COMPARATIVE RANDOM BLOOD GLUCOSE AND BLOOD PRESSURE LEVELS OF PEOPLE IN URBAN AND RURAL AREAS OF SOUTHERN KADUNA, NIGERIA

BY

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MAY, 2015.

DECLARATION

I declare that the work in this thesis entitled 'Comparative random blood glucose and blood pressure levels of people in urban and rural areas of southern Kaduna, Nigeria' has been carried out by me in the Department of Biological Sciences under the supervisions of Dr. C.E. Mbah and Dr. E. Kogi. The information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this thesis was previously presented for another degree or diploma at this or any other Institution.

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CERTIFICATION

This thesis entitled "COMPARATIVE RANDOM BLOOD GLUCOSE AND BLOOD PRESSURE LEVELS OF PEOPLE IN URBAN AND RURAL AREAS OF SOUTHERN KADUNA, NIGERIA" by Deborah Olufunke, AKINOLA, meets the regulations governing the award of the degree of Master of Science of the Ahmadu Bello University, and is approved for its contribution to knowledge and literary presentation.

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DEDICATION

This work is dedicated to the Almighty God, and the entire members of my family. I love you all.

ABSTRACT

Diabetes mellitus and hypertension are interrelated diseases that strongly predispose an individual to artherosclerotic cardiovascular disease. The prevalence of Diabetes mellitus and hypertension is rising in Nigeria and their complications present an immense public health burden. The study determined and compared the random blood glucose and blood pressure levels of people living in the urban and rural areas of Southern Kaduna. A total of 1500 volunteers that were 18 years of age and above were sampled. One thousand (1000) were from ten urban settlements in Southern Kaduna while five hundred (500) volunteers were from ten rural villages in Southern Kaduna. The blood glucose levels were measured using advocate blood glucose monitoring system, the blood pressure levels were measured using advocate automatic memory blood pressure monitor model, weight of individuals were measured using Camry mechanical scale and heights were measured using a graduated rod. There was significant difference in mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and random blood glucose (RBG) levels in relation to urban settlements compared to rural settlements, pensioners compared to other occupations, the elderly compared to other age groups, those who drink alcohol and smoke compared to those who do not drink alcohol nor smoke, and the obese individuals compared to other BMI groups, but the difference in mean SBP, DBP and RBG was not significant ($p > 0.05$) in relation to gender. Hypertension was more prevalent in male (18.6%) compared to female (17.1%); in urban residents (26.3%) compared to rural residents (0.6%); in pensioners (75.0%) compared to other occupations; in elderly (62.5%) compared to the young (14.1%); in smokers (27.3%) compared to non –smokers (17.7%); in alcoholics (28.6%) compared to non- alcoholics (17.5%); obese individuals (55.5%) compared to normal weight individuals (10.9%). Life style modifications like regular exercise, abstinence from smoking and drinking of alcohol must be

promoted and control measures that will lead to high reduction in blood glucose and blood pressure levels in the groups that are at risk should be taken.

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ABREVIATIONS

GLP-1	- Glucagon- like peptide 1
GIP	- Glucose- dependent insulinotropic peptide
NIDDM	- Non- insulin dependent diabetes mellitus
IDF Diabetes Atlas	- International diabetes federation diabetes atlas
NPC	- National Population Commission
WHO	- World Health Organization
NDCs	- Non Communicable Diseases
BMI	- Body Mass Index
PACAP	- Pituitary adenylate cyclase- activating polypeptide
VLDL	- Very low density lipoprptein
SHBG	- Sex- hormone binding globulin
NO	- Nitric oxide
NADPH	- Nicotinamide adenine dinucleotide phosphate
eNOS	- Endothelial enzyme nitric oxide synthase
PAI- 1	-Plasminogen activator inhibitor 1
MAP	- Mitogen activated protein
TNFα	- Tumor necrosis factor alpha
PCOS	- Polycystic ovarian syndrome
OSA	- Obstructive sleep apnoea
T2DM	- Type 2 diabetes mellitus
MODY	- Maturity onset diabetes of the young
NACD	- Nigerian arts/ culture and directory project
NHBPEP	- National High Blood Pressure Education Program

CHAPTER ONE

1.0 INTRODUCTION

The final products of carbohydrate digestion in the alimentary tract are almost entirely glucose, fructose, and galactose with glucose representing, an average 80 percent of these. After absorption from the intestinal tract, much of the fructose and almost all the galactose are rapidly converted into glucose in the liver. Therefore, little fructose and galactose are present in the circulating blood. Glucose thus becomes the final common pathway for the transport of almost all carbohydrates to the tissue cells (Guyton and Hall,2006)

Glucose is a small, polar and, thus, water- soluble monosaccharide. Its importance greatly out- weighs its size for two reasons- the first is that, it has multiple metabolic paths and secondly, neurons have absolute nutritional requirement for a continuous supply of it; in its absence they die. Thus homoeostatic regulation of the concentration of extracellular fluid glucose is vital. It is achieved primarily by the actions of the hormones secreted by the pancreas – insulin and glucagon (Nussey and Whitehead, 2001) and other glucoregulatory hormones which are amylin, glucagon- like peptide 1(GLP-1), glucose-dependent insulinotropic peptide (GIP), epinephrine, cortisol, and growth hormone (Aronoff*et al.*,2004).Plasma glucose concentration is a function of the rate of glucose entering the circulation (glucose appearance) balanced by the rate of glucose removal from the circulation (glucose disappearance). Circulating glucose is derived from three sources: intestinal absorption during the fed state, glycogenolysis – the breakdown of glycogen which is the polymerized storage form glucose, and gluconeogenesis – the formation of glucose primarily from lactate and amino acids during the fasting state. The

major determinant of how quickly glucose appears in the circulation during the fed state is the rate of gastric emptying (Aronoff*et al*., 2004)

Insulin is the important hormone that is concerned with regulation of carbohydrate metabolism and blood sugar level (Aronoff*et al*.,) It is also concerned with metabolism of proteins and fats. Insulin decreases blood sugar level by facilitating transport and uptake of glucose by the cells, increasing peripheral utilization of glucose, increasing conversion of glucose into glycogen in liver and muscle, and inhibiting glycogenolysis and gluconeogenesis. Actions of glucagon are antagonistic to those of insulin. It increases the blood sugar level, increases the peripheral utilization of lipids and facilitates the conversion of proteins to glucose (Sembulingam&Sembulingam, 2006)

The underlying metabolic causes of type 2 -diabetes are the combination of impairment in insulin-mediated glucose disposal (insulin resistance) and defective secretion of insulin by pancreatic β-cells. Insulin resistance develops from obesity and physical inactivity, acting on a substrate of genetic susceptibility (Weir and Bonner- Weir, 2004). Insulin resistance typically precedes the onset of type 2 diabetes and is commonly accompanied by other cardiovascular risk factors like dyslipidemia, hypertension, and prothrombotic factors (Rao, 2001).

Hypertension is the new era pandemic which is the leading cause of mortality in the world and is ranked third as a cause of disability- adjusted life years (Ezatti *et al.*, 2000). Hypertension has become an important worldwide public- health challenge because of its high prevalence and concomitant risks of coronary artery disease, congestive heart failure, stroke, end- stage renal disease, dementia and blindness (Kearney *etal*., 2005). People with hypertension possess two fold higher risk of developing coronary artery

disease, four time higher risk of congestive heart failure and seven times higher risk of cerebrovascular disease compared to normotensive people (Sowers *etal.*,2001)

Diabetes mellitus and Hypertension are interrelated diseases that strongly predispose an individual to artherosclerotic cardiovascular disease (Sowers*et al.*, 2001). Hypertension is about twice as frequent in individuals with diabetes as in those without (Sowers *et al.*, 2001). Life style and genetic factors are important factors contributing to both hypertension and diabetes mellitus(Zhou *et al., 2014*). The prevalence of coexisting hypertension and diabetes mellitus appears to be increasing in industrialized nations because populations are aging and both hypertension and non- insulin dependent diabetes (NIDDM) incidence increases with age. Data obtained from death certificates show that hypertensive disease has been implicated in 4.4% of deaths coded to diabetes, and diabetes was involved in 10% of deaths coded to hypertensive disease (Sowers *et al., 2001*; Zhou *et al., 2014*). Indeed, an estimated 35% to 75% of diabetic cardiovascular and renal complications can be attributed to hypertension (Sowers *et al.*, 2001; Zhou *et al., 2014*). Hypertension also contributes to diabetic retinopathy, which is the leading cause of newly diagnosed blindness in the United States (NHBPEP, 1994). For all these reasons, hypertension and diabetes should be recognized and treated early and aggressively (Levin *et al*., 2015)

Diabetes mellitus does not usually diminish over time despite standard treatment. It is a life long illness that generally worsens with time and often leads to debilitating complications including cardiovascular disease, neuropathy retinopathy and nephropathy (Corkey, 2012)

Diabetes mellitus is now one of the most common non -communicable diseases globally and which for most countries it is the fourth or fifth leading cause of death in most high in-come countries and there is substantial evidence that it is epidemic in many low- and middle- income countries (IDF Diabetes Atlas,2010)

In Nigeria, with over 140 million people (NPC, 2009), an estimated six million people have full blown diabetes mellitus (Sunny, 2014) with prevalence varying from 0.65% in rural Mangu (North) to 11% in urban Lagos (South) and data from WHO suggests that Nigeria has the largest number of people living with diabetes mellitus in Africa (Sunny and Young, 2011). This disease has reached an epidemic proportion in Nigeria according to recent publications and has resulted to premature death of thousands of Nigerians in addition to permanent disabilities like blindness, amputation of limbs, impotence, kidney failures, still births, and pregnancy wastages (Sunny, 2014)

The prevalence of hypertension is highest in the African region at 46% of adults aged 25 and above, while the lowest prevalence at 35% is found in the Americas (WHO, 2013). In Nigeria the prevalence of hypertension is 22.5% (Ogah and Okpechi,2012), about 57 million people are estimated to be hypertensive with many still undiagnosed (Gachomo, 2013)

1.1 Research Problem

Changes in the physical environment and life style which took place in the developed countries in the latter part of 19^{th} and early 20^{th} centuries resulting in a shift from infectious diseases to non- communicable diseases (NCDs) as the major causes of morbidity and mortality. This situation is now being replicated in many developing countries, Southern Kaduna in Nigeria included, as previously traditional communities

adopt a modern way of life. Rapid social, cultural and environmental changes resulting from urbanization, industrialization and migration have been accompanied by major changes in nutrition, physical activity and other life style habits in populations (Zhou*et al.*, 2014).

These unhealthy lifestyles are associated with common modifiable risk factors for chronic diseases such as hypertension, diabetes mellitus, dyslipidaemia and obesity (Sowers *et al.,* 2001; Zhou *et al.,* 2014).It is expected that by 2020 in developing countries, non-communicable diseases will account for 69% of all deaths, with cardiovascular diseases in the lead (Boutayeb and Boutayeb, 2005). The prevalence of diabetes mellitus will almost double in the next 25 years and at least 75% of those affected will be in developing countries. The burden of disease will be worse in these countries, as the majority of sufferers are expected to be in their most productive years, under the age of sixty, of lower socioeconomic status and to suffer from severe disease of premature onset (IDF, 2011).

Further, because of weak health systems and the fact that these co-mobidities rarely cause symptoms in the early stage; the number of people with these co-mobidities who are undiagnosed, untreated and uncontrolled are higher in low and medium countries compared to high income countries (WHO, 2013)

This problem cuts across people of different ages, gender, socio- economic status, socio-cultural back ground and weight.

1.2 Justification

There is paucity of data on diabetes mellitus and hypertension prevalence in many parts of Kaduna state. Thus, burden of diabetes mellitus and hypertension in this population might be under estimated and might leave the disease undiagnosed and untreated. Estimating the prevalence of diabetes mellitus and hypertension and their risk factors in both the urban and rural populations is very crucial as this forms the basis for planning of primary and secondary prevention of diabetes mellitus and hypertension. Hence this field based cross sectional study was undertaken.

1.3 Aim

This research work aims at determining and comparing the random blood glucose and blood pressure levels of people living in the urban and rural areas of Southern Kaduna.

