Kwame Nkrumah University of Science and Technology, Kumasi

COLLEGE OF SCIENCE

DEPARTMENT OF BIOCHEMISTRY AND BIOTECHNOLOGY

PREVALENCE OF PREDIABETES AND DIABETES MELLITUS AMONG CHILDREN AND YOUNG ADULTS IN THE KASSENA NANKANA DISTRICT OF GHANA

SAMUEL SUNYAZI SUNWIALE

SEPTEMBER, 2014

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A THESIS SUBMITTED TO THE DEPARTMENT OF BIOCHEMISTRY & BIOTECHNOLOGY

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF PHILOSOPHY IN BIOCHEMISTRY

SAMUEL SUNYAZI SUNWIALE (BSc)

SEPTEMBER, 2014

DECLARATION

I hereby declare that the experimental work described in this thesis is my own work towards the award of an MPhil degree, and that, to the best of my knowledge, it contains no material previously published by another person or material which has been accepted for the award of any other degree of this university or elsewhere, except where due acknowledgementshavebeen made in the text.

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ABSTRACT

Due to the increasing trend of prediabetes and diabetes, this study investigated the prevalence of these dysglycaemic conditions in children and young people of ages 5 to 20 years old. Furthermore, to assess the presence of some risk factors,the lipid profile of the participants was determined, likewise using a questionnaire to assess information on demographic and lifestyle factors. This study was cross-sectional, and was conducted over a period of five months from January to May of 2012. It was carried out at the Kassena Nankana District in the Upper East Region of Ghana, involving 305 healthy volunteers, randomly sampled from the Navrongo Demographic Surveillance System of the Navrongo Health Research Centre. The socio-demographic characteristics of the participants were investigated, using a structured questionnaire. Anthropometric measurements were also taken, and blood samples from subjects were analysed for fasting blood glucose and lipid profile.The sex distribution of the study participants was 48.2% males and 51.8% females with a mean age of 12.04±4.15 years (± standard deviation). About 49.2% of the respondents were from rural settlements and 50.8% of them were from the urban communities. The mean body mass index (BMI) of the respondents was 18.13±3.6 kg/m^2, whilst 9.8% were overweight and obese, with a BMI $\geq 85^{th}$ percentile specific for age and gender.The mean waist circumference value was 63.3±8.0 cm and 0.63% of the study population had central obesity. The mean fasting blood glucose level was 4.96±0.51 mmol/l, 3.3% and 11.5% of the participants had impaired fasting blood glucose using the WHO/IDF and ADA criteria respectively, while none of the participants had high (diabetic) fasting blood glucose. The mean levels of the lipid profile were as follows; total cholesterol, 3.76±1.14 mmol/l; triglyceride, 0.81±0.51 mmol/l; HDL cholesterol, 1.11±0.36 mmol/l and LDL cholesterol, 2.29±0.94 mmol/l.

Hypertriglyceridaemia was present in 3.0% of the subjects,11.8%of the subjects had high total cholesterol levels, 44.3% of the respondents were with low HDL cholesterol levels whilst high LDL cholesterol was found in 12.8% of the respondents. Through the responses to the questionnaire, 40.3% of the participants and their guardians claimed to have some knowledge of diabetes mellitus. A positive family history of diabetes and hypertension was reported in 7.5% and 23.9% of the participants respectively. There is a positive association between prediabetes and obesity, family history of diabetes and hypertension, total cholesterol, low HDL cholesterol and high LDL cholesterol levels but not with hypertriglyceridaemia. From the prevalence of 3.3% and 11.5% prediabetes obtained in this work, this supports observations from other studies elsewhere that diabetes is a common problem in sub Saharan Africa.Therefore, there is the need for education of the general populace to adopt lifestyles which would not predispose them to hyperglycaemic tendencies, characteristic of prediabetes and diabetes.

ACKNOWLEDGEMENTS

I am grateful and thankful to the Almighty God for seeing me through this programme successfully, especially through all the ups and downs during the research work. May His name be exalted, praised and glorified.

I wish to express my profound gratitude to my supervisors Dr. KwabenaNsiah and Mrs. F.O. Mensah of the Department of Biochemistry and Biotechnology, KNUST for their wonderful supervision, intellectual criticism and guidance throughout this work. I am sincerely grateful for the patience and tolerance they have shown to me during the difficult times of my research work.

My heartfelt gratitude goes to Dr. Abdulai A. Forgor, the Medical Superintendent of the War Memorial Hospital, Navrongo and Dr. Abraham R. Oduro, the Director of the Navrongo Health Research Centre for their advice and invaluable inputs during my sample taking. Furthermore, I appreciate the assistance given to me by the Medical laboratory Scientists of the War Memorial Hospital and Clinical Analysis Laboratory of the Department of Biochemistry, KNUST during the laboratory analysis of my samples.

I am also grateful to the University for Development Studies for granting me the opportunity to pursue a mastersprogramme and for all the assistance during the period of my study.

Finally, my sincere appreciation goes to my family, especially my wife Alice Akulga, my good friend Mr. Yarig Edward Sobe, who in diverse ways contributed to the success of this work. To all I say thank you and God richly bless you.

