifications can be tried for up to six months before initiation of drug therapy (Guleria *et al.*, 2007). However, for those who do not achieve the above blood pressure targets after lifestyle modifications, drug therapy is recommended.

2.6.1 Lifestyle modifications

This is recommended for all patients who are in the prehypertension category as well as those who are hypertensive (Stage I and II). For those who are not hypertensive, lifestyle modification helps to reduce the incidence of hypertension. For those who are hypertensive, lifestyle modification helps to lower blood pressure and also reduce the dosage of drugs required to achieve the blood pressure target.

Interventions with documented efficacy include weight reduction, increased physical activity, limited alcohol consumption, reduced salt intake and DASH diet (Dietary Approach to Stop Hypertension). It should be noted that the effect of implementing these modifications are dose and time dependent and could be greater for some individuals. It should also be noted that the more the interventions tried, the better the outcome (Chobanian *et al.*, 2003).

2.6.1.1 Weight reduction

Overweight or Body Mass index (BMI) of ≥25kg/m^2 is a documented risk factor for blood pressure (Doll *et al.*, 2002; Poulter *et al*.1984; Savitha *et al*., 2007). Reduction of body weight has therefore been shown to significantly reduce blood pressure (He *et al.*, 2000). Reducing 10kg of body weight reduces systolic blood pressure in the range of 5-20 mm Hg (Chobanian *et al.*, 2003)

2.6.1.2 Increased physical activity

Increased aerobic physical activity such as walking, jogging, and swimming has been shown to lower blood pressure (Vriz *et al.*, 2002; Kokkinos *et al.,* 1995; Whelton *et al.,* 2002). Increasing physical activity to the minimum recommended of at least 30 minutes per day for most days of the week reduces systolic blood pressure by between 4 - 9mm Hg (Chobanian *et al.*, 2003)

2.6.1.3 Dietary Approaches to Stop Hypertension (DASH) diet

The algorithm of DASH in the management of hypertension includes advocacy for a diet rich in fruits, vegetables, low- fat daily products, whole grains, white meat (poultry and fish as opposed to red meat) and less saturated fat. This diet is rich in potassium, magnesium, fiber and low in total fat, saturated fat and cholesterol, all which are important in reducing blood pressure (Karanja *et al.*, 1999). The DASH diet has been shown to reduce systolic blood pressure by between 8-14 mm Hg (Chobanian *et al.*, 2003).

Table 2.2 shows the DASH diet together with the significance of each food group in the management of hypertension.

Table 2.2: The Dietary Approaches to Stop Hypertension (DASH) Diet

Food Group	Daily servings	Serving sizes	Significance
Grains and grain products	7 - 8	• 1 slice bread or • 1 cup ready-to eat cereal or • ½ cup cooked rice, pasta or cereal	Carbohydrates and fiber
Vegetables	4-5	• 1 cup raw leafy vegetable or • ½ cup cooked vegetable or • 6 ounces vegetable juice	Potassium, Magnesium and fiber
Fruits	4-5	• 1 medium fruit or • ¼ cup dried fruit or • ½ cup fresh, frozen, or canned fruits	Potassium, Magnesium and fiber
Low-fat or fat free dairy foods	2-3	• 8 ounces milk or • 1 cup yoghurt or • 1.5 ounces cheese	Calcium, protein, potassium and magnesium
Lean meats, poultry and fish	2 or less	• 3 ounces cooked lean meats, skinless poultry or fish	Protein and magnesium
Nuts, seeds and dry beans	4-5 servings per week	• 1/3 cup or 1.5 ounces nuts or • 1 tablespoon or ½ ounces seeds or • ½ cup cooked dry beans	Magnesium. Potassium, protein and fiber

Source: Appel *et al.* (1997)
1 ounce = ~30mls
1 cup = 8 ounces (~240mls)

2.6.1.4 Moderation of alcohol consumption

Alcohol has been documented to be a risk factor for hypertension (Klatsky *et al.,* 1977; Dyer *et al.,* 1977; Cushman *et al.,* 1998). Reducing alcohol intake has therefore been shown to significantly reduce blood pressure (Xin *et al.,* 2001). It has been observed that reducing alcohol intake to no more than two drinks per day, reduces systolic blood pressure by between 2 - 4mm Hg (Chobanian *et al.*, 2003)

2.6.1.5 Reduced salt intake

Excessive consumption of dietary sodium chloride (salt) induces an increase in fluid volume that leads to high blood pressure. Reduction of salt intake to no more than 100 mmol/day (2.4g sodium or 6g sodium chloride) has been shown to significantly reduce blood pressure (He *et al.*, 2000). This reduction in blood pressure has been quantified at between 2-8 mm Hg for systolic blood pressure (Chobanian *et al.*, 2003)

Table 2.3 summarizes the various lifestyle modifications methods that can be used to control hypertension together with the approximate reduction in systolic blood pressure.

Table 2.3: Lifestyle modifications to manage hypertension

Modification	**Recommendation**	**Approximate SBP reduction(Range)**
Weight reduction	Maintain normal body weight (BMI 18.5-24.9kg/m2)	5-20 mmHg/10kg weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables and low fat dairy products with a reduced content of saturated and total fat	8-14 mmHg
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mmol/day (2.4g sodium or 6 g sodium chloride ~ 1 teaspoon of salt)	2-8 mmHg
Physical activity	Engage in regular aerobic physical activity such as brisk walking at least 30 mins/day, most days of the week	4-9 mmHg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks(1oz or 30 ml ethanol) per day in most men and to no more than 1 drink per day in women and lighter persons	2-4 mmHg

Source: Chobanian *et al.* (2003) DASH – Dietary Approaches to Stop Hypertension. SBP-Systolic Blood Pressure

2.6.2 Pharmacologic treatment

Thiazide diuretics are the recommended drugs for managing hypertension stage 1 (SBP 140-159 or DBP 90-99) as they have been proved in many clinical trials as the best in preventing the cardiovascular complications of hypertension. However, if no adequate control is achieved, a second drug may be selected from beta blockers (BBs), Angiotensin Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Blockers (ARBs), or Calcium Channel Blockers (CCBs). A combination of two drugs are usually recommended for management of hypertension stage 2 (SBP≥160 or DBP≥100). These are a thiazide diuretic and either ACEI , ARB, CCB or BB. (Chobanian *et al.,* 2003).

Some of the common oral drugs that are used to manage hypertension, together with their usual dosages, are shown in Table 2.4. Currently, there are no specific contraindications regarding the use of any class of antihypertensive agents in the treatment of HIV-infected patients receiving antiretroviral drugs. However, Calcium Channel Blockers (CCBs) should be used with care as their serum levels can be increased by Protease Inhibitors(PIs) such as ritonavir and atazanavir and hence lead to hypotension and bradycardia (Svetkey and Fan, 2005).