1.4 Objectives

1. To find the relationship between systolic and diastolic blood pressure levels and random blood glucose levels with gender, residence, occupation, age group, habit, and BMI.

2. To find the relationship between blood pressure status (Normal, Pre-hypertensive, Hypertensive) with gender, residence, occupation, age group, habit and BMI.

1.5 Hypotheses

1. Systolic and diastolic blood pressure levels and random blood glucose levels do not vary with gender, residence, occupation, age group, habit, and Body Mass Index (BMI)

2. Blood pressure status (Normotensive, Pre-hypertensive, and Hypertensive) do not correlate with gender, residence, occupation, age group habit and BMI.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Historical Background

The history of diabetes started in approximately 1550BC (Nwaneri, 2015) when an Egyptian papyrus mentions a rare disease that causes the patient to lose weight rapidly and urinate frequently. The term "diabetes" was first coined by Araetus of Cappodocia 81-133AD. Later, the word mellitus (honey sweet) was added by Thomas Willis in 1675 after rediscovering the sweetness of urine and blood of patients which was first noticed by the ancient Indians. It was only in 1776 that Dobson for the first time confirmed the presence of excess sugar in urine and blood as a cause of their sweetness. In modern time, the history of diabetes coincided with the emergence of experimental medicine. An important milestone in the history of diabetes is the establishment of the role of the liver in glycogenesis, and the concept that diabetes is due to excess glucose production by Claude Bernard in 1857. The role of the pancreas in pathogenesis of diabetes was discovered byMering and Minkowski in 1889. Later, this discovery constituted the basis of insulin isolation and clinical use by Banting and Best in 1921(Ahmed,2002).

Subsequently, diabetes mellitus was viewed as a mono-hormonal disorder characterized by absolute or relative insulin deficiency. The recent discovery of additional hormones with glucoregulatory actions has expanded the understanding of how a variety of different hormones contribute to glucose homeostasis. In the 1950s, glucagon was characterized as a major stimulus of hepatic glucose production(Aronoff*et al.,* 2004). This discovery led to a better understanding of the interplay between insulin and

glucagon, thus leading to a bi-hormonal definition of diabetes. Subsequently, the discovery of a second β-cell hormone, amylin, was first reported in 1987. Amylin was determined to have a role that complemented that of insulin, and, like insulin, was found to be deficient in people with diabetes(Aronoff *etal.*, 2004). This more recent development led to a view of glucose homeostasis involving multiple pancreatic hormones(Aronoff*et al.*, 2004).

In the mid-1970s, several gut hormones were identified. One of these, an incretin hormone, glucagon-like peptide-1 (GLP-1), was recognized as another important contributor to the maintenance of glucose homeostasis(Dunning *etal.*, 2005). Based on current understanding, glucose homeostasis is governed by the interplay of insulin, glucagon, amylin, and incretin hormones.

The Greek and Eygptian physicians first theorized that blood circulates through the body more than 2000 years ago but it took a while to prove that blood was driven by pressure (Giuliani *etal.*, 1991). The Egyptian Ebers Papyrus held the concept that all the limbs possess its' vessel, so that the heart speaks from the vessels of every limbs. The first person to measure the pressure of blood was Sir Stephen Hales of Teddington near London. In 1836, English physician Richard Bright observed the effect of hypertension in chronic renal disease patients. The first recording of human blood pressure came in 1847 when Carl Ludwig inserted a catheter into a patient's artery and hooked the catheter to a Kymograph (Garrison, 1929). In 1881, Samuel Karl Ritterr Von Basch invented the sphygmomanometer, which used a water- filled bag to multiply the arterial pulse (Laragh and Brenna, 1995). With this device, he recorded the blood systolic pressure on a thermometer-shaped device. In 1896, Scipine Riva Roche improved on this invention

with a mercury filled sphygmomanometer that used an inflatable cuff on the upper arm to constrict the brachial artery so that blood pressure could be measured (Laragh and Brenna, 1995). The modern sphygmomanometer is based on this prototype. In 1905, Nikolai Korotkoff was the first scientist to observed that arteries made sounds at certain points when the cuff was been inflated and deflated and theorized that these were important. He developed a method to measure the diastolic pressure by the sound arteries made during testing (Sleight and Freis, 1982). This lead to the adoption of the 120 (systolic) over 80 (diastolic) standards for normal blood pressure. While physicians at the time believed that it was unhealthy for blood pressure to be too high or too low, it wasn't until the 1950s that the danger of high blood pressure and its role in stroke and heart attack was fully understood (WHO, 1996)

Diabetes mellitus and hypertension are two non-communicablediseases that frequently co-exist, they are officially considered to be co-mobidities (diseases likely to be present in the same patient) because they tend to share certain physiological traits and common sets of risk factors like body mass, diet and activity level (Weber, 2009). Several studies haveshown that raised blood pressure is common amongpeople with diabetes than in the general population(Sowers *et al.,* 2001; Balogun and Salako, 2011).

Both diseases are independent risk factors forcardiovascular disease (CVD), and when they co-existthey multiply morbidity and mortality of CVD(Gress *etal*., 2000).Hypertension in diabetes accelerates development andprogression of microvascular and macrovascularcomplications in patients with diabetes(Adler *etal.*, 2000).

2.2 Hormonal Regulation of Metabolism

The absorption of energy from the intestine is not continuous; it rises to high levels during a 4- hour period following each meal (the absorptive state) and tapers towards zero between meals, after each absorptive state is concluded (the post absorptive state). The post absorptive state occurs during fasting. Despite this fluctuation, the plasma concentration of glucose and other energy substrates does not remain high during periods of absorption and does not normally fall below a certain level during periods of fasting. During the absorption of digestion products from the intestine, energy substrates are removed from the blood and deposited as energy reserves from which withdrawals can be made during times of fasting. This ensures an adequate plasma concentration of energy substrates to sustain tissue metabolism at all times (Fox, 1999).

The rate of deposit and withdrawal of energy substrates into and from the energy reserves and the conversion of one type of energy substrate into another are regulated by the actions of hormones. The balance between anabolism and catabolism is determined by the antagonistic effects of insulin, glucagon, growth hormone, and thyroxine (Fox, 1999)

2.3 Glucoregulatory Hormones

Glucoregulatory hormonesinclude insulin, glucagon, amylin, glucagon- like polypeptide-1 (GLP-1), glucose-dependent insulinotropic peptide (GIP), epinephrine, cortisol, and growth hormone. Insulin and amylin are derived from the β-cells and glucagon from the α-cells of the pancreas, while GLP-1 and GIP from the L-cells of the intestine (Aronoff*et al*.**,** 2004)

2.3.1 β-Cell Hormones

2.3.1.1 *Insulin*

Until recently, insulin was the only pancreatic β-cell hormone known to lower blood glucose concentration (Aronoff*et al.,* 2004). Insulin is a small protein composed of two polypeptide chains containing 51 amino acids and is a key anabolic hormone that is secreted in response to increased blood glucose and amino acids following ingestion of a meal. Like many hormones, insulin exerts its actions through binding to specific receptors present on many cells of the body, including fat, liver, and muscle cells (Sembulingam and Sembulingam, 2006). The primary action of insulin is to stimulate glucose disappearance(Guyton and Hall, 2006).

Insulin helps control postprandial glucose by sending signals to insulin-sensitive peripheral tissues, primarily skeletal muscle, to increase their uptake of glucose(Guyton and Hall, 2006), acts on the liver to promote glycogenesis and inhibits glucagon secretion from pancreatic α-cells, thus signalling the liver to stop producing glucose via glycogenolysis and gluconeogenesis. Other actions of insulin include the stimulation of fat synthesis, promotion of triglyceride storage in fat cells, promotion of protein synthesis in the liver and muscle, and proliferation of cell growth (Nussey and whitehead, 2001).

Insulin action is carefully regulated in response to circulating glucose concentrations. Insulin is not secreted if the blood glucose concentration is ≤ 3.3 mmol/l, but is secreted in increasing amounts as glucose concentrations increase beyond this threshold(Guyton and Hall, 2006). Postprandially, the secretion of insulin occurs in two phases: an initial rapid release of preformed insulin, followed by increased insulin synthesis and release in

response to blood glucose. Long-term release of insulin occurs if glucose concentrations remain high(Guyton and Hall,2006).

While glucose is the most potent stimulus of insulin, other factors stimulate insulin secretion. These additional stimuli include increased plasma concentrations of some amino acids, especially arginine, leucine, and lysine; GLP-1 and GIP released from the gut following a meal; (Drucker, 2001;Sembulingam and Sembulngam, 2006) acetylcholine, and pituitary adenylatecyclase-activating polypeptide (PACAP), and other counter regulatory hormones like glucagon, glucocorticoides and catecholamines (Bratanova -Tochkova *et al*.,2002).

2.3.1.2 *Amylin*

Amylin was isolated from pancreatic amyloid deposits in the islets of Langerhans and was first reported in the literature in 1987(Dunning*etal*., 2005). Amylin, a 37–amino acid peptide, is a neuroendocrine hormone co-expressed and co-secreted with insulin by pancreatic β-cells in response to nutrient stimuli(Dunning *etal*., 2005;Guyton and Hall, 2006). When secreted by the pancreas, the insulin-to-amylin molar ratio in the portal circulation is approximately 50:1. Because of hepatic extraction of insulin, this ratio falls to ~ 20:1 in the peripheral circulation (Weyer *etal*., 2001).

Amylin complements the effects of insulin on circulating glucose concentration by suppressing post-prandial glucagon secretion(Weyer*et al.*, 2001) thereby decreasing glucagon-stimulated hepatic glucose output following nutrient ingestion,and slows the rate of gastric emptying, thus, the rate at which nutrients are delivered from the stomach to the small intestine for absorption(Samson *etal.,* 2000). In addition to its effects on

glucagon secretion and the rate of gastric emptying, amylin dose-dependently reduces food intake and body weight in animal models. The suppression of post-prandial glucagon secretion is postulated to be centrally mediated via efferent vagal signals. Importantly, amylin does not suppress glucagon secretion during insulin-induced hypoglycemia(Weyer*etal*., 2001)

2.3.2 α-Cell hormone

2.3.2.1 *Glucagon*

Glucagon is a key catabolic hormone consisting of 29 amino acids that is secreted from pancreatic α-cells, described by Roger Unger in the 1950s,and characterized as opposing the effects of insulin(Ivan *et al*., 2008). Glucagon plays a major role in sustaining plasma glucose during fasting conditions by stimulating hepatic glucose production.

Hepatic glucose production, which is primarily regulated by glucagon, maintains basal blood glucose concentrations within a normal range during the fasting state. When plasma glucose level falls below the normal range, glucagon secretion increases, resulting in hepatic glucose production and return of plasma glucose to the normal range (Ivan*et al.*, 2008). This endogenous source of glucose is not needed during and immediately following a meal and glucagon secretion is suppressed. When coupled with insulin's direct effect on the liver, glucagon suppression results in a near-total suppression of hepatic glucose output (Weyer*et al* 2001)

2.3.3 Incretin hormones

2.3.3.1 *GLP-1 and GIP*

By the late 1960s,Perley and Kipnis demonstrated that ingested food caused a more potent release of insulin than glucose infused intravenously. This effect, termed the "incretin effect," suggested that signals from the gut are important in the hormonal regulation of glucose disappearance. Additionally, these hormonal signals from the proximal gut seemed to help regulate gastric emptying and gut motility (Aronoff*et al*., 2004).

Several incretin hormones have been characterized, and the dominant ones for glucose homeostasis are GIP and GLP-1. GIP stimulates insulin secretion and regulates fat metabolism, but does not inhibit glucagon secretion or gastric emptying (Yip and Wolfe, 2000). GIP is a more potent incretin hormone, which is secreted in greater concentrations and is more physiologically relevant in humans (Aronoff*et al.*, 2004). GLP-1 stimulates insulin secretion when plasma glucose concentrations are high but not when plasma glucose concentrations approach or fall below the normal range, inhibits glucagon secretion and slows gastric emptying (Nauck*etal*., 2002). Derived from the proglucagon molecule in the intestine, GLP-1 is synthesized and secreted by the L-cells found mainly in the ileum and colon. Circulating GLP-1 concentrations are low in the fasting state. However, both GIP and GLP-1 are effectively stimulated by ingestion of a mixed meal or meals enriched with fats and carbohydrates(Drucker, 2001; Ivan *etal.*, 2008).