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ABBREVIATIONS

2HrPBG: 2-hour postprandial blood glucose

ADA: American Diabetes Association

ADP: Adenosine diphosphate

AGE(s): Advanced glycated end product(s)

AMP: Adenosine monophosphate

ATP: Adenosine triphosphate

BMI: Body mass index

CDC: Centre for Disease Control and Prevention

CE: Cholesterol esterase

CO: Cholesterol oxidase

CTLA: Cytotoxic T-cell associated antigen

CVD: Cardiovascular Disease

FA: Fatty acid

FBG: Fasting blood glucose

GADab: Glutamic acid decarboxylase antibody

GK: Glycerol kinase

GLUT: Glucose transporter

GPO: Gylcerol-3-phosphate oxidase

HbA_{1c}: Glycosylated haemoglobin

HDL: High density lipoprotein

HLA: Human leucocyte antigen

ICA: Islet cell autoantibodies

IDDM: Insulin dependent diabetes mellitus

IDF: International Diabetes Federation

IDL: Intermediate density lipoprotein

IFG: Impaired fasting glycaemia

IGT: Impaired glucose tolerance

INS: Insulin gene

LADA: Latent autoimmune diabetes of (in) adults

LDL: Low density lipoprotein

MODY: Maturity-onset of diabetes of the young

MRDM: Malnutrition-related diabetes mellitus

NADPH: reduced Nicotinamide adenine dinucleotide phosphate

NCEP ATP III: National Cholesterol Education Programme Adult Treatment Panel III

NDSS: Navrongo Demographic Surveillance System

NHRC: Navrongo Health Research Centre

NIDDM: Non-insulin dependent diabetes mellitus

OGTT: Oral glucose tolerance test

PHC: Primary Health Care

POD: Peroxidase

TC: Total cholesterol

TG: Triglyceride

UNFPA: United Nations Population Fund

VLDL: Very low density lipoprotein

WHO: World Health Organization

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Currently, diabetes mellitus has been established as a chronic disease affecting people all over the world. The number of people affected increases daily in alarming proportions. It is a major non-communicable disease with a higher incidence in the developed countries (WHO, 1985). There is however, demonstrable evidence to show that the incidence is rising in developing countries with prevalence estimates in Africa of 1% in rural areas and 5-7% in urban sub- Saharan Africa, while estimates of up to 13% has been reported in more developed areas in South Africa and Indian populations (Motala *et al.*, 2003). Globally, the number of people with diabetes in the world is expected to almost double in the next two decades, increasing from 194 million in 2003 to 380 million in 2025 (IDF, 2006). Approximately 70% of the growth of diabetes is predicted to occur in the developing world and will increasingly affect people aged younger than 65 years who are still in the productive stages of their life cycle (Aubert *et al*., 1998) and these growths would be as a result of population ageing and urbanization (Green *et al*., 2004; IDF, 2009).

Diabetes mellitus occurs either as a result of lack of insulin or the presence of factors that oppose the action of insulin which brings about an increase in blood glucose levels. Primarily, diabetes mellitus may be classified into type 1 (insulin-dependent) or type 2 (non insulin-dependent). Type 2 diabetes is most common after middle age and occurs most often at 45-70 years of age, affecting both sexes whilst the peak incidence of type 1 diabetes is at 10-12 years which has a small male predominance (Watkins, 2003). Amoah

(2002), reported that approximately 90% of patients with diabetes are categorized as having adult onset type 2 and 10% are diagnosed with type 1 diabetes.

There are 23.6 million children and adults in the United States alone or 7.8% of the population have diabetes, while an estimated 17.9 million have been undiagnosed with diabetes (CDC, 2003). Watkins (2003) has reported that in the United Kingdom more than 3.0% of the population has diabetes and among school children about 2 in 1000 have diabetes. According to Green *et al*. (2004), developing countries including those of sub-Saharan Africa may experience the largest proportional increase in diabetes mellitus with the projected increase for sub-Saharan Africa being 98% (IDF, 2009). The disorder was previously thought to be rare or undocumented in rural Africa, but over the past few decades it has emerged as an important non-communicable disease in sub- Saharan Africa (Levitt, 2008; Motola *et al.*, 2008).

The prevalence of this condition in Ghana was reported in 1976 to be between 0.2 to 0.4%. (Owusu, 1976) and this prevalence of diabetes in Ghana has increased to 6.3% (Amoah *et al.*, 2002), whilst Vuvor *et al.* (2011) also recorded a crude prevalence of 3.9% in Greater Accra region. According to Oakley *et al.* (1975), the percentages of all cases diagnosed at various ages are 5% for 0-20 years, 10% for 20-40 years, 40% occurring in 40-60 years and 45% occurring in 60 years and above.

Little or no data on diabetes is available from the area targeted for the study, hence the need for this study.

1.2 AIMS /OBJECTIVES OF THE STUDY

This study is aimed at the determination of the prevalence of prediabetes and diabetes mellitus among children and young adults of 5 to 20 years in the Kassena Nankana Districts of Ghana.

The specific objectives are to determine the;

a) blood glucose levels of participants in order to obtain the prevalence of prediabetes and diabetes in the population,
b) anthropometric measurements of the participants,
c) lipid profile; namely total cholesterol, triglycerides, high density lipoproteins and low density lipoproteins of the participants,
d) presence of some risks for diabetes in the participants, including participants' knowledge of diabetes mellitus.