Table 2.4: Common oral antihypertensive drugs and their dosages

Class	Drug	Usual dose in mg/day	Usual daily frequency
Thiazide diuretic	Hydrochlorothiazide	12.5-50	1
	Chlorothiazide	125-500	1-2
	Chlorthalidone	12.2-25	1
	Polythiazide	2-4	1
	Indapamide	1.25-2.5	1
	Metolazone	0.5-1.0	1
Beta blockers	Atenolol	25-100	1
	Propranolol	40-160	2
	Propranolol long acting	60-180	1
	Metoprolol	50-100	1-2
	Timolol	20-40	2
	Nadolol	40-120	1
	Betaxolol	5-20	1
ACEIs	Enalapril	5-40	1-2
	Captopril	25-100	2
	Lisinopril	10-40	1
	Benazepril	10-40	1
	Fosinopril	10-40	1
	Moexipril	7.5-30	1
	Perindopril	4-8	1
	Quinapril	10-80	1
	ramipril	2.5-20	1
ARBs	Losartan	25-100	1-2
	Valsartan	80-320	1-2
	Candesartan	8-32	1
	Eprosartan	400-800	1-2
	Olmesartan	20-40	1
	Irbesartan	150-300	1
	Telmisartan	20-80	1
CCBs	Nifedipine long acting	30-60	1
	Amlodipine	2.5-10	1
	Felodipine	2.5-20	1
	Nicardipine sustained release	60-120	2

Source – Chobanian *et al.*, 2003
ACEIs – Angiotensin Converting Enzyme Inhibitors
ARBs – Angiotensin II Receptor Blockers
CCBs – Calcium Channel Blockers

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study design

This was a cross-sectional study carried out over two months between 15th September and 10th November 2008 and involved systematic random sampling of 200 participants. A cross-sectional study was selected because one of the objectives of the study was to determine the prevalence of hypertension in HIV-positive people.

3.2 Study site

The study was conducted at the out-patient based Comprehensive Care Centre (CCC) at Thika District Hospital (Figure 3.1). The hospital was selected as it had a big number of patients at the clinic which was ideal for a prevalence study (there were about 6,000 patients registered at the clinic as at 1st September, 2008 with a daily attendance of about 70-100 patients). The hospital is located in Thika District in Central Province of Kenya, about 48 kilometers north-east of Nairobi and has a catchment population of about 652,000 people. About 60% of the catchment population is from Thika District with the rest coming from neighboring districts such as Maragua, Gatundu, Kirinyaga, Yatta and parts of Nairobi.

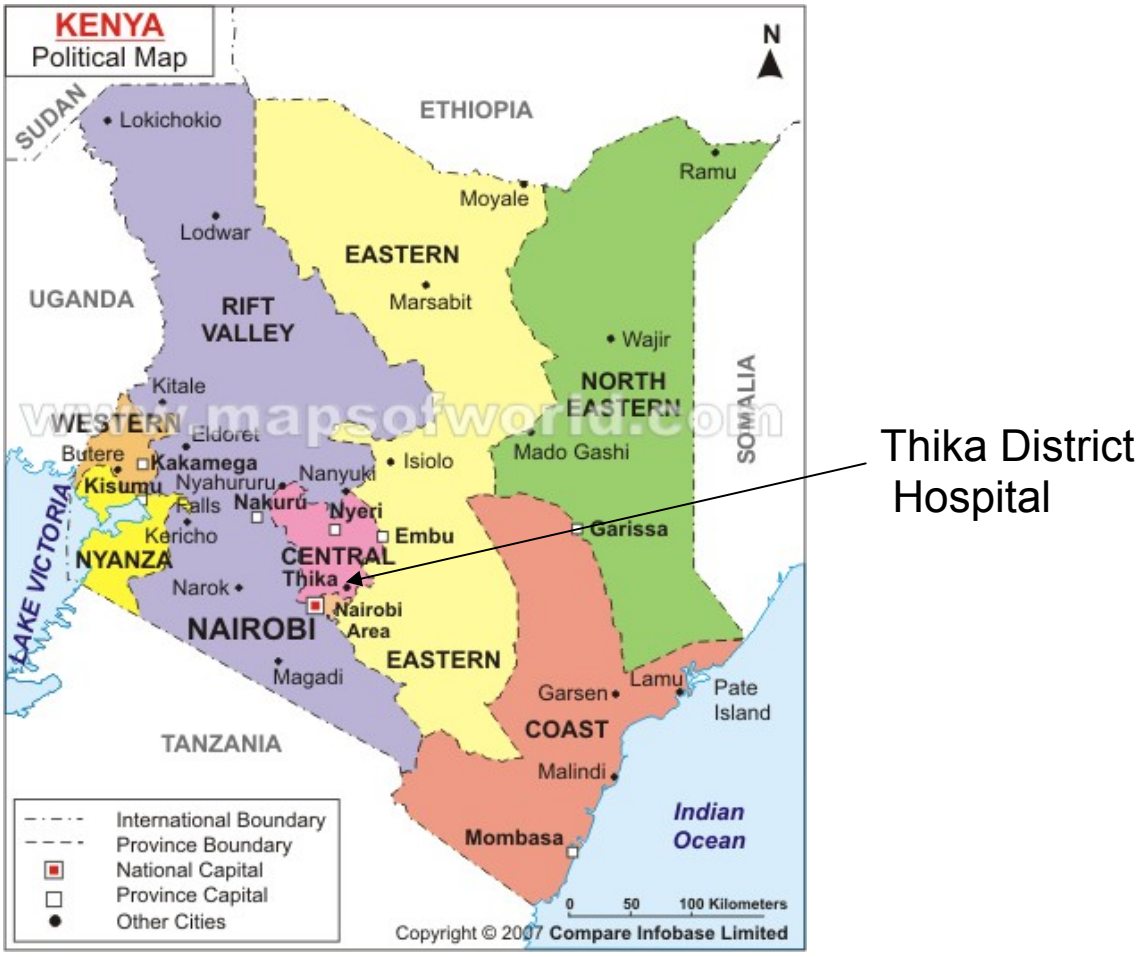

Figure 3.1: Map of Kenya

3.3 Study population

The study population was adult HIV positive patients attending the out-patient based CCC at Thika District Hospital.