Infusion of GLP-1 lowers postprandial glucose as well as overnight fasting blood glucose concentrations (Nauck *etal*.,2002). The postprandial effect of GLP-1 is partly due to

inhibition of glucagon secretion. Yet while GLP-1 inhibits glucagon secretion in the fed state, it does not appear to blunt glucagon's response to hypoglycemia(Nauck *etal*., 2002). GLP-1 helps regulate gastric emptying and gastric acid secretion (Drucker, 2001), perhaps by signalling GLP-1 receptors in the brain and thereby stimulating efferent tracts of the vagus nerve(Nauck*etal*., 2002). As gastric emptying slows, the postprandial glucose excursion is reduced. Administration of GLP-1 has been associated with the regulation of feeding behavior and body weight(Zander *etal*., 2002). In addition, there have been reported observations of GLP-1 improving insulin sensitivity and enhancing glucose disposal(Zander *etal.*, 2002).

Of significant and increasing interest is the role GLP-1 may have in preservation of β-cell function and β-cell proliferation(Drucker, 2003). In animal studies, GLP-1 has been shown to enhance functional β-cell mass(Drucker, 2003).

2.4 Insulin Resistance

Insulin resistance is defined where a normal or elevated insulin level produces an attenuated biological response (Cefalu,2001) classically this refers to impaired sensitivity to insulin mediated glucose disposal(Reaven, 2004).*Compensatory hyperinsulinaemia* occurs when pancreatic β cell secretion increases to maintain normal blood glucose levels in the setting of peripheral insulin resistance in muscle and adipose tissue.

2.4.1 Mechanisms of insulin resistance

Physiologically, at the whole body level, the actions of insulin are influenced by the interplay of other hormones. Insulin, though the dominant hormone driving metabolic

processes in the fed state, acts in concert with growth hormone and Insulin- like growth factor 1(IGF-1); growth hormone is secreted in response to insulin, among other stimuli, preventing insulin-induced hypoglycaemia (Giorgino*et al.*, 2005) Other counter-regulatory hormones include glucagon, glucocorticoids and catecholamines. These hormones drive metabolic processes in the fasting state. Glucagon promotes glycogenolysis, gluconeogenesis and ketogenesis. The ratio of insulin to glucagon determines the degree of phosphorylation or dephosphorylation of the relevant enzymes(Nussey and Whitehead, 2001). Catecholamines promote lipolysis and glycogenolysis; glucocorticoids promote muscle catabolism, gluconeogenesis and lipolysis. Excess secretion of these hormones may contribute to insulin resistance in particular settings, but does not account for the vast majority of insulin resistant states (Gisela, 2005).

Insulin resistance in most cases is believed to be manifest at the cellular level via post-receptor defects in insulin signalling. Despite promising findings in experimental animals with respect to a range of insulin signalling defects, their relevance to human insulin resistance is presently unclear. Possible mechanisms include down-regulation, deficiencies or genetic polymorphisms of tyrosine phosphorylation of the insulin receptor, insulin receptor substrate (IRS) proteins or phosphatidylinositol- 3,4,5-triphosphate (PIP-3) kinase, or may involve abnormalities of GLUT 4 function (Wheatcroft *et al.*, 2003)

2.4.2 Sites of insulin action and manifestations of insulin resistance

The effects of insulin, insulin deficiency and insulin resistance vary according to the physiological function of the tissues and organs concerned, and their dependence on insulin for metabolic processes. Those tissues defined as insulin dependent, based on intracellular glucose transport, are principally adipose tissue and muscle. However, insulin's actions are pleotropic and widespread, as are the manifestations of insulin resistance and the associated compensatory hyperinsulinaemia (Reaven, 2004).

2.4.2.1 *Muscle*

Glucose uptake into muscle is essentially insulin dependent via GLUT 4, and muscle accounts for about 60–70% of whole-body insulin mediated uptake (Smith, 2002). In insulin resistance, muscle glycogen synthesis is impaired; this appears largely mediated by reduced intracellular glucose translocation (Guyton and Hall, 2006).

2.4.2.2 *Adipose tissue*

Intracellular glucose transport into adipocytes in the postprandial state is insulin-dependent via GLUT 4; it is estimated that adipose tissue accounts for about 10% of insulin stimulated whole body glucose uptake (Smith, 2002).In insulin resistance, peripheral uptake of triglycerides from very low density lipoprotein (VLDL) is diminished this contribute to the observed hypertriglyceridaemia of insulin resistance(Krauss and Siri,2004).

2.4.2.3 *Liver*

While glucose uptake into the liver is not insulin-dependent, it accounts for about 30% of whole body insulin-mediated glucose disposal (Smith, 2002), with insulin being needed to facilitate key metabolic processes. Resistance to insulin's metabolic effects results in increased glucose output via increased gluconeogenesis (as in starvation), however, unlike starvation, compensatory hyperinsulinaemia depresses sex- hormone binding globulin(SHBG) production and promotes insulin's mitogenic effects. Alterations in lipoprotein metabolism represent a major hepatic manifestation of insulin resistance. Increased free fatty acid delivery, and reduced VLDL catabolism by insulin resistant adipocytes, results in increased hepatic triglyceride content and VLDL secretion (Krauss and Siri, 2004).

2.4.2.4 *Endothelium and vasculature*

Insulin and its actions play an important role in various aspects of endothelial function, e.g. nitric oxide (NO) production, while insulin resistance is strongly associated with endothelial dysfunction. Whether these associations are causal, or mediated by common mechanisms, awaits clarification. The functions of vascular endothelial cells are critical to many aspects of cardiovascular biology, with endothelial dysfunction being seen at a very early stage of atherosclerosis and its associated clinical risk factors. Endothelial cells not only provide the physical lining of the blood vessels but secrete various factors influencing vessel tone, platelet function, coagulation and fibrinolysis. Clinical problems develop when these processes are in imbalance (Wheatcroft *etal.*, 2003).

Nitric oxide is the major factor in large arteries mediating endothelial dependent relaxation. It also inhibits platelet aggregation, cell adhesion and smooth muscle cell

proliferation (Zhou, 2014). NO is synthesised from L-arginine, molecular oxygen and nicotinamide adenine dinucleotide phosphate (NADPH), via the activity of endothelial enzyme nitric oxide synthase (eNOS), and its cofactors tetrahydrobiopterin, flavin adenine dinucleotide and flavin mononucleotide. Interestingly, arginine is a potent secretatogue for insulin and there is a final common pathway for the intracellular signalling of both eNOS and insulin. Insulin enhances tetrahydrobiopterin production by stimulating its biosynthetic enzyme GTP cyclohydrolase, and stimulates eNOS by calcium-independent phosphorylation of eNOS at serine and threonine residues via PIP-3 kinase and Akt (protein kinase B). Thus nitric oxide production is enhanced. Insulin also promotes release of the vasoconstrictor endothelin while TNFα decreases eNOS expression and induces von Willebrand Factor release (Horita*et al*., 2011). Ininsulin resistance tetrahydrobiopterin levels are reduced, the pathways for eNOS stimulation are down-regulated, and vasodilator responses to insulin and cholinergic agonists are impaired. Insulin's ability to counteract the TNFα-mediated Aktdephosphorylation in endothelial cells is also lost. Free fatty acids, elevated in insulin resistant states, also inhibit eNOS activity, decreasing NO production (Wheatcroft*etal*., 2003).

The compensatory hyperinsulinaemia that accompanies insulin resistance is associated with increased levels of pro-coagulant factors such as plasminogen activator inhibitor 1 (PAI-1). These factors are thought to contribute to the enhanced platelet aggregation seen in insulin resistant states. Endothelin 1 secretion is stimulated by insulin and elevated in insulin resistant states. Endothelin 1, a potent vasoconstrictor also inhibits insulin signalling via PIP-3 kinase and competes with NO resulting in endothelial dysfunction. Whilst the metabolic effects of insulin are variably affected in insulin resistance, the

mitogenic properties, mediated via the mitogen activated protein (MAP) kinase pathway, remain intact. These mitogenic effects of insulin on endothelial smooth muscle cell proliferation probably contribute to atherosclerosis(Wheatcroft*etal*, 2003).

2.4.3 Physiological influences on insulin action and insulin resistance

2.4.3.1 *Diet and starvation*

Chronic excess energy consumption promotes hyperinsulinaemia and insulin resistance through stimulation of insulin secretion, triglyceride synthesis and fat accumulation with down-regulation of insulin receptors and post receptor signaling(Gisela, 2005).

High fat diets tend to be associated with insulin resistance, particularly with respect to saturated fat(Lichentenstein and Schwab, 2000) and trans-fatty acids (Bray *etal.*, 2002). Fatty acid composition is thought to play a role in the long term development of insulin resistance, via effects on the composition of membrane lipids. Long chain polyunsaturated fatty acids play a physiological role in maintaining cell membrane fluidity and cell signalling; they also influence gene expression and are endogenous ligands for peroxisome proliferator receptors (Sampath and Ntambi, 2004).

Chronic overfeeding with sucrose has been reported to increase visceral adipose tissue deposition in rodents, which may have long-term implications for insulin resistance (Gisela, 2005). Whilst there is concern that high carbohydrate diets may exacerbate the clinical manifestations of the insulin resistance syndrome, this likely depends on the type of carbohydrate and intake of dietary fibre which has a favourable effect (Davey and Melby, 2003).Moderate alcohol consumption has been reported to augment the

postprandial increment in insulin and reduce the postprandial increment in glucose following a low carbohydrate meal (Greenfield, 2004). Population studies report a U-shaped curve with respect to level of alcohol consumption and insulin resistance (Magis*etal,* 2003).Chromium deficiency has been associated with glucose intolerance and insulin resistance in patients on long-term parenteral nutrition (Gisela, 2005), Iron accumulation is associated with impaired insulin sensitivity and type 2 diabetes, and features of the metabolic syndrome (Fernandez *etal*., 2002).

2.4.3.2 *Exercise and physical activity*

A large body of evidence supports the role of exercise in improving insulin sensitivity and its beneficial outcomes in insulin resistant states. Epidemiological studies such as the US Physicians Health Study have reported substantial decreases in the relative risk of type 2 diabetes with lifelong regular physical activity (Rao, 2001). Large scale randomised controlled clinical trials such as the Diabetes Prevention Program (Knowler*etal*., 2002) and the Finnish Prevention Study (Milehto *etal.*, 2001) demonstrate a 58% reduction in progression of impaired glucose tolerance to type 2 diabetes by intensive lifestyle modification which included a minimum of 20–30 minutes of exercise per day.

2.4.3.3 *Stress*

Insulin resistance is typically seen in the catabolic stress of severe illness with implications for morbidity and mortality (Gisela, 2005)

2.4.3.4 *Sleep and sleep deprivation*

Acute sleep deprivation in healthy young adults has been reported to raise fasting blood glucose concentrations in association with altered diurnal cortisol secretion and reduced heart rate variability (Spiegel *etal.,* 1999). These effects suggest increased counter-regulatory hormone secretion via hyper-arousal with activation of the hypothalamo-pituitary adrenal axis (Vgontzas*etal.,* 1999). There is also accumulating evidence that chronic sleep deprivation may impact on insulin and insulin resistance. Recent epidemiological studies report that reduced sleep duration is associated with increased BMI (Vorona*etal*., 2005).

Sleep deprivation is associated with decreased plasma concentrations of leptin, the adipocyte peptide hormone regulating fat mass and appetite, and increased concentrations of ghrelin, which increases appetite (Spiegel *etal*., 1999). Growth hormone is secreted during slow wave sleep, sleep declines with age (Mullington*etal*., 1996) and growth hormone deficiency in adults has been associated with central adiposity and insulin resistance (Hew *etal*., 1998), but whether sleep deprivation acts through these mechanisms is not clearly established. Obstructive sleep apnoea (OSA), where sleep disturbance results from obstruction to breathing during sleep, is associated with impaired glucose tolerance independent of adiposity (Tassone*etal.,* 2003), and improves with continuous positive airway pressure treatment (Yee *etal*., 2004) but whether this is due to resolution of hypoxia and hypercapnia, or to effects on sleep quality, is unclear.