1.3 HYPOTHESIS

Diabetes mellitus is a worldwide problem and occurs in all categories of people, though type 2 diabetes is mainly a condition of adults, recent studies highlight its increasing prevalence in adolescents and children (Reinehr and Wabitsch, 2005). It is therefore hypothesized that some children or young adults in the Kassena-Nankana District of Ghana suffer from diabetes mellitus or have the risk of developing diabetes. Through the study, the hypothesis would be either rejected or proven.

1.4 PROBLEM STATEMENT

Diabetes mellitus has reached epidemic levels worldwide, both in the developed and developing nations; and the health of a large number of people is threatened (King *et al.*, 1998). In type 1 diabetes mellitus (insulin-dependent) there is the loss of insulin production as a result of the destruction of the β-cells of the islets of Langerhans of the pancreas. A combination of environmental and genetic factors that trigger an autoimmune attack on the β-cells is responsible for this destruction and occurs in susceptible individuals. Children and adolescents form a large group of these susceptible individuals and thus can be affected by type 1 diabetes mellitus or become prediabetic individuals. The transition from the early metabolic abnormalities that precede diabetes, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), to diabetes may take many years; however, current estimates indicate that most individuals (perhaps up to 70%) with these pre-diabetic states eventually develop diabetes (Vendrame and Gottlieb, 2004; Santaguida, *et al.,* 2006). The determination of blood glucose levels of individuals is important to identify individuals in the general population, the siblings and the families of diabetic patients who are at higher risk of developing this disease because of their genetic predisposition to diabetes. Complications of diabetes mellitus have been found to set in long before clinical manifestation of the disease (Harris *et al*., 1998; Young and Mustard, 2001). The onset of complications of diabetes mellitus can be reduced if the diagnosis is made early and appropriate treatment is commenced promptly. Diabetes mellitus has a serious impact on those affected and their families, hence the need for early detection and prompt and adequate management.

Prediabetes is a common disorder in most populations and the prevalence appear to vary

among populations with different ethnic backgrounds (Dunstan *et al*., 2002). It is the state in which blood glucose levels are above normal but have not reached those of diabetes. It is an intermediate metabolic state between normal and diabetic glucose homeostasis. It comprises two distinct states, those of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) or a combination of both but by itself is not diabetes. Prediabetes is reported as America's largest health care epidemic and affects about 56 million people in America (Jellinger, 2009). Prediabetes is a long, asymptomatic preclinical phase of diabetes mellitus and it provides an opportunity to intervene to prevent progression to overt diabetes and reduce the associated health and economic burdens (Vinicor *et al.*, 2003). Sometimes, it goes undetected even up to twelve years (Harris *et al.*, 1992).

In Ghana, little studies have been done on prediabetes or diabetes among children and young adults, so this study is intended to fill that knowledge gap.

1.5 EXPECTED BENEFITS

This study would provide baseline information on the prevalence of prediabetes and possibly, undiagnosed diabetes in children and young adults in the study location. Those who are highly at risk would be advised to modify their lifestyle, like increase physical activity and control of their diet so that they can prevent the onset of the disease as well as its complications. Epidemiological data on diabetes mellitus and dyslipidaemia in children and young adults would be provided and this would support measures to be adopted for the prevention and management of the disease and other cardiovascular diseases (CVDs) and this in the long term, would go to improve the health status of people in the district in particular and in Ghana as a whole.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 DIABETES MELLITUS

Diabetes mellitus is a non-communicable disease with a worldwide increasing prevalence. It is a chronic metabolic disease that requires life-long management. It was recognized almost four thousand (4000) years ago and can affect the entire body system and tends to run in families (Mayer, 1981). Generally, diabetes mellitus is a metabolic disorder with multiple aetiology (Alberti and Zimmet, 1998).

Diabetes is as a result of lack of insulin action on carbohydrates, protein and fat metabolism, but abnormalities in glucose metabolism is thought to be the primary disturbance. In some patients, this defect is caused by decrease or non-production of insulin and in others by impaired effectiveness of the insulin that is produced (Mayer, 1981). These result in an increase in blood glucose concentration, known as hyperglycaemia. Uncontrolled chronic hyperglycaemia results in long-term damage, particularly failure of the eyes, heart, blood vessels, nerves and kidneys (Mayer, 1981).

2.2 PREDIABETES

Prediabetes is a state in which blood glucose levels are above normal but have not reached those of diabetes. It is often described as “grey area” between normal blood glucose and diabetic level (Jellinger, 2009). While in this range, individuals are at an increased risk for not only developing diabetes, but also for cardiovascular complications (Jellinger, 2009). It is an asymptomatic state, as the signs of diabetes do not develop at this point. Approximately, 10% to 20% of the general population have prediabetes and

without intervention, approximately two thirds of individuals will develop diabetes within 6 years (Unwin *et al.,* 2002). According to the American Diabetes Association (ADA), people with prediabetes have the likelihood to develop diabetes in about ten (10) years time, unless they lose 5 to 7% of their body weight, by making changes in their diet and level of physical activity. According to Nathan *et al.* (2007), for those with prediabetes, the progression to diabetes mellitus is not inevitable and it is approximately 25% over three to five years. Prediabetes is also referred to as borderline diabetes, impaired glucose regulation; that is, impaired glucose tolerance (IGT), and impaired fasting glucose (IFG).This is a metabolic state intermediate between normal glucose homeostasis and diabetes mellitus (Jellinger, 2009). Even in this state, individuals with prediabetes are at an increased risk of complications associated with diabetes and thus have higher morbidity and mortality than individuals with normal glucose homeostasis (Singleton *et al.,* 2003).