Criteria for inclusion into the study

- HIV positive patients attending CCC who were aged ≥18 years

Criteria for exclusion

- Patients aged <18years
- Patients over 18 years who declined participation
- Patients who were too sick to participate

3.4 Sampling

3.4.1 Sample size:

The formula according to Fisher *et al*. (1991) was used to determine the minimum sample size. Assuming a prevalence rate of hypertension of 15% in this group, a confidence level/deviation of ±5% in the estimated prevalence and a confidence interval of 95%, the calculated sample size was 196. The prevalence assumption of 15% was made based on an unpublished survey which was done in Muranga, Kenya in 2006 and which found that 15% of patients attending the Comprehensive Care Clinic were hypertensive.

$$n = z^2 p (1-p)/d^2$$

$$= 1.96 \times 1.96 \times 0.15 \times 0.85/0.05^2$$

$$= 196$$

Where;

n = sample size

p = estimated prevalence of hypertension

d = deviation from the estimated prevalence

z =z-score at 95% CI

3.4.2 Sampling method

Sampling was done using systematic random sampling of patients attending the Comprehensive Care Centre. Patients were given numbers on arrival at the clinic and the first participant selected randomly between 1 and 10. Every 10^{th} patient was subsequently selected and requested to participate in the study. Those who declined to take part and those who had already been interviewed on a previous date were excluded from the sampling frame.

3.5 Data collection

3.5.1 Semi-structured questionnaire

A semi-structured questionnaire was designed to collect data on selected variables. Two nurses were then trained on the questionnaire and assisted in piloting and subsequent collection of the main data. The variables of interest included age, sex, education, occupation, marital status, income, family history of hypertension, history of diabetes and kidney disease, smoking and alcohol. Others included physical activity, diet, duration of HIV infection, use of antiretroviral drugs, and duration of treatment. Weight, height, blood pressure and blood sugar measurements were also taken and captured by the questionnaire.

Information collected on alcohol included details of whether the participants had ever taken alcohol and if they were taking alcohol at the time study. Information on the duration and quantity of alcohol taken was also collected. For smoking, information collected included whether participants had ever smoked, if they were current

smokers, duration of smoking and number of sticks smoked per day. Physical inactivity was defined as staying in the house or office the whole day without doing any manual(strenuous) work and not walking more than 3 kilometers per day (approximately 30 minutes of walking per day).

Data on the types of antiretroviral drugs being taken by the participants was also collected. The drugs were then classified into their respective categories. Antiretroviral drugs are generally classified into 3 categories

i. Nucleoside Reverse Transcriptase Inhibitors (NRTI) e.g. Zidovudine, Stavudine, Lamivudine, Didanosine, Abacavir
ii. Non-Nucleoside Reverse Transcriptase Inhibitors(NNRTI) e.g. Nevirapine, Efavirenz , Delavirdine
iii. Protease inhibitors(PI) e.g. Lopinavir/Ritonavir(Kaletra), indinavir, Ritonavir, Nelfinavir, Saquinavir

A combination of three drugs from the 3 categories is usually recommended for treatment with the most common being 2NRTI+1NNRTI and 2NRTI+1PI.

3.5.2 Weight and Height

The weight was measured in kilograms using a standard manual weighing machine with the participants having minimal clothes (no jackets, coats or pullovers) and no shoes. The height was measured in centimeters using a height rule after the participants had removed their shoes. These two measurements were used to calculate

body mass index (BMI). The BMI was calculated as weight (kg) divided by the square of the height (m^2).

3.5.3 Blood pressure measurement

All the blood pressure measurements were taken by the principal investigator in order to minimize variation in the readings. The measurements were taken non-invasively using a mercury column sphygmomanometer (first and fifth phases of Korotkoff sounds taken as systolic (SBP) and diastolic blood pressure (DBP), respectively) after the participants had rested for 5 minutes in sitting position. The consecutive measurement was done after 5 minutes and an average of the two readings taken. Any participant who had a history of hypertension since being diagnosed with HIV, those who were already on treatment for hypertension and those whose systolic blood pressure (SBP) was ≥140 and/or a diastolic blood pressure (DBP) was ≥90 mm Hg were regarded as hypertensive (WHO, 2003).

3.5.4 Random blood sugar measurement

A random blood sugar test was used to screen all participants who were not known to be diabetic in order to find out if they were diabetic. Those who had a random blood sugar of ≥11.1 mmol/l had their fasting blood sugars taken on a different day. A fasting blood sugar of ≥7.0 mmol/l was used to confirm participants as being diabetic (WHO, 2006). All those who were newly diagnosed in this study, plus those who were already on treatment were classified as diabetics.

3.6 Data Management

3.6.1 Data entry and storage

Data was entered, cleaned and stored into the computer using Epi info statistical software version 3.3.2.

3.6.2 Data analysis

Data was analyzed using the same Epi info statistical software. Prevalence odds ratio was used to establish any association of risk factors with hypertension. Chi-square test and t-test were used to test for statistical significance for discrete and continuous data, respectively. Stepwise multivariable logistical regression was used to develop the final model for risk factors that were significantly associated with hypertension in the bivariate analysis. All p-values reported are two-sided and all confidence intervals (CI) are 95% intervals. Statistical significance was defined as $p \leq 0.05$

3.7 Ethical considerations

Research authorization was given by the Ministry of Higher Education, Science and Technology, Thika District Medical Officer of Health (DMOH) and Thika District Hospital Medical Superintendent. Informed consent was obtained before the questionnaires were administered to the participants. In particular, the purpose and benefits of the study was explained to the participants. Participants were also informed that participation was absolutely voluntary and that they were free to decline participation or stop at any time if they so wished. Data obtained was treated with strict confidentiality to ensure it was not accessed by unauthorized people. Data

was stored in the computer and was password- protected to ensure no unauthorized access while questionnaires were kept under lock and key.

CHAPTER FOUR: RESULTS

4.1 Demographic and socio-economic characteristics

4.1.1 Age and sex

Majority of the participants were relatively young with 71% (142) being below the age of 44 years. Sixty six percent of the participants were in the age group 25-44 years. Only 29% (58) of the participants were aged 45 years and above (Figure 4.1). One hundred and forty two (71%) participants were female with only 58 (29%) being male.

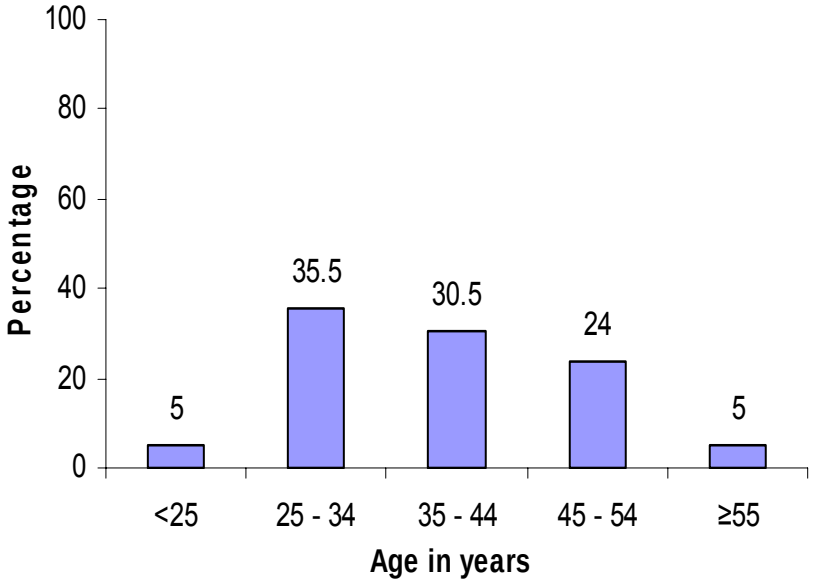

Figure 4.1 Age of participants

4.1.2 Education level

Ninety six percent (192) of the study participants had at least primary level education although only 37.5% (75) had gone past primary school. Only 5.5% had gone to college (Figure 4.2).