2.4.3.5 *Pregnancy*

Normal pregnancy is characterised by insulin resistance (Nussey and Whitehead, 2001) which is greatest in the third trimester. This appears to be an adaptive response, diverting

glucose and lipids to the developing foetus(Butte, 2000) and thought due to the combined effects of human placental lactogen, progesterone, oestradiol and cortisol, which act as counter-regulatory hormones to insulin. Exaggeration of the insulin resistance normally seen in pregnancy is associated with gestational diabetes mellitus and gestational hypertension (Seeley and Solomon, 2003).

2.4.3.6 *Obesity*

Increased adipose tissue, especially that in an upper body or "android" deposition, was first associated with diabetes and vascular disease by French endocrinologist Jean Vague in 1956 (Gisela, 2005). Insulin resistance increases with increasing body mass index, waist circumference and in particular waist-hip ratio (Aronne and Segal, 2002). These reflect increased adiposity especially increased levels of visceral adipose tissue. Visceral adipose tissue refers to intra-abdominal fat around the intestines and correlates with liver fat. Visceral adipose tissue has metabolic characteristics which differ from that of subcutaneous fat. It is more metabolically active with regard to free fatty acid turnover; the increased flux of free fatty acids promotes insulin resistance at a cellular level and increases hepatic VLDL production (Giorgino *etal.*, 2005).Adipose tissue produces a number of cytokines which have been associated with insulin resistance, including those with pro-inflammatory activity e.g. tumor necrosis factor alpha (TNFα), interleukins, and PAI-1. Muscle insulin resistance is associated with increased intramyocellular triglyceride, derived from adipose tissue lipolysis (Perseghin*etal*., 2003).

The insulin resistance seen in obesity is believed to involve primarily muscle and liver, with increased adipocyte-derived free fatty acids promoting triglyceride accumulation in

these tissues(Perseghin *etal*., 2003). This is more likely where adipocytes are insulin resistant (Frystyk and Orskof, 1997). Free fatty acid flux is greater from visceral adipose tissue and more likely in those individuals with genetically mediated adipocyte insulin resistance. Whilst individual differences in the effects of increasing adiposity exist, weight gain worsens and weight loss improves insulin resistance in those so predisposed (Reaven, 2003).

2.4.4 Pharmacological influences on insulin action and insulin resistance

A wide range of pharmacological agents have been associated with impaired glucose tolerance. Antihypertensive agents such as diuretics and β-blockers, corticosteroids, oral contraceptives, nicotinic acid and antipsychotic agents have been reported to impair glucose tolerance (Ananth *etal*., 2004)as have the anti-retroviral protease inhibitors used to treat human immunodeficiency virus infection (Chen *etal*., 2002). The mechanisms vary; β-blockers impair insulin secretion from the pancreas by blockade of β-adrenoceptors, thiazide diuretics are thought to act by depleting potassium levels, corticosteroids and oral contraceptives have counter-regulatory hormonal activity (Ananth *etal*., 2004), and the HIV-1 protease inhibitors result in partial lipodystrophy with loss of peripheral subcutaneous fat and accumulation of truncal adipose tissue leading to insulin resistance (Chen *etal*., 2002).

Metformin, a biguanide, reduces hepatic glucose output and to a lesser extent peripheral insulin resistance and is used in type 2 diabetes and polycystic ovarian syndrome (PCOS). Its cellular actions are less well characterised. Recently, a class of agonists for peroxisome proliferator gamma receptors has been available and these agents are more

potent than metformin in reducing peripheral insulin resistance. They promote the differentiation of subcutaneous adipocytes and favour redistribution of triglycerides from hepatic and visceral adipose fat depots to the periphery. They improve insulin resistance in adipose tissue but not in muscle. Thiazolidinediones such as rosiglitazone and pioglitazone are used in type 2 diabetes (Lebovitz, 2004) and have been effective in PCOS (Hunter and Garvey, 1998). However, there are concerns regarding the safety of thiazolidinediones in pregnancy; moreover the long term pregnancy outcome of all these insulin-sensitizing agents, including metformin, is unknown (Ehrmann, 2005).

2.4.5 The insulin resistance syndrome

The insulin resistance syndrome describes the cluster of abnormalities which occur more frequently in insulin resistant individuals. These include glucose intolerance, dyslipidaemia, endothelial dysfunction and elevated procoagulant factors, haemodynamic changes, elevated inflammatory markers, abnormal uric acid metabolism, increased ovarian testosterone secretion and sleep-disordered breathing (Reaven, 2004). Clinical syndromes associated with insulin resistance include type 2 diabetes, cardiovascular disease, essential hypertension, polycystic ovary syndrome, non-alcoholic fatty liver disease,and certain forms of cancer and sleep apnoea (Reaven, 2004).

2.4.6 Clinical syndromes associated with insulin resistance

Type 2 diabetes and the Metabolic Syndrome would be the most common clinical syndromes associated with insulin resistance. Others include hypertension, PCOS, non-alcoholic fatty liver disease, certain forms of cancer and OSA (Reaven, 2004), which some authors consider a component of the metabolic syndrome per se. There are also

relatively common conditions where insulin resistance is a secondary phenomenon; these include acute illness, hepatic cirrhosis, renal failure, pregnancy, hyperthyroidism, Cushing's disease and Cushing's syndrome as well as acromegaly and phaeochromocytoma which are less common (Withers and white, 2000). In many of these, the insulin resistance is due to increased production of counter-regulatory hormones.

2.4.7 Common conditions associated with insulin resistance

2.4.7.1 *Type 2 diabetes (T2DM)*

Insulin resistance was reported to be a characteristic feature of T2DM in the early 1970s (Reaven, 2004). A progressive inability of the β cells to compensate for the prevailing insulin resistance by sufficient hyperinsulinaemia, heralds the clinical onset of this disorder (Reaven, 2004). While twin studies and linkage analyses are consistent with a strong genetic component in the development of type 2 diabetes, several decades of research have failed to identify a predominant genetic abnormality in the majority of cases (Withers and White, 2000). The aetiology of T2DM is thought to be polygenic, with environmental factors being superimposed upon this basic predisposition.

Insulin resistance typically predates the development of diabetes and is commonly found in unaffected first-degree relatives (Rao, 2001). The morbidity of the disorder relates both to the severity of hyperglycaemia and the metabolic consequences of insulin resistance itself. The primary defects in insulin action appear to be in muscle cells and adipocytes, with impaired GLUT 4 translocation resulting in impaired insulin-mediated glucose transport (Guyton and Hall, 2006).

Compensatory hyperinsulinaemia develops initially, but the first phase of insulin secretion is lost early in the disorder. Additional environmental and physiological stresses such as pregnancy, weight gain, physical inactivity and medications may worsen the insulin resistance. As the β cells fail to compensate for the prevailing insulin resistance, impaired glucose tolerance and diabetes develops. As glucose levels rise, β cell function deteriorates further, with diminishing sensitivity to glucose and worsening hyperglycaemia. The pancreatic islet cell mass is reported to be reduced in size in diabetic patients; humoral and endocrine factors may be important in maintaining islet cell mass (Nielson*etal.*, 2001). In contrast to most forms of type 2 diabetes, the genetic basis of Maturity Onset diabetes of the Young (MODY) has been well characterised and relates to defects in glucokinase, hence intracellular glucose transport (Withers and White, 2000).

2.4.7.2 *Hypertension*

Essential hypertension has been associated with insulin resistance in up to 50% of cases (Reaven, 2003). There is a strong correlation of blood pressure with body weight. The significance of insulin resistance in hypertension is subject to some controversy, as 50% of essential hypertensives appear not to have insulin resistance. Proposed mechanisms have included increased renal sodium retention and increased sympathetic nervous system activity from compensatory hyperinsulinaemia (Reaven, 2004). However endothelial dysfunction from resistance to insulin-mediated nitric oxide formation is thought to be of clearer significance (Wang, 2004).

2.4.8 Signs and Symptoms of Diabetes Mellitus

Various manifestations of diabetes mellitus develop because of three major set -backs of insulin deficiency, which are increased blood sugar level (300- 400 mg/dl) due to reduced utilization by tissue, mobilization of fats from adipose tissue for energy purpose, leading to elevated fatty acid content in the blood which causes deposition of fat on the wall of arteries and the development of atherosclerosis and depletion of protein from the tissue (Sembulingam and Sembulingam, 2006)

The following are the features of diabetes mellitus:

2.4.8.1 Glucosuria

Loss of glucose in the urine is called glucosuria. Normally glucose does not appear in urine but when glucose level rises above the threshold (180mg/dl) in blood, glucose appears in urine (sembulingam and Sembulingam, 2006).

2.4.8.2 Osmotic diueresis

Diueresis due to osmoyic effects is called osmotic dieresis. The excess glucose in the renal tubules develops osmotic effect which decreases the reabsorption of water from renal tubules in dieresis and eventually leads to polyuria and polydipsia (Sembulingam and Sembulingam, 2006)

2.4.8.3 Polyuria

Excess urine formation with increase in frequency of voiding urine is called polyuria which is due to the osmotic dieresis caused by increase in blood glucose level

2.4.8.4 Polydipsia

The increase in water in- take is called polydipsia. The excess loss of water decreases water content and increases salt content in the body which stimulates the thirst centre in

hypothalamus, hence the increase in water in –take (Sembulingam and Sembulingam, 2006)

2.4.8.5 Polyphagia

It means the in- take of excess food and it is very common in diabetes

2.4.8.6 Asthenia

The loss of strength is called asthenia. The body becomes weak because of lack of insulin which causes decrease in protein synthesis and increase in protein break down. Protein depletion also occurs due to the utilization of proteins for energy in the absence of glucose utilization (Sembulingam and Sembulingam, 2006)

2.4.8.7 *Acidiosis*

During insulin deficiency glucose cannot be utilized by peripheral tissues for energy. So a large amount of fat is broken down to release energy which causes the formation of excess ketoacids leading to acidosis. Ketoacids are also excreted in combination with sodium ions through urine(ketonuria), sodium is exchanged for hydrogen ions which diffuse from the renal tubules into ECF adding to acidosis

2.4.8.8 Acetone breathing

In cases of severe ketoacidosis, acetone is expired in the respiratory air, giving the characteristic acetone or fruity breath odor. It is a life- threatening condition of severe diabetes (Sembulingam and Sembulingam, 2006).

2.4.8.9 Kussmaul breathing

Severe acidosis increases the rate and depth of respiration which is known as kussmaul breathing.

2.4.8.10 Circulatory shock

The osmotic dieresis leads to dehydration, which causes circulatory shock. It occurs only in severe diabetes.

2.4.8.11 Coma

Due to kussmaul breathing, large amount of carbondioxide is lost during expiration. It leads to drastic reduction in the concentration of bicarbonate ions causing severe acidosis and coma. It occurs in severe cases of diabetes mellitus. Increase in blood glucose level develops hyperosmolar coma (Sembulingam and Sembulingam, 2006).

2.4.9 Physiology of Diagnosis of Diabetes Mellitus

The usual methods for diagnosing diabetes are based on various chemical tests of the urine and the blood.

2.4.9.1 Urinary glucose

Simple office tests or more complicated quantitative laboratory tests may be used to determine the quantity of glucose lost in urine. In general, a normal person loses undetectable amounts of glucose, whereas a person with diabetes loses glucose in small to large amounts, in proportion to the severity of disease and the intake of carbohydrates (Guyton and Hall, 2006).

2.4.9.2 Fasting blood glucose and insulin levels

The fasting blood glucose level in the early morning is normally 80- 90mg/100ml, and 110mg/100ml is considered to be the upper limit of normal. A fasting blood glucose level above this value often indicates diabetes mellitus or at least marked insulin resistance. In type 1 diabetes mellitus, plasma insulin levels are very low or undetectable during fasting and even after a meal. In type 2 diabetes mellitus, plasma insulin concentration may be

seven fold higher than normal and usually increases to a greater extent after ingestion of a standard glucose load during a glucose tolerance test (Guyton and Hall, 2006)

2.4.10 Treatment of diabetes mellitus

The theory of treatment of type 1 diabetes mellitus is to administer enough insulin so that the patient will have carbohydrate, fat, and protein metabolism that is as normal as possible. Insulin is available in several forms. Regular insulin has a duration of action that lasts from 3 to 8 hours, whereas other forms of insulin (precipitated with zinc or with various protein derivatives) are absorbed slowly from the injection site and therefore have effects that last as long as 10 to 48 hours. Ordinarily a patient with severe type 1 diabetes is given a single dose of one of the longer- acting insulins each day to increase overall carbohydrate metabolism throughout the day. Then additional quantities of regular insulin are given during the day at those times when the blood glucose level tends to rise too high, such as at meal times. Thus, each patient is provided with an individualized pattern of treatment (Sembulingam and Sembulingam, 2006).