2.3 MAINTENANCE OF BLOOD GLUCOSE LEVELS

Blood glucose levels are maintained within a very narrow range, although the nature of the diet varies widely and the normal person eats periodically during the day and fasts between meals and at night (Dawn, 1999). Even under circumstances when a person does not eat for extended periods of time, blood glucose levels decrease only slowly.

The major hormones that regulate blood glucose levels are insulin and glucagon. Other regulatory hormones are epinephrine (adrenaline), growth hormone, thyroxine and cortisol. During fasting, the liver maintains blood glucose levels by the processes of glycogenolysis and gluconeogenesis. Within the first few hours of fasting, glycogenolysis

is responsible for maintaining blood glucose levels; as a fast progresses and glycogen store decreases, gluconeogenesis becomes an important additional source of blood glucose and after 30 hours, when liver glycogen stores are depleted, gluconeogenesis becomes the only source of blood glucose (Dawn, 1999).

2.3.1 Insulin

Insulin is a small protein (*M*r 5,800) composed of 51 amino acid residues with two polypeptide chains, A and B, joined by two disulfide bonds (Nelson and Cox, 2005). It is synthesized in the pancreas as an inactive single-chain precursor, preproinsulin, with an amino-terminal "signal sequence" that directs its passage into secretory vesicles. Proteolytic removal of the signal sequence and formation of three disulfide bonds produces proinsulin, which is stored in secretory granules in pancreatic β cells. When elevated blood glucose triggers insulin secretion, proinsulin is converted to active insulin by specific proteases, which cleave two peptide bonds to form the mature insulin molecule (Nelson and Cox, 2005).

When glucose enters the bloodstream from the intestine after a carbohydrate-rich meal, the resulting increase in blood glucose causes increased secretion of insulin (and decreased secretion of glucagon).

2.3.2 Mechanism of insulin release in normal pancreatic β-cells.

Insulin production is more or less constant within the beta cells, irrespective of blood glucose levels. It is stored within vesicles pending release, via exocytosis, which is primarily triggered by food, chiefly food containing absorbable glucose. The chief trigger is a rise in blood glucose levels after eating (Longanathan *et al*., 2012).

When blood glucose rises, glucose uptake by the β cells is facilitated by GLUT-2 transporters, where it is immediately converted to glucose 6-phosphate by hexokinase IV (glucokinase). The increased rate of glucose catabolism raises the concentration of ATP, causing the closing of ATP-gated K^+ channels in the plasma membrane. Reduced efflux of K^+ depolarizes the membrane, thereby opening voltage-sensitive Ca^{2+} channels in the plasma membrane. The resulting influx of Ca^{2+} triggers the release of insulin by exocytosis. A simple feedback loop limits hormone release. Insulin lowers blood glucose by stimulating glucose uptake by tissues; the reduced blood glucose is detected by the β cell as a diminished flux through the hexokinase reaction; this slows or stops the release of insulin. This feedback regulation holds blood glucose concentration nearly constant despite large fluctuations in dietary intake (Nelson and Cox, 2005).

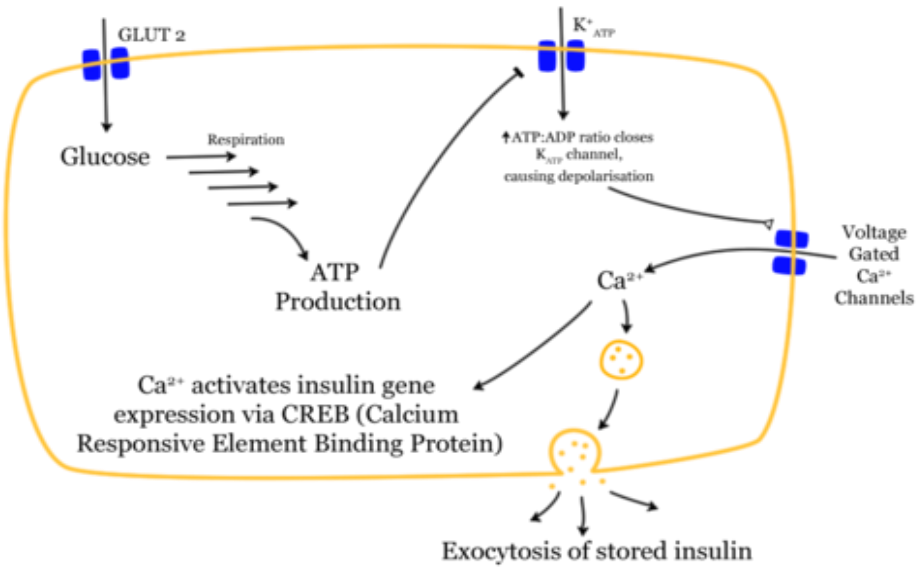


Figure 2.1: Mechanism of insulin release in the β cells of the pancreas (Adapted from Longanathan *et al.*, 2012).

2.3.3 Blood glucose levels in the fed state

After consumption and digestion of a meal, glucose and amino acids are transported from the intestine to the blood. The dietary lipids are packaged in the villi of the small intestines, into chylomicrons and transported to the blood by the lymphatic system (Jeremy *et al.*, 2005). This fed condition leads to the secretion of insulin, in essence, insulin release signals the fed state, as it stimulates the storage of fuels and the synthesis of proteins in a variety of ways. For instance, insulin initiates protein kinase cascades; it stimulates glycogen synthesis in both muscle and the liver and suppresses gluconeogenesis by the liver (Jeremy *et al*., 2005). Insulin also accelerates glycolysis in the liver, which in turn, increases the synthesis of fatty acids.