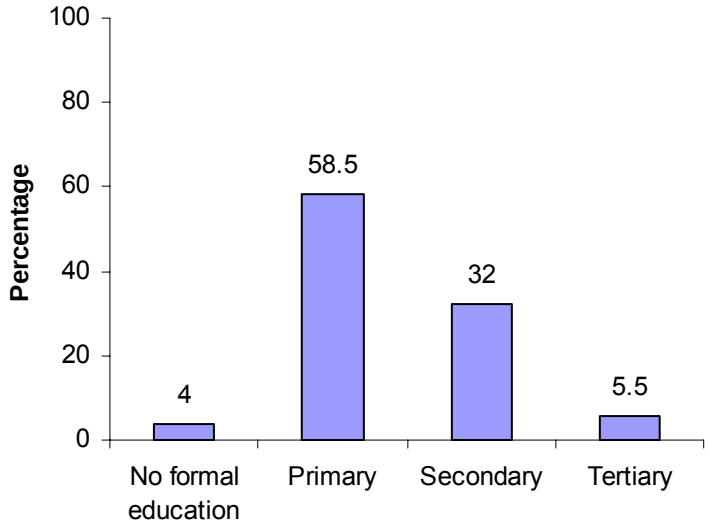

Figure 4.2: Highest level of education

4.1.3 Marital status

One hundred (50%) participants were separated, divorced or widowed. A further 81(40%) participants were married with only 19 (9.5%) being single (Figure 4.3).

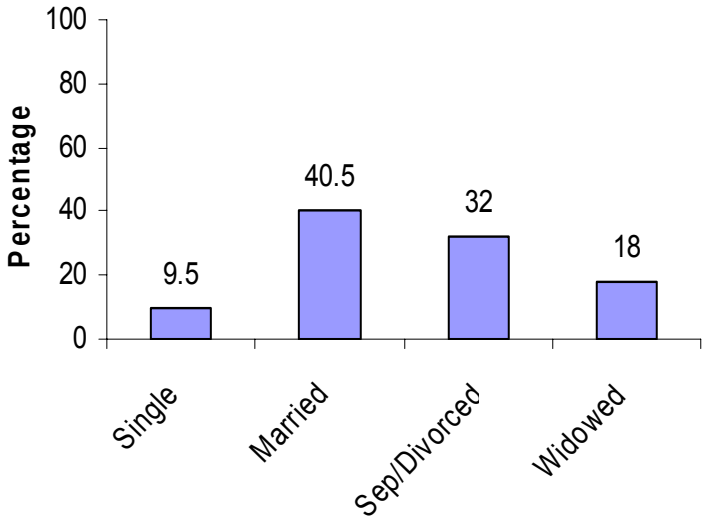

Figure 4.3: Marital status

4.1.4 Monthly income

One hundred and forty nine (75%) participants earned a monthly salary of less than Ksh 5,000 with only 19 (10%) earning more than ten thousand shillings (Figure 4.4).

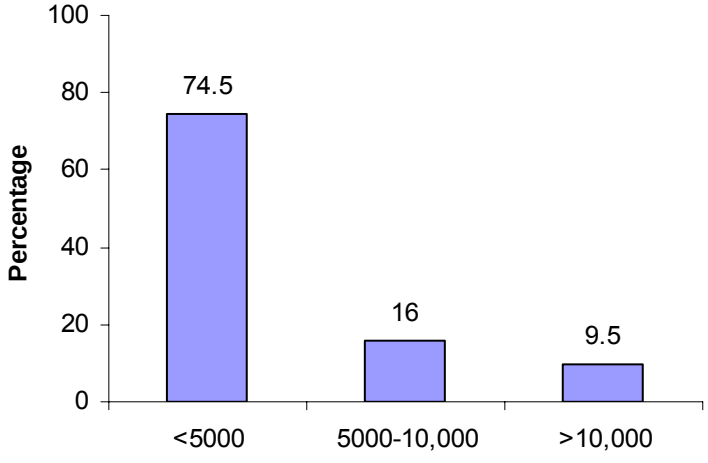

Figure 4.4: Monthly income (K sh)

4.1.5 Comparative analysis of demographic and socio-economic characteristics

When the hypertensive and the normotensive groups were compared, the mean age was significantly higher in the hypertensive group as compared to the normotensive group (p-value = 0.001). However, there was no significant difference between the two groups in terms of sex, education, marital status, occupation and monthly income (Table 4.1)

Table 4.1: Comparison of the demographic and socio-economic characteristics between the hypertensive and normotensive groups

	Hypertensive group n=35 (17.5%)	Normotensive group n=165 (82.5%)	P-value
Age (years) - mean	43.3 ±10.4	37.4 ±9.3	0.001
Gender			NS
Male	7 (20%)	50 (30.3%)	
Female	28 (80%	115 (69.7%)	
Education			NS
No formal education	3 (8.6%)	5 (3%)	
Primary	19 (54.3%)	98(59.4%)	
Secondary	11 (31.4%)	53 (32.1%)	
College/University	2 (5.7%)	9 (5.5%)	
Marital status			NS
Single	3 (8.6%)	16 (9.7%)	
Married	14 (40%)	67 (40.6%)	
Separated/Divorced	10 (28.6%)	54 (32.7%)	
Widowed	8 (22.9%)	28 (17%)	
Occupation			NS
Unemployed	6 (17.1%)	29 (17.6%)	
Informal employment	22 (62.9%)	92 (55.8%)	
Formal Employment	7 (20%)	44 (26.7%)	
Monthly Income (Kshs)			NS
<5000	26 (74.3%)	123 (74.5%)	
5000-10,000	5 (14.3%)	27 (16.4%)	
>10,000	4(11.4%)	15 (9.0%)	

Continuous data given as, means ±SD. NS = Not Significant

4.2 Prevalence of hypertension in HIV positive patients

Thirty five (18%) of the participants were hypertensive (95% CI: 12.5-23.5%). The mean systolic blood pressure was 142.3 mm Hg in the hypertensive group and 109.6 mm Hg in the normotensive group (p <0.0001). The diastolic blood pressure was 95.5 mm Hg in the hypertensive group and 76.2 mm Hg in the normotensive group (p <0.0001) (Table 4.2).