In persons with type 2 diabetes, dieting and exercise are usually recommended in an attempt to induce weight loss and to reverse the insulin resistance. If this fails, drugs may be administered to increase insulin sensitivity or to stimulate increased production of insulin by the pancreas. In many persons, however, exogenous insulin must be used to regulate blood glucose (Sembulingam and Sembulingam, 2006).

2.4.11 Complications of diabetes mellitus

Prolonged hyperglycemia in diabetes mellitus causes dysfunction and injury of many tissues resulting in some complications. Development of these complications is directly proportional to the degree and duration of hyperglycemia. However, the patients with

well controlled diabetes mellitus can postpone the onset or reduce the rate of progression of these complications (Sembulingam and Sembulingam,2006).

Initially the untreated chronic hyperglycemia affects the blood vessels resulting in vascular complications like atherosclerosis. The vascular complications are responsible for the development of most of the complications of diabetes such as: cardiovascular complications like hypertension and myocardial infarction; degenerative changes in retina called diabetic retinopathy; degenerative changes in kidney known as diabetic nephropathy; and degeneration of autonomic and peripheral nerves called diabetic neuropathy (sembulingam and Sembulingam, 2006; Long and Jack, 2011).

2.5 Relationship between Diabetes and Hypertension

The coexistence of Diabetes mellitus and Hypertension can be viewed as a cause- effect relationship (Diabetes mellitus as a cause of Hypertension or vice versa) or as a non-causal association (Manoocher, 2015). Insulin can increase blood pressure via several mechanisms by increased renal sodium reabsorption, activation of the sympathetic nervous system, alteration of transmembrane ion transport, and hypertrophy of resistance vessels. Conversely, hypertension can cause diabetes mellitus by altering the delivery of insulin and glucose to skeletal muscle cells, resulting in impaired glucose uptake. For example, hypertension can impair vasodialation of skeletal muscle as a result of vascular structural changes and rarefaction, and increased response to vasoconstrictor stimuli (Horita *et al*., 2011; Levin *et al*., 2015; Manoocher, 2015)

Also, the prevalence of muscle type 2b fibres (fast twitch fibres) may contribute to the development of insulin resistance. The common paths genetic mechanism for both insulin

resistance and hypertension could be activation of the sympathetic nervous system. This result in vasoconstriction and may contribute to the genesis of vascular structural changes and increase the number of fast twitch fibres (Horita *et al*., 2011; Levin *et al*., 2015; Manoocher, 2015)

Finally, hypertension and insulin resistance can be viewed as a non-causal association, because they may represent two independent consequences of the same metabolic disorder (intracellular free calcium accumulation) or because insulin resistance is a genetic marker and / or a pathogenetic mechanism of multiple metabolic abnormalities frequently associated with hypertension (Manoocher, 2015).

Diabetes and hypertension tend to occur together so frequently that they are officially considered to be co-morbidities (diseases likely to be present in the same patient). They tend to occur together because they share certain physiological traits, that is, the effects cause by one tend to make the other disease likely to occur (Weber, 2008). In the case of diabetes and high blood pressure these effects include increased fluid volume, increased arterial stiffness and impaired insulin handling (Weber, 2008)

Though these biological traits partially explain why diabetes and blood pressure are such a common pair. In many cases the two diseases are likely to occur together simply because they share a common set of risk factors like body mass index, diet and activity level (Weber, 2008)

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study Area

The global location of Kaduna State is between latitude 90^0 and 140^0 north of the equator and longitude 70^0 and 100^0 east of the Greenwich meridian. It occupies a landmass of about 70,210 square kilometers on the map of Nigeria. Its topography is that of an undulating Plateau that forms part of the rich tourist attractions in areas like Kufena, Kagoro, Kwoi and Gwantu. These areas have protruding hard resistant granite rocks that are so attractive for sightseeing. Its main rivers are River Kaduna, River Gurara, River Kogum, and River Kubani(NACD, 2014).

Kaduna State has two distinct seasons. The dry season lasts from November to Mid-April while the rainy reason, which is cool and lasts between 5-6 months, starts from mid-April to October. The State extends from the tropical grassland known as the Guinea Savannah to Sudan Savannah. Vegetation is thick and grasses about 3.6 meters tall with big trees, which grow shorter as one approaches the Sudan Savannah. The two climatic conditions in the State greatly influence activities of the people, who are predominantly occupied in agriculture (NACD, 2014).

3.2 Sample size

Four hundred and eighteen being the minimum sample size that could have been taken but a sample size of one thousand and five hundred was decided on to account for contingencies such as non-responses or recording error.

There are about two thousand, nine hundred settlements in southern Kaduna (NPC, 2009). Using the criteria for selecting urban and rural settlements stipulated by United Nations, these settlements were divided into urban and rural settlements. Ten settlements from the rural area of southern Kaduna were selected randomly by writing all the names of the settlements in the rural areas one at a time on a piece of a paper. The pieces of paper were folded and put in a container, the container was shaken properly and the settlements were picked from the container one at a time. Ten settlements from the urban area of southern were selected randomly by writing all the names of the settlement in the urban areas one at a time on a piece of a paper. The pieces of paper were folded and put in a container, the container was shaken properly and the settlements were picked from the container one at a time

A total of 1500 samples which were made up of 500 males and 500 females were collected from the urban area and 500 samples which were made of 250 males and 250 females were collected from the rural areas. All persons were aged 18 and above

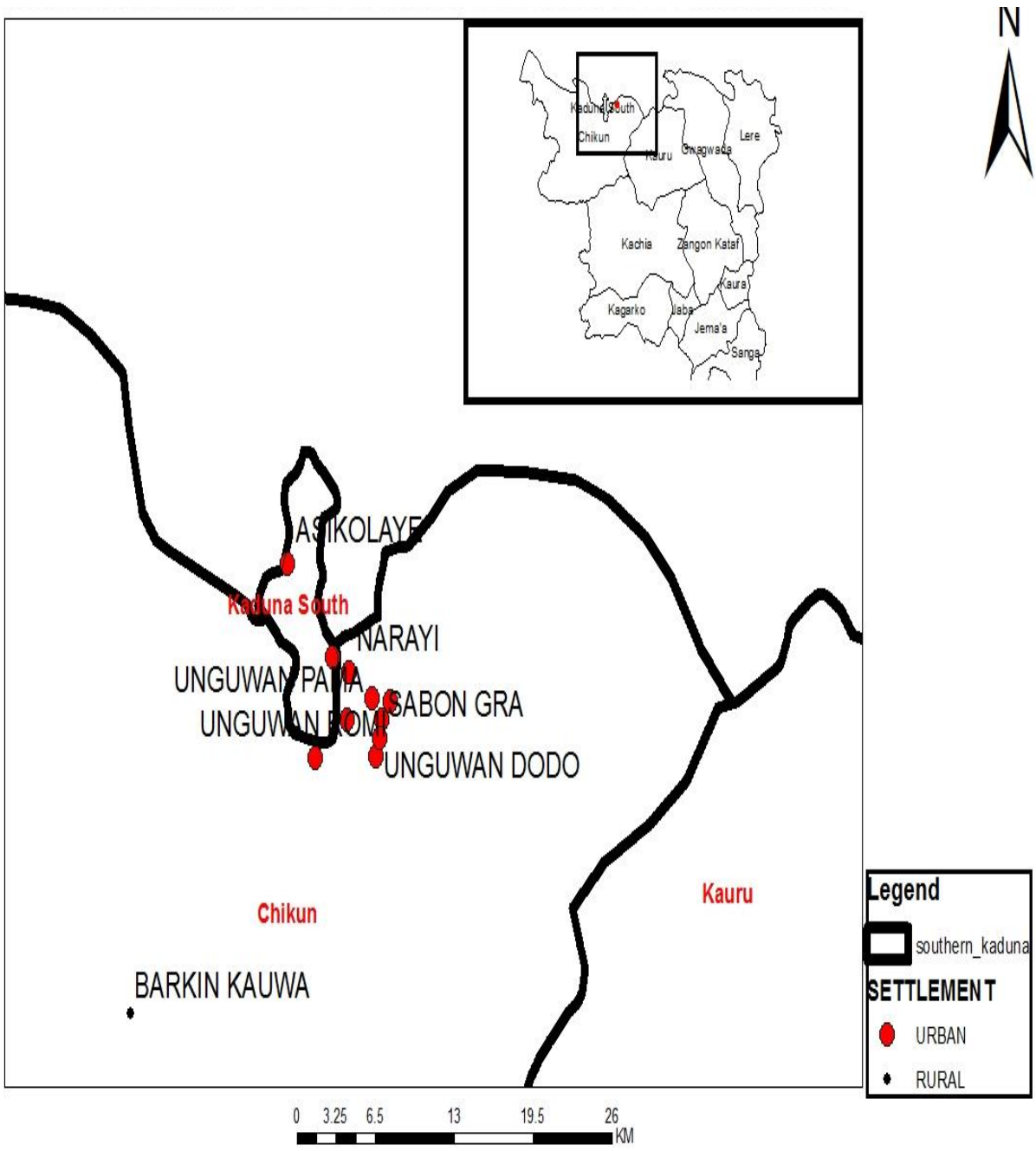
3.3 Population

Kaduna State is one of the most densely populated States in Nigeria. This is as a result of the liberal nature of its people. It accommodates peoples from all parts of the country who have come to see Kaduna as their home. According to the 2003 census population figure it has more than 6 million people (NACD, 2014). Spatial distribution of the

selected ten urban and ten rural settlements from the numerous settlements in the state from where the samples were collected are shown in fig. 3.1 and fig 3.2 respectively.