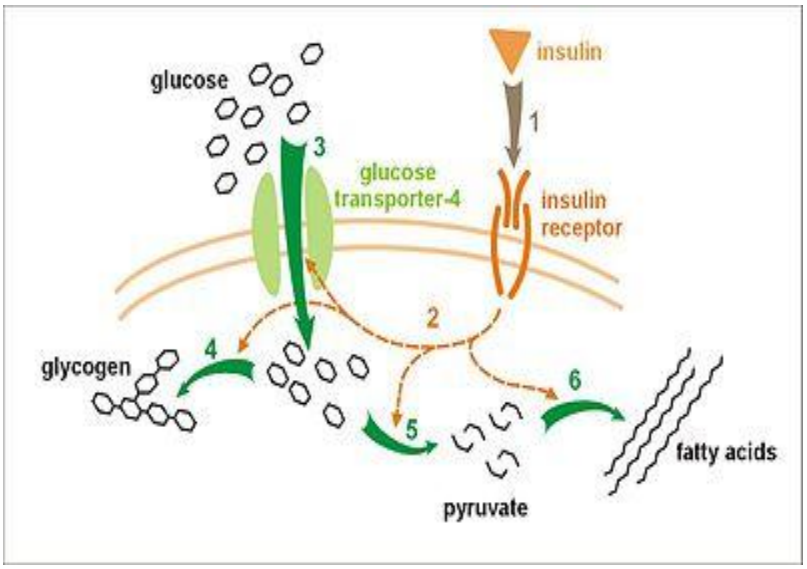


Figure 2.2: Mechanism of insulin regulation of glucose metabolism in the myocytes and adipocytes (Adapted from http://: en wikipedia.org/wiki image: Glucose-insulin-release*).* Insulin binds to its receptor (1) on the cell membrane which in turn, starts many protein activation processes (2). These include: translocation of GLUT-4 transporter to

the plasma membrane and influx of glucose (3), glycogen synthesis (4), glycolysis (5) and fatty acid synthesis (6).

The liver helps to limit the amount of glucose in the blood during times of plenty by storing it as glycogen so as to be able to release glucose in times of scarcity. Insulin accelerates the uptake of blood glucose into the liver by GLUT-2. The level of glucose 6-phosphate in the liver rises because of high levels of glucose in the blood. Glucokinase is active only when blood-glucose levels are high, consequently, the liver forms glucose-6-phosphate more rapidly as the blood glucose level rises. The increase in glucose 6-phosphate, coupled with insulin action leads to a build-up of glycogen stores. The hormonal effects on glycogen synthesis and storage are reinforced by a direct action of glucose itself (Jeremy *et al.*, 2005). On the other hand, glucagon levels decrease as blood glucose levels increase; this prevents the breakdown of glycogen to glucose.

2.3.4 Blood glucose levels in the fasting state

In normal subjects, fasting blood glucose is maintained constant by control of hepatic glucose output. After an overnight fast, approximately 75 % of hepatic glucose output is accounted for by glycogenolysis and the rest by gluconeogenesis from lactate, alanine, glycerol and pyruvate in decreasing order of importance (Hers and Hue, 1983). Hepatic glucose output is controlled by basal levels of insulin and glucagon. The blood-glucose level begins to drop several hours after a meal, leading to a decrease in insulin secretion and a rise in glucagon secretion; glucagon is secreted by the α-cells of the pancreas in response to a low blood-sugar level in the fasting state. Just as insulin signals the fed state, glucagon signals the fasting state. It serves to mobilize glycogen stores when there is no dietary intake of glucose. The main target organ of glucagon is the liver.

Glucagon stimulates glycogen breakdown and inhibits glycogen synthesis by triggering the cyclic AMP cascade, leading to the phosphorylation and activation of phosphorylase *a* and the inhibition of glycogen synthase. Glucagon also inhibits fatty acid synthesis by diminishing the production of pyruvate and by lowering the activity of acetyl CoA carboxylase by maintaining it in an unphosphorylated state (Jeremy *et al*., 2005). In addition, glucagon stimulates gluconeogenesis in the liver and blocks glycolysis by lowering the level of fructose-2,6- bisphosphate (F-2,6-BP). All known actions of glucagon are mediated by protein kinases that are activated by cyclic AMP (Jeremy *et al.*, 2005).

2.4 CLASSIFICATION OF DIABETES MELLITUS

According to Watkins (2003), type 1 and type 2 diabetes mellitus are the two commonest forms of primary diabetes. This division is important both clinically in assessing the need for treatment, and also in understanding the causes of diabetes (Watkins, 2003). Diabetes mellitus can also be classified into four principal types (WHO, 1999). These include type 1 diabetes, type 2 diabetes, other specific types of diabetes, and gestational diabetes mellitus.