Table 4.2: Blood pressure measurements of study participants

	Hypertensive group n=35 (17.5%)		Normotensive group n=165 (82.5%)		
	Mean ±SD	Range	Mean ±SD	Range	P- value
SBP	142.3±11.7	123-170	109.6±12.8	90-138	<0.0001
DBP	95.5±5.9	85-115	76.2±7.4	50-89	<0.0001

SBP=Systolic Blood Pressure DBP=Diastolic Blood Pressure

4.3 Risk factors for hypertension

4.3.1 HIV infection and antiretroviral drugs

The mean duration of known HIV infection was 21.14 months (range=1-84) in the hypertensive group and 21.89 months (range 1-180) in the normotensive groups. The two groups were therefore similar as far as duration of infection was concerned (p=0.86).

There were 27 (77%) participants in the hypertensive group and 108 (65%) in the normotensive group who were on antiretroviral drugs (Table 4.3). However, this difference was not statistically significant (OR: 1.78; 95% CI: 0.71-4.58); p=0.25). The mean cumulative duration of antiretroviral therapy was 20.1 months (Range= 1-

52) in the hypertensive group and 16.4 months (Range=1-55 months) in the normotensive group. However, this difference was not statistically significant (p=0.20).

Majority of the participants were on the 1st line regimen which consisted of Stavudine, Lamivudine and Nevirapine (Table 4.3). Twenty seven (77%) participants were on NRTI in the hypertensive group as compared to 108 (65%) in the normotensive group (OR: 1.78; 95% CI: 0.71-4.58; p=0.25). There were 26 (74%) participants on NNRTI in the hypertensive group as compared to 108 (65%) in the normotensive group (OR: 1.52; 95% CI: 0.63-3.78; p=0.42). Only one participant was on a protease inhibitor and this class of drugs was therefore not analyzed.

When specific drugs were analyzed, there were twenty five (93%) participants on Stavudine in the hypertensive group and 104 (96%) in the normotensive group (OR 0.48; 95% CI: 0.07-4.03; p=0.34). Twenty six participants (96%) were on Lamivudine in the hypertensive group as compared to 108 (100%) in the normotensive group (p=0.2). Only 1(3.7%) participant was on Zidovudine in the hypertensive group as compared to 4 (3.7%) in the normotensive group (OR=1). Twenty five participants (71.4%) were on Nevirapine in the hypertensive group as compared to 93 (56.3%) in the normotensive group (OR: 1.94; 95% CI: 0.82-4.64; p=0.15). Only 1(2.9%) participant was on Efavirenz in the hypertensive group as compared to 15(9.1%) in the normotensive group (0.29; 95% CI: 0.01-2.25; p=0.31).

Table 4.3: Types of antiretroviral drugs used by the study participants (n=135)

Type of drugs used	Hypertensive group n=27	Normotensive group n=108
Stavudine/Lamivudine/Nevirapine (1st line regimen)	24(88.9%)	89(82.4%)
Stavudine/Lamivudine/Efavirenz	1(3.7%)	15(13.9%)
Zidovudine/Lamivudine/Nevirapine	1(3.7%)	4(3.7%)
Didanosine/Abacavir/Kaletra	1(3.7)	0

4.3.2 Body Mass Index (BMI)

The mean BMI was significantly higher (23.53 Kg/M^2) in the hypertensive group than in the normotensive group (21.96 Kg/M^2) (p=0.03). Fourteen (40%) participants in the hypertensive group and 36 (21.8%) in the normotensive group had a BMI of ≥25 (Table 4.4). This difference was statistically significant (OR: 2.39; 95% CI: 1.03-5.52; p=0.04).

4.3.3 Age

The mean age was 43.3 years (range=22-70) in the hypertensive group and 37.4 (range=19-73) in the normotensive group. This was significantly higher by 6 years in the hypertensive group (p=0.001). When age was analyzed using different cut-offs, the age of ≥35 years was found to be a risk factor for hypertension with 29 (82.9%) of the hypertensives and 90 (54.5%) of the normotensives being aged ≥35 years (Table 4.4). Therefore, an age of ≥35 was significantly associated with hypertension (OR: 4.03; 95% CI: 1.49-11.47; p=0.004).

4.3.4 Family history of hypertension

There were 10 (28.6%) participants in the hypertensive group with a positive family history of hypertension from a first degree relative as compared to 20 (12.1%) in the normotensive group (Table 4.4). This difference was found to be statistically significant (OR: 2.90; 95% CI: 1.11-7.49; p=0.03).

4.3.5 Kidney disease

There were 3 (8.6%) participants in the hypertensive group with a history of having been diagnosed with a kidney disease as compared to 2 (1.2%) in the normotensive group (Table 4.4). Although these figures were small, the difference was found to be significant (p=0.04).

4.3.6 Diabetes

There was only 1 person with diabetes in each group, representing 2.9% and 0.6% in the hypertensive and normotensive groups, respectively (Table 4.4). This difference was not statistically significant (p=0.32).

4.3.7 Physical inactivity

There were 42.9% (15) participants in the hypertensive group that fell in the Minimal/Physical inactivity category compared to 26% (43) in the normotensive category (Table 4.4). However, this difference was not statistically significant (OR: 2.13; 95% CI: 0.94-4.82); p=0.07)

4.3.8 Smoking

Only 34 (17%) of all participants had ever smoked cigarettes, of whom 2 (5.7%) were in the hypertensive group and 32 (19.4%) in the normotensive group (Table 4.4). This difference was not statistically significant (OR: 0.25; 95% CI: 0.04-1.16; p= 0.09). Among the 34 participants who had ever smoked, only 7 (21%) were smokers at the time of the study, all of whom were in the normotensive group. There were no current smokers in the hypertensive group. Again, there was no significant difference between the numbers of current smokers in both groups (p=0.61).

Of the 34 participants who had ever smoked, 27(79%) had stopped smoking at the time of the study. Twenty two (81%) of ex-smokers had stopped smoking within the last 5 years mostly after they started attending the HIV clinic. There was no significant difference between the hypertensive and the normotensive groups as far as the period of stopping smoking was concerned.

Thirty (88%) of all-time smokers had smoked for more than six years with 21(62%) having smoked for more than 11 years. There was no significant difference regarding the duration of smoking in both groups. Of all time smokers, 26(76%) smoked less than 10 cigarettes per day. There was no significant difference between the two groups regarding the number of cigarettes smoked per day

4.3.9 Alcohol

Only 85 (42.5%) of all study participants had ever taken alcohol for a period exceeding three months. This comprised 14 (40%) in the hypertensive group and 71(43%)in the normotensive group (Table 4.4). However, only 2 (5.7%) of the hypertensives and 11 (6.7%) of the normotensives were taking alcohol at the time of the study. This difference was not statistically significant. For the 72 participants who had already stopped taking alcohol at the time of the study, 55 (76%) had done so within the last five years. In terms of the time they stopped taking alcohol, there was no significant difference between the hypertensive and the normotensive groups. Eighty five percent of participants who reported being current drinkers and 65% of ex-drinkers had taken alcohol for more than 6 years. Nonetheless, no significant difference was found between the two groups regarding the duration of taking alcohol.