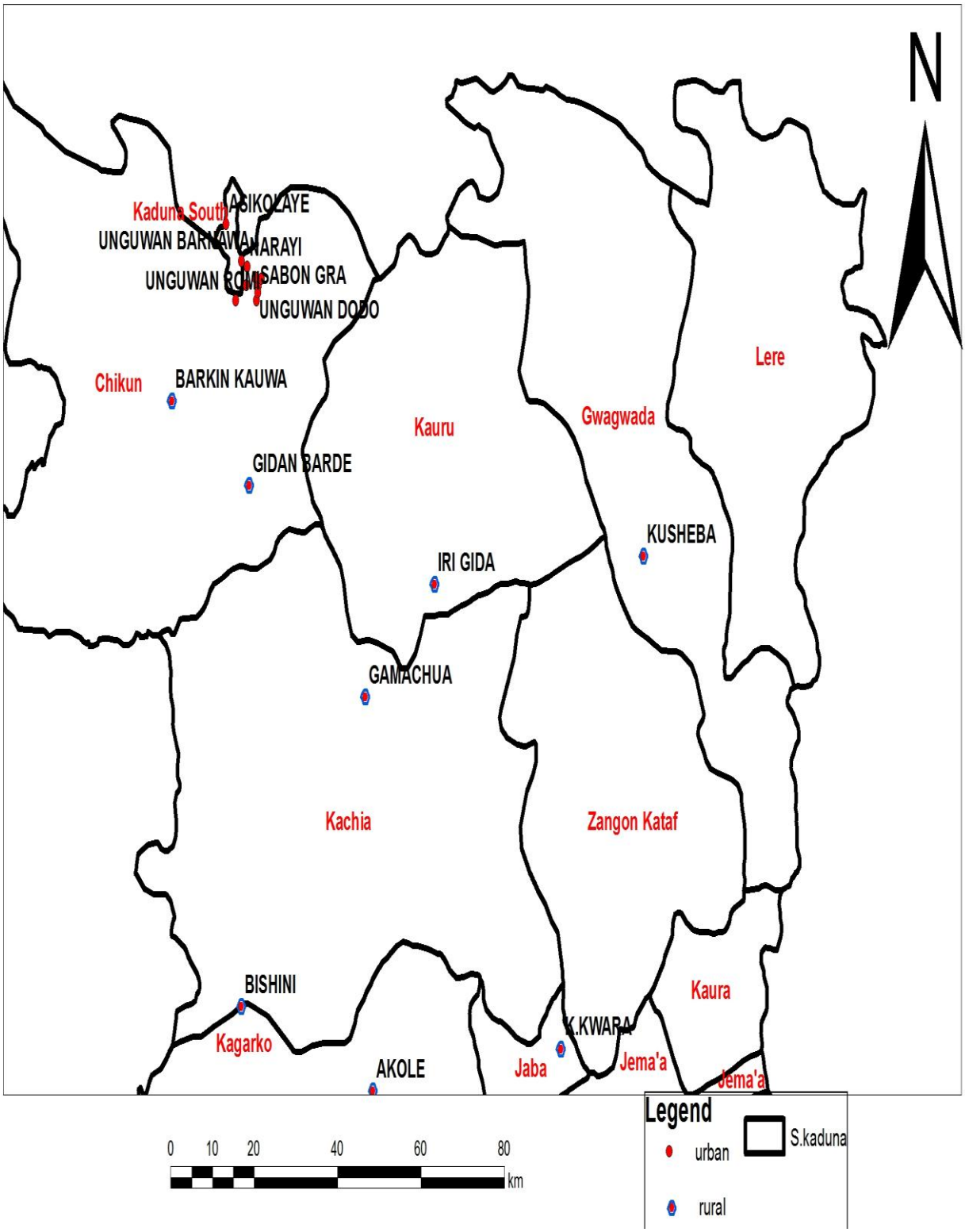
3.4 Measurement of Blood Sugar Level

Blood sugar levels of all the 1500 volunteers were measured using ADVOCATE®Blood Glucose Monitoring System TD- 4223 S/B 311- 4223000-001, VERSION 1.0 NOVEMBER 2006 (plate I). This test kit consists of a Meter, Test strips and Lancets. When the test strip is inserted into the meter, it automatically turns the meter on.



Source: Adapted and modified from Administrative Map of Kaduna State

Fig: 3.1 Spatial Distributions of Selected Urban Settlements in Southern Kaduna Metropolis



Source: Adapted and modified from Administrative Map of Kaduna State

Fig 3.2:Spatial Distribution of Selected Urban and Rural Settlements in Southern Kaduna state

Plate I: Advocate® Blood Glucose Monitoring System TD-4223 S/B 311 – 4223000-001, version 1.0 November 2006

The lancet was used to prick any of the five fingers after the finger had been cleaned with a cotton wool that was soaked in 70% alcohol and allowed to air dry. Blood from the pricked finger was applied unto the absorbent hole of the test strip until the confirmation window was fully covered with blood. The result of the blood glucose test was displayed on the meter screen. After the test result was recorded the test strip was removed and discarded. The procedure was repeated for each individual of the 1500 volunteers using a new lancet and test strip. This test was conducted in the morning.

3.5 Measurement of Blood Pressure Level

Blood pressure of all the volunteers in the sample was measured one at a time using ADVOCATE® Automatic Memory Blood Pressure Monitor Model KD -575 (Plate II). The air-tube of the arm cuff was connected to the air socket of the monitoring device. The arm cuff was coiled on bare skin 1- 2cm above the elbow joint (on the bicep) at the same level with the heart. The start button on the monitoring device was pressed for more than two seconds to get the machine ready for measurement after cuffing the arm. The start button was pressed again for the machine to begin to pressurize the person's arm. After pressurization was completed, the machine deflated regularly and automatically. Pressure decreased gradually while the pulse is checked. After a beeping sound, the automatic measurement was completed; the measured blood pressure value appeared on the screen. After the blood pressure value was recorded for a particular individual in the sample, the start button was pressed for three seconds to shut down the machine. The cuff was removed and the procedure was repeated for the next person. The test was conducted in the morning.

Plate II: Advocate®Blood Pressure Monitor Model KD -575

3.6 Measurement of Weight

Weight of each person was measured using a CAMRY®Mechanical Scale Model BR9011 (plate III). The individuals stood one at a time on the scale bare footed and wearing light clothing. The spring of the measuring scale that was stationery at zero kg before an individual stood on the scale deflected to another number which is the weight

of that individual that was standing on the scale. The value was recorded and that individual stepped down from the scale. The spring then returns to zero kg.

3.7 Measurement of Height

A graduated rod was placed vertically against a wall each individual stood uprightly backing the graduated rod. The heights of all the individuals were taken using this procedure one at a time.

3.8 Determination of BMI

BMI is was calculated as the ratio of weight in kilogram to the square of height in meters (Losos*et al.,* 2002)

$$BMI = \frac{W}{H^2}$$

3.9 Questionnaire Administration

A structured questionnaire was used to collect information on socio economic status, eating and drinking habits and presence or absence of any ailment that they are taking medication for.

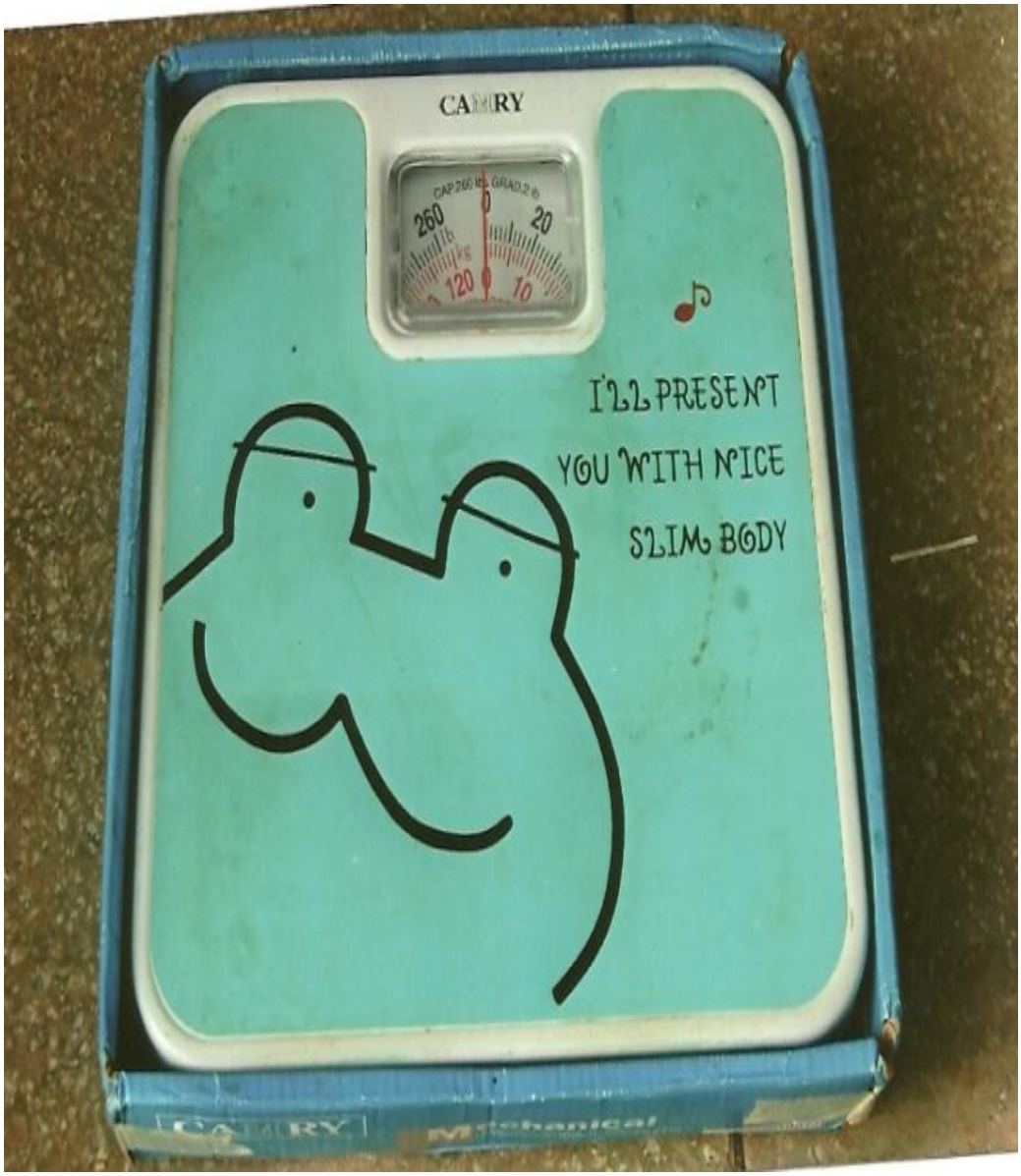


Plate III:Camry® Mechanical Scale Model BR9011

3.10 Statistical Analysis

The statistical package used for the statistical analysis of the data that was collected is SPSS version 20. Students't-test was used to find the difference in the meansof systolic

and diastolic blood pressure levels and random blood sugar levels with gender, residence, occupation, age group, habit and BMI

Chi -square was used to find the association between blood pressure status, gender, residence, occupation, age group, habit and BMI and correlation Analysis was used to determine the strength of relationship between all the parameters measured

CHAPTER FOUR

4.0 RESULTS

4.1 Mean Systolic Blood Pressure(SBP), Diastolic Blood pressure(DBP) and Random Blood Glucose(RBG)in Relation to Gender

The male gender had higher but statistically non-significant ($p>0.05$) mean SBP, DBP, and RBG values of 128.03mmHg, 84.65mmHg and 4.69Mmol/l compared to the female gender as shown in table 4.1.

4.2 Mean Systolic Blood Pressure(SBP), Diastolic Blood pressure (DBP)and Random Blood Glucose(RBG)in Relation to Respondents' location

In the urban settlements Angwanpama had the highest mean SBP, DBP and RBG values of 140.56mmHg, 92.11mmHg and 6.02Mmol/l, the lowest mean SBP, DBP values of 129.36mmHg, 87.12mmHg were recorded in AngwanMaigero and RBG value of 5.03Mmol/l was recorded in Barnawa while in the rural areas the highest mean SBP value of 123.14mmHg was recorded in Kusheba, DBP value of 82.92mmHg was recorded in BarkinKasuwa, RBG value of 4.07Mmol/l was recorded in Chakwama and the lowest mean SBP, DBP values of 112.58mmHg, 72.58mmHg were recorded in Chakwama, RBG value of 3.57Mmol/l was recorded in BarkinKasuwa as shown in table 4.2

4.3 Mean systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Random Blood Glucose(RBG) in Relation to Respondents' Residence

The urban settlements had high and significant ($p < 0.05$) mean SBP, DBP and RBG values of 133.56mmHg, 88.30mmHg, 5.22Mmol/l as shown in table 4.3 compared to the respondents in the rural areas.

Table 4.1: Mean Values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Glucose Levels In Relation To Respondents' Gender

Gender	**No. of individuals**	**SBP (mmHg)**	**DBP (mmHg)**	**RBG (mmol/l)**
Male	750	128.03±0.62	84.65±0.37	4.69±0.05
Female	750	127.79±0.66	84.22±0.42	4.83±0.07

Note: Values are expressed as mean ± SEM. Means along column with the same superscripted alphabets are not different at P>0.05)

Table 4.2: Mean values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Random Blood Glucose Levels in Relation To Respondents' location.