2.4.1 Type 1 diabetes mellitus:

Type 1 diabetes, formerly called insulin-dependent diabetes mellitus (IDDM) is due to an autoimmune destruction of the β-cells of the pancreatic islets of Langerhans, with resulting loss of insulin production. There is therefore, lack of insulin in the body to maintain normal levels of blood glucose. It can be immune-mediated or idiopathic (Watkins, 2003), thus the subclasses of type 1 diabetes are the type 1 autoimmune

diabetes and the type 1 idiopathic diabetes. Type 1 diabetes is also called juvenile-onset diabetes because it primarily occurs in younger people, but may occur in individuals of any age. Children are usually affected by this type of diabetes, although it occurs at all ages and the clinical presentation can vary with age. A combination of environmental and genetic factors is responsible for this because they trigger an autoimmune attack on the β-cells, leading to their destruction, and this occurs in genetically susceptible individuals (Watkins, 2003).

According to Mayer (1981), the characteristics of type 1 diabetes are;

- Patients are insulinopenic (lacking insulin production) and thus depend on exogenous insulin for sustaining life.
- Patients are ketosis-prone, unless treated appropriately.
- There is a frequent presence of pancreatic islet-cell antibodies at diagnosis.
- There is a genetic association between diabetes and certain human leucocytes antigens (HLA) of the major histocompatibility system.

Type 1 autoimmune diabetes mellitus results from an inflammatory autoimmune and T-cells- mediated destruction of the insulin producing beta-cells of the pancreas, usually leading to an absolute insulin deficiency. Insulin resistance does not play a major role in its pathogenesis (Atkinson and Maclaren, 1994). The rate of destruction of beta cells is quite variable, being rapid in some individuals and slow in others (Zimmet *et al.*, 1994). The rapidly progressive form is commonly observed in children, but also may occur in adults (Humphrey *et al.*, 1998). The slowly progressive form generally occurs in adults and is sometimes referred to as latent autoimmune diabetes in adults (LADA).

Type 1 idiopathic diabetes mellitus is a subclass of type 1 diabetes mellitus that has no known aetiology, but it is likely related to insulin resistance and transient β-cell dysfunction, perhaps because of glucose desensitization (Ramamruthan and Westphal, 2000). In most patients with idiopathic type 1 diabetes, insulin therapy is better in terms of glycaemic control than either oral hypoglycaemic agents or diet therapy alone and that long-term glycaemic control is better maintained with insulin treatment (Pinero-Pilona *et al.*, 2001).

2.4.2 Type 2 diabetes mellitus:

Type 2 diabetes mellitus, formerly non-insulin dependent diabetes mellitus (NIDDM), is due to a decreased secretion of insulin or an inability of the body to respond to insulin action (insulin resistance) either of which may predominate, but both of which are usually present, thus leading to a rise in blood glucose level. It is the most common type of diabetes and was formerly called maturity-onset diabetes, because it mostly occurs from middle-age to old-age. A long asymptomatic stage of diabetes is known to exist causing cellular damage and complications prior to clinical diagnosis (Ramachandran *et al.*, 1996). There are multiple causes to this type of diabetes.

The main characteristics of type 2 diabetes mellitus are as follows;

- High, low or normal insulin level.
- No ketosis, even without treatment.
- Onset primarily at more than 40 years of age but may occur at any age.
- Maturity-onset diabetes of the young (MODY; i.e. occurring in childhood or adolescence.
- Obesity in more than 60% of patients.

- Family history of type 2 diabetes (Mayer, 1981).

Type 2 diabetes is a complex metabolic disorder, triggered by lifestyle factors superimposed on a genetic predisposition, is responsible for approximately 90% of all diabetes, and accounts for most of the public health and cost burden attributable to diabetes (Dunstan *et al*., 2002). Further, although type 2 diabetes is mainly a condition of adults, recent studies highlight its increasing prevalence in adolescents and children (Reinehr and Wabitsch, 2005). The rapid rise of childhood obesity and its causal link to diabetes has led Olshansky and colleagues (2005) to forecast that type 2 diabetes has the potential to result in a decline in the overall life expectancy of the population within the first half of the twenty-first century.

2.4.3 Gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy (Metzger and Coustan, 1998). It occurs when women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy (especially during third trimester of pregnancy). It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy. Women who become pregnant and who are known to have diabetes mellitus which antedates pregnancy do not have gestational diabetes mellitus but have "diabetes mellitus and pregnancy" and should be treated accordingly before, during and after the pregnancy. Approximately 7% of all pregnancies are complicated by GDM (ADA, 2004). The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed (ADA, 2004).

Babies born to mothers with gestational diabetes are typically at increased risk of problems, such as being large for gestational age (which may lead to delivery complications), low blood sugar, and jaundice (Meztger *et al.*, 2008). Gestational diabetes is a treatable condition and women who have adequate control of glucose levels can effectively decrease these risks. Women with gestational diabetes are at increased risk of developing type 2 diabetes mellitus (or, very rarely, latent autoimmune diabetes of Type 1) after pregnancy, as well as having a higher incidence of pre-eclampsia and caesarean section; their offspring are prone to developing childhood obesity, with type 2 diabetes later in life.

The precise mechanisms underlying gestational diabetes remain unknown. The hallmark of GDM is increased insulin resistance. Pregnancy hormones and other factors are thought to interfere with the action of insulin as it binds to the insulin receptor. The interference probably occurs at the level of the cell signaling pathway behind the insulin receptor (Carr and Gabbe, 1998). Since insulin promotes the entry of glucose into most cells, insulin resistance prevents glucose from entering the cells properly. As a result, glucose remains in the bloodstream, where glucose levels rise. More insulin is needed to overcome this resistance; about 1.5-2.5 times more insulin is produced than in a normal pregnancy (Carr and Gabbe, 1998). Insulin resistance is a normal phenomenon emerging in the second trimester of pregnancy, which progresses thereafter to levels seen in non-pregnant patients with type 2 diabetes. It is thought to secure glucose supply to the growing foetus. Women with GDM have an insulin resistance they cannot compensate with increased production in the β-cells of the pancreas. Placental hormones, and to a

lesser extent, increased fat deposits during pregnancy, seem to mediate insulin resistance during pregnancy (Carr and Gabbe, 1998).