Table 4.4 shows the bi-variate analysis results of the risk factors for hypertension

Table 4.4: Bivariate analysis of risk factors for Hypertension

	Hypertensives n=35	**Normotensives n=165**	**OR (95% CI)**	**P-value**
HIV infection				
Duration of known HIV Infection(month)	21.14±19.4	21.89±24.0		0.86
ARVs				
Any ARVs	27(77%)	108(65%)	1.78(0.71-4.58)	0.25
NRTI	27(77%)	108(65%)	1.78(0.71-4.58)	0.25
NNRTI	26(74%)	108(65%)	1.52(0.63-3.78)	0.42
Duration of ARVs use (months)	20.1±15.7	16.4±12.7		0.20
Male Gender	7(20%)	50(30%)	0.57(0.21-1.50)	0.31
Age Mean	43.3	37.4		**0.001**
≥35 years	29(82.9%)	90(54.5%)	4.03(1.49-11.47)	**0.004**
BMI Mean	23.53	21.96		**0.03**
≥25	14(40%)	36(21.8%)	2.39(1.03-5.52)	**0.04**
Family history of hypertension	10(28.6%)	20(12.1%)	2.90(1.11-7.49)	**0.03**
History of kidney disease	3(8.6%)	2(1.2%)	7.64(0.98-68.63)	**0.04**
Diabetes	1(2.9%)	1(0.6%)	4.82(0-181.72)	0.32
Smoking				
Ever smoked	2(5.7%)	32(19.4%)	0.25(0.04-1.16)	0.09
Current smoking	0(0%)	7(4.2%)	0(0-3.9)	0.60
Alcohol				
Ever taken alcohol	14(40%)	71(43%)	0.88(0.39-1.97)	0.88
Current alcohol	2(5.7%)	11(6.7%)	0.85	NS
Physical inactivity	15(42.9%)	43(26.1%)	2.13(0.94-4.82)	0.07

ARVs – Antiretroviral drugs. BMI – Body Mass index
NRTI – Nucleoside Reverse Transcriptase Inhibitors
NNRTI - Non-Nucleoside Reverse Transcriptase Inhibitors
NS – Not statistically significant

Only 4 risk factors were found to be significantly associated with hypertension in bi-variate analysis. These were:

- Age ≥35 years (OR: 4.03; 95%CI: 1.49-11.47; p-value =0.004)
- BMI ≥25 (OR: 2.39; 95% CI: 1.03-5.52; p-value =0.04)
- Family history of hypertension (OR: 2.90; 95% CI: 1.11-7.49; p-value=0.03)
- Kidney disease (OR: 7.64; 95% CI:0.98-68.63; p-value=0.04)

These 4 risk factors were further analyzed alongside others that had a p-value of ≤0.25 (Table 4.4) using unconditional logistical regression. In the final model, only three factors were found to be significant (Table 4.5).

Table 4.5: Multivariate analysis of risk factors for hypertension (Logistical regression model)

Risk Factor	OR (95% CI)	P-value
Age ≥35 years	4.55(1.72-12.03)	0.002
BMI ≥25	3.01(1.32-6.85)	0.009
Kidney disease	13.38(1.81-98.73)	0.01

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

Systemic hypertension was present in 18% of HIV infected adults in this study. This prevalence was higher than the 13% reported in Spain (Jerico *et al.,* 2005). Contrastingly, a higher prevalence of 29% in Germany (Jung *et al*., 2004), 26% in USA (Khalsa *et al.,* 2007) and 26% in Switzerland (Glass *et al*., 2006) has been reported. An Italian study that focused only on patients on antiretroviral drugs found a prevalence of 34.2% (Gazzaruso *et al.,* 2002). Therefore, the prevalence of hypertension in HIV infected patients seems to vary from country to country.

Although there were no similar published studies that were available in Africa, the prevalence found in this study was lower than that found in most developed countries. One possible explanation for this could be differences in lifestyles between people in Africa and those of developed countries. Some studies that have been done have found people from developed countries to be generally heavier than those in Africa. Consequently, their BMI is higher than that of most Africans and hence more at risk of hypertension (Cooper *et al.,* 1997).

Being overweight (BMI ≥25 Kg/m^2) was significantly associated with hypertension in this study (OR: 3.0; 95% CI=1.32-6.85; p-value=0.009. This suggests that those who had a BMI of 25 or more were three times more likely to have hypertension. The

mean BMI was also significantly higher in the hypertensive than in the normotensive group (23.53 Vs 21.96; p-value=0.03). These findings compare very well with other studies that have found an increased BMI to be a risk factor for hypertension in HIV (Jerico *et al.,* 2005; Thiebaut *et al.,* 2005; Khalsa *et al.,* 2007).

The hypertensive group was 6 years older than the normotensive group (p-value=0.001) with the risk of hypertension increasing with advanced age. These findings are in agreement with those of several other researchers that have found increasing age to be a risk factor for hypertension in HIV infected patients (Jerico *et al.,* 2005; Jung *et al.,* 2004 Khalsa *et al.,* 2007; Thiebaut *et al.,* 2005). When different ages were analyzed for the cut-off age, the age of ≥35 years was found to be significantly associated with hypertension (OR: 4.55; 95% CI: 1.72-12.03; p-value=0.002). This means that people who were 35 years or older were more than four times more likely to be hypertensive than those who were younger. Other researchers who have also found significant increase in blood pressure from the age of 35 years include Poulter *et al.* (1984) and Wolf-Maier *et al.* (2003)

Having had a kidney disease was significantly associated with hypertension in HIV infected persons (p-value=0.01). This finding is not surprising as kidney disease is one of the major causes of secondary hypertension with chronic glomerulonephritis, and chronic pyelonephritis being major causes in developing countries. However, this

finding should be interpreted with care as this study was a cross-sectional study and did not try to find out whether having kidney disease preceded hypertension or not.

Family history of hypertension from a first degree relative was found to be associated with hypertension in bi-variate analysis but not in multivariate analysis (logistical regression). Considering that several studies have found hypertension to be hereditary, it is possible that the information obtained in this study was not complete and hence the marginal results obtained.

There was no difference in the duration of known HIV infection between the hypertensive and the normotensive groups (p-value=0.86). Although the actual time of infection could not be established, the reported duration of HIV infection was therefore not associated with hypertension in this study. These findings are in agreement with several other studies that have not found any association between duration of HIV infection and hypertension (Khalsa *et al.,* 2007; Jung *et al.,* 2004).