Residence		**No of individuals**	**SBP (mmHg)**	**DBP (mmHg)**	**RBG (mmol/l)**
Urban	AngwanBoro	100	137.06	89.33	5.84
	AngwanPama	100	140.56	92.11	6.02
	AngwanMaigero	100	129.36	87.12	5.07
	Angwan Sunday	100	133.77	88.30	5.04
	Sabo GRA	100	132.33	88.13	5.14
	Angwan Dodo	100	133.32	88.12	5.15
	Narayi	100	130.85	86.15	4.79
	Barnawa	100	130.17	87.32	5.03
	Asikolaiye	100	134.44	87.75	5.24
	AngwaRomi	100	133.69	88.65	4.84
	Mean	**1000**	**133.56**	**88.30**	**5.22**
Rural	BarkinKasuwa	50	120.16	82.92	3.57
	Kusheba	50	123.14	82.10	3.81
	GidanBarde	50	119.34	80.36	3.79
	IriGida	50	115.78	75.78	3.78
	Gama Chuwa	50	116.62	76.94	3.74
	Bishni	50	118.00	77.10	3.81
	Akole	50	113.80	72.84	3.89
	K. Kwara	50	112.82	73.20	4.03
	Chakwama	50	112.58	72.58	4.07

Kasabere	50	113.98	73.42	3.95
Mean	**500**	**116.62**	**76.71**	**3.84**

Table 4.3: Mean Values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Glucose Levels In Relation To Respondents' Residence

Residence	**No. of individuals**	**SBP (mmHg)**	**DBP (mmHg)**	**RBG (mmol/l)**
Urban	1000	133.56±0.58[a]	88.30±0.32[a]	5.22±0.06[a]
Rural	500	116.62±0.36[b]	76.71±0.33[b]	3.84±0.03[b]

Note: Values are expressed as mean ± SEM. Means along column with the different superscripted alphabets are different at $P<0.05$)

4.4 Mean Systolic Blood Pressure(SBP), Diastolic Blood pressure (DBP)and Random Blood Glucose (RBG)in Relation to Occupation

It was observed from the study as seen in table 4.4 that pensioners had the highest SBP, DBP and RBG in this study with 147.67mmHg, 93.3mmHg and 6.74Mmol/l respectively which was significantly higher ($p< 0.05$) than the other occupations while, students were observed tohave the lowest SBP, DBP and RBG of 123.68mmHg, 82.22mmHg and 4.42Mmol/l respectively at $P<0.05$. The difference in the SBP, DBP and RBG among civil servants, unemployed and business person were found to be statistically non-significant ($p< 0.05$).

4.5 Mean systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Random Blood Glucose(RBG)in Relation to Age Group

The elderly age group had significantly ($p<0.05$) higher SBP, DBP and RBGmean values of 149.06mmHg, 92.31mmHg and 6.42Mmol/l respectively than the young and middle-aged group at $P<0.05$ as shown in table 4.5. Although, there was no significant difference between the DBP and RBG among the young and middle-aged, while significant difference was noted between the SBP in young and middle aged. Generally SBP, DBP, RBG increased with increase in age.

4.6 Mean Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Random Blood Glucose(RBG)in Relation to Smoking Habit

Cigarette smokers had significantly ($p< 0.05$) higher mean SBP and DBP values of 142.64mmHg and 92.91mmHg compared to non-smokers with SBP and DBP values of 127.80 mmHg and 84.37mmHg. The difference in the means of their RBG was found to be statistically non -significant at $P <0.05$ as shown in table 4.6

Table 4.4: Mean Values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Glucose Levels In Relation To Respondents' Occupation

Occupation	No. of individuals	SBP (mmHg)	DBP (mmHg)	RBG (mmol/l)
Civil servant	178	134.88±1.39^{b}	89.20±0.89^{b}	4.99±0.08^{bc}
Unemployed	130	134.57±2.16^{b}	87.03±1.06^{b}	5.30±0.20^{b}
Pensioner	12	147.67±7.25^{a}	93.33±2.84^{a}	6.74±1.06^{a}
Businessperson	312	132.18±1.22^{b}	86.46±0.68^{b}	5.25±0.14^{b}
Student	868	123.68±0.42^{c}	82.22±0.31^{c}	4.42±0.04^{c}

Note: Values are expressed as mean ± SEM. Means along column with the different superscripted alphabets are different at $P<0.05$)

Table 4.5: Mean Values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Glucose Levels In Relation To Respondents' Age Group

Age group	**No. of individuals**	**SBP (mmHg)**	**DBP (mmHg)**	**RBG (mmol/l)**
Young (<40)	1227	126.15±0.42[c]	83.62±0.28[b]	4.64±0.04[b]
Middle-aged (40-65)	257	135.02±1.61[b]	87.80±0.90[b]	5.22±0.14[b]
Elderly (>65)	16	149.06±6.00[a]	92.31±2.00[a]	6.42±0.80[a]

Note: Values are expressed as mean ± SEM. Means along column with the different superscripted alphabets are different at P<0.05)

Table 4.6: Mean Values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Glucose Levels In Relation To Respondents' Habit (I smoke, I don't smoke)

Smoke	No. of individuals	SBP (mmHg)	DBP (mmHg)	RBG (mmol/l)
Yes	11	142.64±7.78[a]	92.91±3.30[a]	5.17±0.32[a]
No	1489	127.80±0.45[b]	84.37±0.28[b]	4.76±0.04[a]

Note: Values are expressed as mean ± SEM. Means along column with the different superscripted alphabets are different at $P<0.05$)

4.7 Mean Systolic Blood Pressure (SBP), Diastolic Blood pressure (DBP) and Random Blood Glucose(RBG)in Relation to Drinking of Alcohol

Habit of drinking alcohol amongst respondents indicated significant (P<0.05)high mean SBP, DBP and RBSvalues as shown in Table 4.7 compared to those who didn't drink.

4.8 Mean Systolic Blood Pressure(SBP), Diastolic Blood pressure (DBP)and Random Blood Glucose (RBG)in Relation to Body Mass Index (BMI)

SBP increased significantly (p <0.05) with an increase in BMI, the highest value of 145.45mmHg was recorded by obese respondents and the lowest was recorded by the underweight respondents. DBP increased with increase in BMI but the difference between the mean value of the normal respondents and the overweight respondents was statistically non-significant (p< 0.05). RBG also increased with increase in BMI but the difference between the mean valuesof the underweight and normal respondents werenon-significant (p <0.05) as shown in table 4.8

4.9 Blood Pressure Status Distribution between Gender

The male gender had a higher but non-significant (p> 0.05) prevalence of high blood pressure compared to the female gender as shown in Table 4.9.The male gender had 18.3% hypertensive, 51.1% pre- hypertensive and 30.7% persons who had blood pressure in the normal range. The female gender had 17.2% hypertensive, 49.1% pre-hypertensive and 33.7%persons who had blood pressure in the normal range.

Table 4.7: Mean Values Of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Sugar Levels In Relation To Respondents' Habit (I drink, I don't drink)

Alcohol	**No. of individuals**	**SBP (mmHg)**	**DBP (mmHg)**	**RBS (mmol/l)**
Yes	42	136.81±2.40[a]	90.74±1.52[a]	5.40±0.14[ay,]
No	1458	127.65±0.46[b]	84.25±0.28[b]	4.74±0.04[b]

Note: Values are expressed as mean ± SEM. Means along column with the different superscripted alphabets are different at $P<0.05$)

Table 4.8: Mean Values of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), And Random Blood Sugar Levels In Relation To Respondents' Body Mass Index (BMI)

BMI	No. of individuals	SBP (mmHg)	DBP (mmHg)	RBS (mmol/l)
Underweight (<18.5)	45	119.09±1.97[d]	79.02±1.12[c]	4.41±0.22[c]
Normal (18.5-24.9)	907	125.03±0.48[c]	82.99±0.33[b]	4.47±0.04[c]
Overweight (25-29.9)	438	130.38±0.81[b]	85.50±0.50[b]	5.04±0.10[b]
Obesity (30& above)	110	145.45±2.78[a]	94.32±1.27[a]	6.17±0.24[a]

Note: Values are expressed as mean ± SEM. Means along column with the different superscripted alphabets are different at P<0.05)

Table 4.9: “Blood Pressure Status” Distribution In Relation To Respondents’ Gender

Gender	No of individuals	Blood Pressure Status: Frequency (%)			Chi-square	Df	P value
		Normal	Pre-hypertension	Hypertension			
Male	750 (100)	230 (30.7)	383 (51.1)	137 (18.3)	1.635n.s	2	0.441
Female	750 (100)	253 (33.7)	368 (49.1)	129 (17.2)			

n.s = non-significant at P > 0.05.

4.10 Blood Pressure Status Distribution by Respondents' location

In the urban settlements respondents in Asikolaiye had the highest number of people whose blood pressure were within the normal range, respondents in AngwanMaigero had the highest number of people that were pre- hypertensive and the highest number of people that were hypertensive was found in AngwanPama. In the rural settlements the highest number of people with normal blood pressure was found in Kasabere, Kusheba had the highest number of pre- hypertensive and hypertensive individuals as shown in Table 4.10.

4.11 Blood pressure status distribution by respondents' residence

Respondents in the urban settlements had higher and highly significant ($p<0.05$) prevalence of hypertension compared to respondents in the rural settlements.

4.12 Blood Pressure Status Distribution by Occupation

Pensioners had the highest prevalence of hypertension that was highly significant ($p<0.05$) compared to other occupations. Civil servants and students have the highest percentage of pre-hypertensive individuals while students have the highest percentage of individuals with normal blood pressure status with a prevalence of 39.2% as shown in Table 4.12.

4.13 Blood Pressure Status Distribution by Age Category

Blood pressure level increased with an increase in age. The young age group had the lowest prevalence followed by the middle aged group and highest prevalence was found among the elderly age group. The differences in their prevalence were highly significant ($p< 0.05$) as shown in table in 4.13

Table 4.10: “Blood Pressure Status” Distribution In Relation To Respondents’ Location

Blood Pressure Status: Frequency (%)				
Settlement	**No of individuals**	**Normal (mmHg)**	**Pre-hypertension (mmHg)**	**Hypertension (mmHg)**
AngwanBoro	100	10	58	32
AngwanPama	100	11	49	40
AngwanMaigero	100	13	72	15
Angwan Sunday	100	12	61	27
Sabo GRA	100	14	62	24
Angwan Dodo	100	18	55	27
Narayi	100	17	61	22
Barnawa	100	19	62	19
Asikolaiye	100	20	50	30
AngwanRomi	100	19	54	27
TOTAL	**1000**	**153(15%)**	**584(58.4%)**	**263(26.3%)**
BarkinKasuwa	50	24	26	0
Kusheba	50	15	33	2
GidanBarde	50	25	25	0
IriGida	50	40	9	1
Gama Chuwa	50	33	17	0
Bishni	50	32	18	0
Akole	50	38	12	0
K. Kwara	50	40	10	0
Chakwama	50	40	10	0
Kasabere	50	43	7	0
TOTAL	**500**	**330(65.5%)**	**167(32.9%)**	**3(0.6%)**

** = highly significant at $P < 0.05$.

Table 4.11: “Blood Pressure Status” Distribution In Relation To Respondents’ Residence

Residence	No of individuals	Blood Pressure Status: Frequency (%)			Chi-square	Df	P value
		Normal	Pre-hypertension	Hypertension			
Urban	1000 (100)	153 (15.3)	584 (58.4)	263 (26.3)	431.860**	2	0.000
Rural	500 (100)	330 (66.0)	167 (33.4)	3 (0.6)			

** = highly significant at $P < 0.05$.

Table 4.12: “Blood Pressure Status” Distribution In Relation To Respondents’ Occupation

Occupation	No of individuals	Blood Pressure Status: Frequency (%)			Chisquare	Df	P value
		Normal	Pre-hypertension	Hypertension			
Civil servant	178 (100)	27 (15.2)	94 (52.8)	57 (32.0)	157.694**	8	0.000
Unemployed	130 (100)	30 (23.1)	63 (48.5)	37 (28.5)			
Pensioner	12 (100)	2 (16.7)	1 (8.3)	9 (75.0)			
Businessperson	312 (100)	83 (26.6)	139 (44.6)	90 (28.8)			
Student	868 (100)	340 (39.2)	454 (52.3)	74 (8.5)			

** = highly significant at $P < 0.05$.

Table 4.13: “Blood Pressure Status” Distribution In Relation To Respondents’ Age Category

Age Group	No of individuals	Blood Pressure Status: Frequency (%)			Chi-square	Df	P value
		Normal	Pre-hypertension	Hypertension			
Young (<40)	1226 (100)	408 (33.3)	645 (52.6)	173 (14.1)	65.566**	4	0.000
Middle-aged (40-65)	256 (100)	72 (28.1)	100 (39.1)	84 (32.8)			
Elderly (>65)	16 (100)	12 (12.4)	4 (25.0)	10 (62.5)			

** = highly significant at $P < 0.05$.

4.14 Blood Pressure Status Distribution by Smoking Habit

Respondents who had the habit of smoking had 63.6% prevalence of pre-hypertensive, 27.3% hypertensive and just 9.1% respondents having normal blood pressure compared to non-smokers that had 50.0% individuals pre-hypertensive and 17.7% are hypertensive but higher number of individuals with normal blood pressure status with prevalence of 32.3%. No significant ($p<0.05$) difference was statistically found for the parameter as shown in Table 4.14

4.15 Blood Pressure Status Distribution by Drinking Habit (Alcohol)

Respondents who consumed alcohol had a higher and highly significant ($p< 0.05$) prevalence of hypertension compared to the non- alcoholics who had32.9% normal, 49.6% pre- hypertensive and 17.5% hypertensive individuals as shown in Table 4.15.