It is unclear why some patients are unable to balance insulin needs and develop GDM, however a number of explanations have been given, similar to those in type 2 diabetes, autoimmunity, single gene mutations, obesity, and other mechanisms (Buchanan and Xiang, 2005).

When glucose travels across the placenta (through diffusion facilitated by GLUT-3 carriers), the foetus is exposed to higher glucose levels. This leads to increased foetal levels of insulin (insulin itself cannot cross the placenta). The growth-stimulating effects of insulin can lead to excessive growth and a large body of the baby (macrosomia) (Kelly *et al.,* 2005). After birth, the high glucose environment disappears, leaving these newborns with ongoing high insulin production and susceptibility to low blood glucose levels (Kelly *et al.*, 2005)

2.4.4 "Other specific types" of diabetes

"Other specific types" of diabetes include those due to genetic disorders, infections, diseases of the exocrine pancreas, endocrinopathies, and chemicals or drugs. This last type of diabetes is relatively uncommon. A type of diabetes called MODY (Maturity-onset of Diabetes of the Young) is increasingly seen in adolescents, but this is classified as diabetes due to a specific cause and not as type 2 diabetes (The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997). Diabetes mellitus with a known aetiology, such as secondary to other diseases, known gene defects, trauma or surgery, or the effects of drugs, is more appropriately called secondary diabetes mellitus or diabetes due to a specific cause. Examples include diabetes mellitus caused by

haemochromatosis, pancreatic insufficiencies, or certain types of medications for example, the long-term use of steroids (http://en.wikipedi.org/w/index.php?title=Diabetesmellitustype2&oldid=424946479). Genetic defects in β-cell function and genetic defects in insulin action are examples of causes of other specific types of diabetes (ADA, 2012).

2.5 DIAGNOSIS OF DIABETES MELLITUS

The diagnosis of diabetes must always be established by a blood glucose measurement made in an accredited laboratory (Watkins, 2003). It is often prompted by the presence of symptoms such as increased thirst, frequent urination, excessive hunger, unexplained weight loss and others. It is worth to note that the risk factors associated with diabetes cannot be used to diagnose diabetes. The tests used for the diagnosis of diabetes are fasting blood glucose, random (casual) blood glucose and blood glucose after 2-hours of glucose load.

The oral glucose tolerance test (OGTT), previously recommended by the National Diabetes Data Group has been replaced with the recommendation that the diagnosis of diabetes mellitus be based on two fasting plasma glucose levels of 126 mg/dL (7.0 mmol/L) or higher. Other options for diagnosis include 2-hour postprandial blood glucose (2hrPBG) readings of 200 mg/dL (11.1 mmol/L) or higher after a glucose load of 75 g (essentially, the criterion recommended by WHO) or two casual glucose readings of 200 mg/dL (11.1 mmol/L) or higher. Measurement of the fasting blood glucose level is the preferred diagnostic test, but any combination of two abnormal test results can be used. Fasting blood glucose was selected as the primary diagnostic test because it predicts

adverse outcomes (e.g., retinopathy), is much more reproducible than the oral glucose tolerance test and easier to perform in a clinical setting (Jennifer, 1998). The use of glycated haemoglobin (HbA1c) was also recommended for the diagnosis of diabetes mellitus with a cut-point of 6.5% or higher (International Expert Committee, 2009) , provided the test was carried out using a method that is certified by the National Glycohaemoglobin Standardization Program (NGSP) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay.

The choice of the new cut-off point for fasting blood glucose levels is based on strong evidence from a number of populations, linking the risk of various complications to the glycaemic status of the patient. The risk of retinopathy greatly increases when the patient's fasting blood glucose level is higher than 109 to 116 mg/dL (6.05 to 6.45 mmol/L) or when the result of a 2hrPBG test is higher than 150 to 180 mg/dL (8.3 to 10.0 mmol/L). However, the committee decided to maintain the cut-off point for the 2hrPBG test at 200 mg per dL (11.1 mmol/L) because so much literature has already been published using this criterion. They selected a cut-off point for fasting blood glucose of 126 mg/dL (7.0 mmol/L) or higher. This point corresponded best with the 2hrPBG level of 200 mg/dL (11.1 mmol/L). The risk of other complications also increases dramatically at the same cut-off points (Jennifer, 1998).

Blood glucose levels above the normal level but below the criterion established for diabetes mellitus indicate impaired glucose homeostasis. According to ADA (2012), persons with fasting blood glucose levels ranging from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) are said to have impaired fasting glucose (IFG), while those with a 2-hour OGTT level between 140 - 200 mg/dL (7.8 – 11.1 mmol/L) are said to have impaired

glucose tolerance (IGT). It is recommended by WHO/IDF consultation that, fasting blood glucose ranging from 110 to 125 mg/dl (6.1 to 6.9 mmol/l) is considered IFG (WHO, 2006) Both impaired fasting glucose and impaired glucose tolerance are termed prediabetes and are associated with an increased risk of developing type 2 diabetes mellitus. Lifestyle changes, such as weight loss and exercise, are warranted in these patients.