Being on antiretroviral drugs was not associated with hypertension in this study (p value=0.25). Specifically, use of NRTIs (p-value=0.25) and NNRTIs (p-value= 0.42) was also not associated with hypertension. These findings are in agreement with results from several other studies done elsewhere which did not find any association between the use of antiretroviral drugs and hypertension ((Jerico *et al.,* 2005; Jung *et al.,* 2004; Khalsa *et al.,* 2007; Bergersen *et al.,* 2003). However, 99% of those on

antiretroviral drugs were on NRTIs and NNRTIs combination which is the current 1st line regimen in Kenya. It was therefore not possible to assess whether PIs are associated with hypertension or not and cannot argue against the findings of those studies that have found an association between some PIs and hypertension (Cattelan, *et al.*, 2001; Chow *et al.*, 2003).

The hypertensive and the normotensive groups were comparable in terms of other factors including gender, education, occupation, income, alcohol, smoking and physical activity.

5.2 Conclusions

5.2.1 Prevalence of hypertension among HIV positive patients

Hypertension among HIV patients is not uncommon in Kenya. The prevalence was found to be 18% (Approximately 1 in 5 people) in this study.

5.2.2 Risk factors for hypertension among HIV positive patients

Older age, being overweight and having had kidney disease were risk factors significantly associated with hypertension among HIV infected patients. These factors are similar to those found in the general population.

5.3 Recommendations

5.3.1 Routine screening of hypertension

There should be routine screening of hypertension in the HIV clinics. This will enable early detection, control and treatment of these patients.

5.3.2 Health education

As in the general population, there is need to educate patients on the various the risk factors for hypertension so that they can prevent or delay the onset of hypertension. Specifically, patients need to be educated on how to deal with the three risk factors that were associated with hypertension in this study i.e. being overweight, older age and kidney disease.

5.3.3 Further research

More studies should be done to compare the prevalence of hypertension in both the HIV positive and negative groups as this was not done in this study.

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APPENDICES

Appendix 1 - Questionnaire

Questionnaire

Questionnaire number _____ Date of interview_____

Interviewer's name _____

Details of person being interviewed

Province_____ District_____Location_____
Sub location_____

Demographic and Socio-economic information	
1.	Age in years_____
2.	Sex [ ] Male [ ] Female
3.	Highest level of education [ ]None [ ]Lower primary [ ]Upper primary [ ]Secondary [ ]College/University
4.	Marital status [ ]Single [ ]Married/Cohabiting [ ]Separated/Divorced [ ]Widowed
5.	Occupation [ ] Unemployed [ ] Peasant farmer/small scale business e.g. small shop, hawker [ ] Commercial farming/Large scale business e.g. wholesaler/distributor [ ] Employed by others e.g. by government or private firms [ ] Student [ ] Others (specify) _____
6.	Income a) Average monthly *personal income* (Ksh) [ ]<5,000 [ ]5,000-10,000 [ ]11,000-15,000 [ ]16,000-20,000 [ ]21,000-40,000 [ ]>40,000 b)Average monthly *family income* (Ksh) [ ]<5,000 [ ]5,000-10,000 [ ]11,000-15,000 [ ]16,000-20,000

	[ ]21,000-40,000 [ ]>40,000
Risk factors for hypertension	
Family history of hypertension and other illnesses -	
7.	i) Do you suffer from high blood pressure or have you ever been told you have high blood pressure since you were diagnosed with HIV? [ ] Yes [ ] No
	ii) Is there any member of your family (blood related) who has ever been diagnosed with high blood pressure? (e.g. your father, mother, brothers, sisters, grandparents) [ ] Yes [ ] No [ ] don't know
8.	i) Have you ever been diagnosed with diabetes? [ ] Yes [ ] No ii) If yes, when_____
9.	i) Have you ever been diagnosed with kidney disease? [ ] Yes [ ] No ii) If yes when_____
Smoking	
10.	a) Have you ever been a smoker in your life? [ ] Yes [ ] No
	b) If yes, are you a current smoker? [ ] Yes [ ] No
For *ex-smokers* only (Question 10c)	

	c) i) How long ago did you stop smoking? [ ] <1 year ago [ ]1-5 years ago [ ]6-10 years ago [ ]11-20years ago [ ] >20 years ago
	ii) For how long did you smoke? [ ] <1 year [ ]1-5 years [ ]6-10 years [ ]11-20 years [ ] >20 years
	iii) How many sticks did you smoke on average per day? [ ] <5 [ ] 5-10 [ ] 11-15 [ ] 16-20 [ ] >20
For *current smokers* only (Question 10d)	
d)	i) How long have you smoked? [ ] <1 year [ ]1-5 years [ ]6-10 years [ ]11-20 years [ ] >20 years
	ii) How many sticks do you smoke per day? [ ] <5 [ ] 5-10 [ ] 11-15 [ ] 16-20 [ ] >20
Alcohol	
11.	a) Have you ever taken alcohol [ ] Yes [ ] No
	b) If yes, do you still take alcohol? [ ] Yes [ ] No
For *Ex-drinkers* only (Question 11c) - Tick or Answer as appropriate	
	c) i) How long ago did you stop drinking [ ] <1 year [ ] 1-5 years [ ] 6-10 years [ ] >10 years
	ii) How long did you drink alcohol? [ ] <1 year [ ] 1-5 years [ ] 6-10 years [ ] 11-20 years [ ] >20 years

	iii) What alcohol type did you usually take e.g. Tusker, pilsner, allsops, vodka, whisky, wine, keroche, Muratina, Chang'aa, busaa etc _____
	iv) How much did you drink per week/month (bottles, glasses, milliliters, tots etc?) Week_____ Month_____
For *Current alcohol drinkers* only (Question 11d)	
	d) i) How long have you drunk alcohol? [ ] <1 year [ ] 1-5 years [ ] 6-10 years [ ] 11-20 years [ ] >20 years
	ii) What alcohol type do you usually take e.g. Tusker, pilsner, allsops, vodka, whisky, wine, keroche, Muratina, Chang'aa, busaa etc ----------
	iii) How much do you drink per week/month (bottles, glasses, milliliters, tots etc?) Week_____ Month_____
Physical activity	
12.	a) What do you do as your daily occupational activity (e.g. farming, carpentry, teaching, shopkeeper, etc)? _____
	b) How do you usually get to your area of work? [ ]It is within my compound/Shamba [ ]Walking [ ] Cycling [ ] Public transport [ ] Personal car
	c) How long do you usually walk per day on average? [ ] < ½ km [ ] ½-1km [ ] 1km – 3km [ ] 3 - 5km [ ] >5km
	d) Do you do any of the following activities? i) *Gardening/Tilling* the land ……..… [ ] Y [ ] N How many days per week (or per month) _____