4.16 Blood Pressure Status Distribution by Body Mass Index (BMI)

Blood pressure value increased highly significantly ($p< 0.05$) with increase in body weight. Obese individuals had the highest prevalence of 55.5% while the lowest prevalence of 4.4%was found among those that were under weight as shown in Table 4.16.

4.17 Correlation coefficient of measured parameters

There was a strong, positive, and significant relationship between BMI and WEIGHT, a positive and significant relationship between SBP and DBP, a slight positive relationship also existed between RBS, SBP and DBP. Every other parameter had weak but positive relationship with each other except BMI that had a negative relationship with HEIGHT as shown in table 4.17.

Table 4.14: Blood Pressure Status" Distribution In Relation To Respondents' Habit (I smoke, I don't smoke)

Smoke	No of individuals	Blood Pressure Status: Frequency (%)			Chisquare	Df	P value
		Normal	Pre-hypertension	Hypertension			
Yes	11 (100)	1 (9.1)	7 (63.6)	3 (27.3)	2.797n.s	2	0.247
No	1489 (100)	481 (32.3)	744 (50.0)	264 (17.7)			

n.s = non-significant at P > 0.05.

Table 4.15: Blood Pressure Status" Distribution In Relation To Respondents' Habit (I drink, I don't drink)

Alcohol	No of individuals	Blood Pressure Status: Frequency (%) Normal	Pre-hypertension	Hypertension	Chisquare	df	P value
Yes	42 (100)	2 (4.8)	28 (68.7)	12 (28.6)	15.269**	2	0.000
No	1458 (100)	480 (32.9)	723 (49.6)	255 (17.5)			

** = highly significant at $P < 0.05$.

Table 4.16: Blood Pressure Status" Distribution In Relation To Respondents' Body Mass Index (BMI)

BMI	No of individuals	Blood Pressure Status: Frequency (%)			Chi-square	df	P value
		Normal	Pre-hypertension	Hypertension			
Underweight (<18.5)	45 (100)	26 (57.8)	17 (37.8)	2 (4.4)	173.387**	6	0.000
Normal (18.5-24.9)	907 (100)	336 (37.0)	472 (52.0)	99 (10.9)			
Overweight (25-29.9)	438 (100)	110 (25.1)	223(50.9)	105 (24.0)			
Obesity (30& above)	110 (100)	10 (9.1)	39(35.5)	61(55.5)			

** = highly significant at P < 0.05.

Table 4.17 Pearson correlation Coefficient between the measured parameters

	RBS	SBP	DBP	WEIGHT	HEIGHT	BMI	AGE
RBS	1						
SBP	0.463	1					
DBP	0.408	0.684*	1				
WEIGHT	0.227	0.326	0.290	1			
HEIGHT	0.009	0.053	0.012	0.003	1		
BMI	0.265	0.329	0.286	0.801**	-0.240*	1	
AGE	0.222	0.276	0.213	0.345	0.059	0.301	1

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

CHAPTER FIVE

5.0 DISCUSSION

The prevalence of hypertension in the urban areas was 26.4% and 0.6% in the rural. The urban prevalence rate was similar to those reported by Imaad, (2012) in his study conducted in India where he got a prevalence of 23.7% in urban but 18.3%in rural although different methodology was used.

In the present study male had a higher prevalence of hypertension compared to female. The prevalence of hypertension was 18.6% in male and 17.1% in female, but this difference was found to be statistically insignificant. Imaad, (2012)reported 23.5% in male and 19.2% in female. A large number of epidemiological studies have inferred that prevalence of hypertension is more in male compared to female. This is because during adolescent and middle age male have a higher blood pressure compare to female. The female hormones estrogen and progesterone have a protective effect on blood pressure. Later in life this difference diminishes mainly because of the postmenopausal changes (WHO, 1996).

The present study found increasing age to be an important non- modifiable risk factor for the development of hypertension. The prevalence of hypertension was 14.1% in the age group 18- 39, which increased to 62.5% for people of age 65 and above. The main reason for increase in blood pressure with increase in age is that arteries and arterioles become less elastic due to artherosclerotic changes as people age. Changes in life style and stress are also important contributors. Imaad, (2012) reported 6% in the age group of 20- 29 and 52.4% for people age 70 and above.

Pensioners had the highest prevalence of hypertension, followed by civil servant and business persons in this present study. All these occupation have sedentary type of job and higher mental stress as a common factor which may have a contributory factor in the development of hypertension. Students have the lowest prevalence of hypertension of 8.5%. A study conducted by Ghosh*etal.*, (1983) in Shimla found the prevalence of hypertension to be more among professionals, executives and traders as compared to the occupation involving semi-skilled and unskilled persons. This is because physical activity can slow the initiation and development of diabetes and the sequence of CVD through its effect on body weight, insulin sensitivity, glycemic control, blood pressure, fibrinolysis, endothelial function and inflammatory defense systems (Bassuk and Manson, 2005), Physical activity can also lessen triglycerides and have an effect on both LDL and HDL particles sizes (Szapary*et al* 2003)

The prevalence of hypertension was 27.3% among smokers and 17.7% among non-smokers. Tobacco smoke contains various toxic substances like nicotine, tar, acetone, benzene, hydrogen cyanide, carbon- monoxide which are known to increase the blood pressure by their vaso- constriction action. Smoking is assumed to cause coronary thrombosis by increasing the formation of coronary plagues, destabilizing coronary plagues, promoting plague split, increasing platelet activation and causing endothelial dysfunction. In addition, smoking causes coronary spasms by increasing catecholamine release (Glick, 2002). The frequency and duration of use are also important factors which influence the development of hypertension in people who smoke.

Alcohol consumption was found to be a highly significant risk factor for the development of hypertension. The prevalence of hypertension was 28.6% among people who

consumed alcohol and 17.5% among those who were non- alcoholic. The mechanisms by which alcohol causes elevation of blood pressure include a direct pressor effect of alcohol on the vessel wall, a sensitization of resistance vessels to pressor substances, stimulation of sympathetic nervous system and increased production of adrenocorticoid hormones (Anand, 1995). Imaad, (2012) observed a prevalence of 29.8% among people who consumed alcohol and 19.7% among those who were non- alcoholic.

Highly significant association was found between body mass index and hypertension. The prevalence of hypertension was 55.5% among those that are obese while the prevalence among those with normal BMI was 10.9%. Obesity causes hypertension by activating the rennin- angiotensin- aldosterone system, increasing sympathetic activity, promoting insulin resistance and leptin resistance, increased cholesterol levels, increased procoagulatory activity and by endothelial dysfunction. Further mechanisms include increased renal sodium reabsorption, causing a shift to the right of the pressure natriuresis relationship and resulting in volume expansion (Wofford and Hall, 2004). Majority of researchers have found increased BMI to be a risk factor for hypertension. Imaad, (2012) reported 39.5% among those who had BMI $\geq$ to 25. Similar results were obtained by Tesfaye, (2009) in Sweden where it was reported that BMI $\geq$ 25 is significantly associated with both systolic and diastolic blood pressure.

CHAPTER SIX

6.0 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

6.1 SUMMARY

The prevalence of hypertension was 17.8% in the present study, which is comparable to the estimates given by WHO. Around32% in the population had blood pressure in the normal range and 50% of the population had pre-hypertension. The prevalence of hypertension was 26.4% in the urban areas and0.6% in the rural areas. The difference was found to be statistically highly significant. Increasing age, sedentary occupation, alcohol consumption and body mass index were identified as risk factors for the development of hypertension

6.2 CONCLUSIONS

I. Systolic and Diastolic blood pressure and Random blood sugar levels were higher in the male gender compared to the female gender; higher in urban settlements compared to rural settlements; higher in people who engaged in occupation with less activity level but higher mental stress compared to people who engaged in active but less mental stress; in alcoholics and smokers as compared to people who do not drink alcohol or smoke; increased with an increase in age and BMI

II. From this investigation, it can be concluded that hypertension is more prevalent in the male gender (18.3%) compared to the female gender (17.2%), in urban settlements (26.3%) compared to the rural settlements (0.6%).Obese individuals (55.5%) are at risk of hypertension compared to normal weight people (10.9%);people who consumed alcohol (28.6%) compared to those who don’t consume alcohol (17.5%);people who

hadoccupation with less activity level but higher mental stress (75.0%)compared to people engaged in active and less mental stressed occupation (8.5%); in older people (62.5%) as compared to the young and middle aged people (32.8%); in people who smoke (27.3%) as compare with peoplewho do not smoke (17.7%).

6.3 RECOMMENDATIONS

Inlight of the findings of the present study the following recommendations are made regarding prevention and control of diabetes mellitus and hypertension:

I. A relatively large proportion of the population (17.8%) is suffering from hypertension, it is imperative to have a dedicated national health programme focusing solely on prevention and control of diabetes mellitus and hypertension and not as a subcomponent of any national health programe. This programme should promote the prevention of diabetes mellitus and hypertension by providing culturally sensitive educational messages and lifestyle support services. High risk screen and prompt treatment should be done.

II. Inculcation of healthy lifestyles should be promoted. These include regular physical exercise, abstinence from smoking tobacco chewing and alcohol consumption.

III. High risk screening is preferable to mass screening of population for early diagnosis of diabetes mellitus and hypertension in a developing country like Nigeria because of financial constraints. In the current study around 47.7% of hypertensive were age more than 40years, hence high risk screening is recommended in all people aged more than 40 years

IV. Primordial prevention can play a very crucial role in preventing the occurrence of hypertension and diabetes mellitus. This can be achieved by inculcating habits in

children, as many risk factors of diabetes mellitus and hypertension identified in the current study are known to originate during childhood. Primordial prevention should be a part of school health services involving active participation of teachers to prevent emergence of risk factors of diabetes mellitus and hypertension. This has an added advantage that along with the prevention of hypertension and diabetes mellitus these activities will also reduce many other non- communicable diseases

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APPENDICE I

1.1 Sample Size

1.1.1 Sample size Calculation for Diabetes Mellitus

Sample size was calculated using the formula $n = \frac{t^2 x\ p\ (1-p)}{m^2}$

Where n = required sample size

t= confidence level at 95% (standard value of 1.96)

p= estimated prevalence of hypertension and diabetes

m= margin of error at 5% (standard value of 0.05)

$$n = \frac{1.96^2 x 0.11\ (1 - 0.11)}{0.05^2}$$

$$= \frac{0.3761}{0.0025}$$

$$= 150$$

1.1.2 Sample Size Calculation for Hypertension

$$n = \frac{1.96^2 x 0.225\ (1 - 0.225)}{0.05^2}$$

$$= \frac{0.6699}{0.0025}$$

$$= 268$$

Total sample size is =150+268

=418

APPENDICE II

DEPARTMENT OF BIOLOGICAL SCIENCES, AHMADU BELLO UNIVERSITY, ZARIA, KADUNA STATE.

QUESTIONNARIE

I am a student of the above named institution and would like to conduct a study on my project titled; COMPARATIVE STUDY OF RANDOM BLOOD GLUCOSE AND BLOOD PRESSURE LEVELS IN URBAN AND RURAL SETTLEMENTS OF SOUTHERN KADUNA, KADUNA STATE, NIGERIA.

Your participation in this questionnaire is voluntary and anonymous, I.e. the information will not be associated with names. The information will remain confidential and data will be used for research purposes.

I appreciate and it is very important to me that you answer all questions to the best of your knowledge.

LOCATION Urban ( ) Rural ( )

GENDER Male ( ) Female ( )

AGE

OCCUPATION

SMOKING HABIT I do ( ) I don't ( )

ALCOHOL CONSUMPTION I do ( ) I don't ( )