	How many minutes/hours per day on average_____ ii) *Cycling* …… [ ] Y [ ] N How many days per week (or per month) _____ How many minutes/hours per day on average_____ iii) *Sporting* (e.g. running, jogging, swimming, soccer)…[ ] Y [ ] N How many days per week (or per month) _____ How many minutes/hours per day on average_____
	e) What do you do in your leisure time as part of your recreation activity? How many days per week? Activity Days per week or month _____ _____ _____ _____ _____ _____
Diet	
13.	a) i) Which of the following green vegetables have you eaten in the last 7 days? Tick as appropriate √ [ ]Sukumawiki [ ]Spinach [ ]Cabbage [ ]Terere [ ]Managu [ ]Thabai Others(specify)_____ ii) In summary, how many days in the last 7 days have you taken green vegetables? _____
	b) How many of these fruits have you eaten in the last 7 days? i) Bananas _____ ii) Oranges_____iii) Pineapple_____iv) Passion_____ v) Avocado_____ vi) Pawpaw_____vii) Watermelon_____ Others(specify)_____
	c) i)) How much tea(with milk) do you take per day_____cups ii)How much plain milk(fresh+lala) do you take per day?_____glasses iii) Source of milk [ ] Shop (Packaged milk) [ ] My cows/farm [ ] Vendors

	d) Where do you usually get your maize flour from? [ ] Posho mill(unprocessed flour) [ ] Shop (Processed flour)
HIV illness and ARVs	
14.	a) How long ago is it since you were diagnosed with HIV? Years_____ Months_____
	b) i) Are you on ARVs [ ] Y [ ] N ii) If yes, how long? Years_____ Months_____
	c) If on ARVs, which of the following are you on (tick as appropriate)? i)*Nucleoside Reverse Transcriptase Inhibitors(NRTIs*) [ ] Stavudine(d4T) [ ] Lamivudine(3TC) [ ] Zidovudine(AZT) [ ] Didanosine(ddi) [ ] Abacavir(ABV) [ ] Zalcitabine (ddc) ii) *Non-Nucleoside Reverse Transcriptase Inhibitors(NNRTIs)* [ ] Nevirapine (NVP) [ ] Efavirenz(EFV) [ ] Delavirdine(DLV) iii) *Protease inhibitor(PIs)* [ ] Lopinavir/Ritonavir(NLF) [ ] Indinavir [ ] Ritonavir [ ] Nelfinavir [ ] Saquinavir
Measurements	
15.	*a)Blood Pressure (mm Hg)* • Blood pressure reading 1 Systolic_____ Diastolic_____ • Blood pressure reading 2 Systolic_____ Diastolic_____ (After 5 minutes)

	(Average of the above) Systolic_____ Diastolic_____
	b) Height (in Meters, without shoes) _____M
	c) *Weight* in Kilogrammes (light clothes only, no shoes) _____Kg
	d) *Random Blood Sugar* (RBS) _____mmol/l

******END******

Appendix 2 – Informed Consent Form

Informed Consent

Study: Prevalence and Risk factors for hypertension in HIV + patients

Introduction
My name is Dr James W. Njeru. I work for the Ministry of Health. I am conducting a study on the prevalence of hypertension (high blood pressure) and its associated risk factors among HIV+ patients. I will have some research assistants to help me.

Purpose of the study
This study will help us to estimate the burden and risk factors for hypertension in this clinic and hence help us in better management of the patients.

Study design/Procedure
This is a cross-sectional study and we are recruiting participants for this study from this clinic through systematic random sampling of the clinic attendants as they come to see the clinician. That means that anybody can be selected depending on their assigned number. An interviewer administered questionnaire will be used to collect information from the participants. In addition their height, weight, blood pressure and blood sugar will be taken. This should take no more than 30 minutes.

Benefits
The participants will be able to have their blood pressure, blood sugar and Basal Mass Index (BMI) taken. Appropriate advice and management will be given at the end of the interview, if necessary.

Risks
There are no anticipated risks in this study

Voluntary Participation
This study is absolutely voluntary and participants can decide to decline participation or can abandon it half way if they feel uncomfortable with it.

Confidentiality
The information obtained will be treated with confidentiality and will not be shared with any other unauthorized people. In addition, participant's names will not be taken.

Contact
In case of any questions or clarifications please contact the principal investigator below:

Dr James W. Njeru
Ministry of Health /JKUAT
Tel 0727 764 164
Email: iannjeru75@yahoo.com

Consent Form

I declare that the content of the informed consent has been read and explained to me in a way that i can understand. I do hereby voluntarily consent to participate in this study

Name of Participant_____

Signature/Thumb print_____

Interviewer's name_____

Interviewer's signature_____

Witness_____

Appendix 3 – Research authorization letter (Ministry of Higher Education, Science and Technology)

REPUBLIC OF KENYA

MINISTRY OF HIGHER EDUCATION SCIENCE & TECHNOLOGY

Telegrams: "SCIENCE TEC", Nairobi
Telephone: 02-318581
E-Mail:ps@scienceandtechnology.go.ke

JOGOO HOUSE "B"
HARAMBEE AVENUE,
P.O. Box 9583-00200
NAIROBI

When Replying please quote
Ref. MOHEST 13/001/ 38 C/535/2

5th September 2008

Dr.James Ian Njeru
Jomo Kenya University of Agriculture
and Technology
NAIROBI

RE: RESEARCH AUTHORIZATION

Following your application for authority to carry out research on, ***'Prevalence and Associated Risk Factors for Hypertension in HIV Positive Patients attending Comprehensive Care Centre at Thika District Hospital,***

I am pleased to inform you that you have been authorized to undertake research in Thika District Hospital for a period ending 30th July 2009.

You are advised to report to the District Commissioner and the District Education Officer Medical Officer of Health Thika District before embarking on your research.

On completion, you are expected to submit two copies of your research report to this office.

M. GATOBU
FOR: PERMANENT SECRETARY

Copy to:

The District Commissioner
THIKA DISTRICT

The District Medical Officer of Health
THIKA DISTRICT

Appendix 4 – Request to conduct study at Thika District Hospital

Dr James Ian Njeru
Box 69
Muranga

10th September, 2008

To
Medical Superintendent,
Thika District Hospital,

Dear Sir,

Re: Request to conduct research at Thika District Hospital

I am a doctor working for the Ministry of Health and currently a student at the Jomo Kenyatta University of Agriculture and Technology pursuing Master of Science in Applied Epidemiology. I would like to request for permission to conduct research for my thesis at the Comprehensive Care Centre in your hospital.

My thesis is entitled "*Prevalence and Risk factors for hypertension in HIV positive patients attending Comprehensive Care Centre at Thika District Hospital*". The study will be a cross-sectional study and data collection will take approximately 3-4 months.

Attached please find authorization letter from the Ministry of Higher Education, Science and Technology

Yours truly,

James Ian Njeru

CC

District Medical Officer of Health, Thika

District Education Officer, Thika

District Commissioner, Thika