2.6 AETIOLOGY OF DIABETES MELLITUS

The aetiology of diabetes is complicated. In the great majority of cases, there seems to be no single cause of the condition. Among the factors thought to be important in causing diabetes are: age, sex, body weight, genetics, viral factors, immune deficiency, trauma, environment, etc. (Oakley *et al.*, 1975). Type 1 diabetes has a complex aetiology, involving genetic susceptibility and environmental factors. According to Colaguiri (2004), individuals with the common factors as indicated in figure 2.3 are more predisposed to type 2 diabetes;

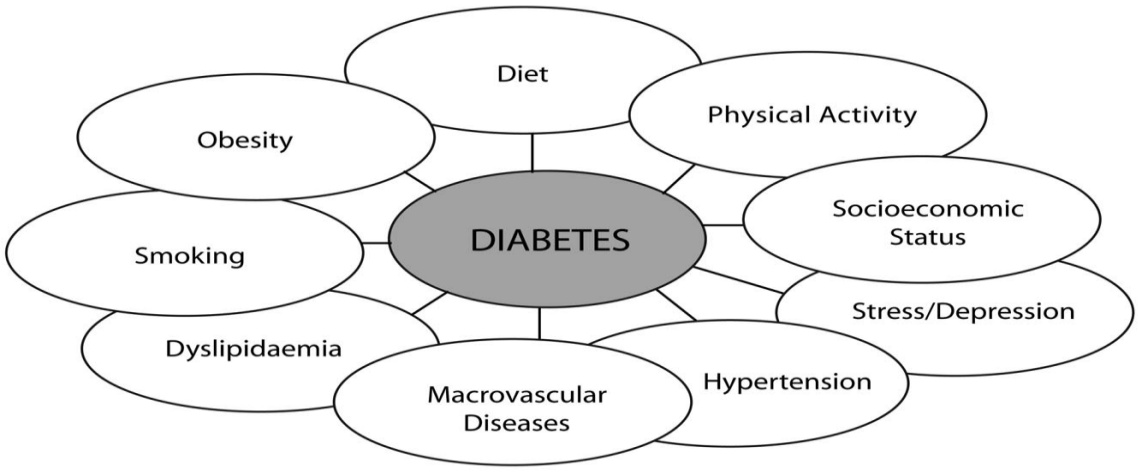


Figure 2.3: **Factors associated with type 2 diabetes as a 'composite' chronic disease.** (Adapted from Colaguiri, 2004).

2.6.1 Age and ethnicity

Age and ethnicity are the two main non modifiable risk factors of diabetes in Africa. Glucose intolerance in sub-Saharan Africa, as in other regions of the world, increases with age in both men and women. According to King *et al.* (1998), in most developed communities the peak of occurrence falls in the age group of 65 years or older, whereas in developing countries it is in the age group 45 to 64, and in sub-Saharan Africa it is in the age groups 20 to 44 and 45 to 64 years. At a later period of the diabetes epidemic, the age at onset will shift to younger age groups and then early-onset type 2 diabetes will emerge (Mbanya *et al.,* 2010).

Two studies in sub-Saharan Africa have examined ethnic differences in the prevalence of diabetes. A difference was found between Indians, Blacks, and Caucasians in South Africa, where Indians had the highest predisposition and were followed by Blacks and Caucasians (Levitt *et al.,* 1999). In a Tanzanian study, the indigenous African population had lower diabetes prevalence than the migrant Asian group (1.1 percent as opposed to 7.1 to 9.1 percent) (Ramaiya *et al.,* 1991). The prevalence of diabetes appears to be substantially higher in African-origin populations living abroad than in indigenous Africans.

2.6.2 Urban-rural differences

Residence seems to be a major determinant of diabetes in sub-Saharan Africa, since many studies have shown that urban residents have two to five times increased risk of diabetes or impaired fasting glycaemia than their rural counterparts (Unwin *et al*., 2006; Mayosi *et al.,* 2009). This is attributable to lifestyle changes associated with urbanization and Westernization. Urban lifestyle in Africa is characterized by changes in dietary habits,

involving an increase in the consumption of refined sugars and saturated fat and a reduction in fibre intake (Mennen *et al*., 2000). Sobngwi and colleagues (2002), have reported an increase in fasting plasma glucose in those whose lives have been spent in an urban environment, suggesting that both lifetime exposure to and recent migration to or current residence in an urban environment are potential risk factors for obesity and diabetes mellitus. The disease might represent the cumulative effects over years of dietary changes, decrease in physical activity, and psychological stress (Sobngwi *et al.*, 2002).

The population of Africa is predominantly rural, but the 1995–2000 urban growth rate was estimated at 4.3 percent (compared with 0.5 percent in Europe). Thus, more than 70 percent of the population of Africa will be urban residents by 2025 (UNFPA, 2000). There will therefore be a tremendous increase in the prevalence of diabetes, attributable to rapid urbanization. In addition, life expectancy at birth is rapidly increasing. An increase in diabetes prevalence simply because of the change in the age structure of the population is therefore expected.

2.6.3 Family history of diabetes

Family history is an important risk factor for the development of type 1 and type 2 diabetes. Studies have shown that people with one or more first-degree relatives who are affected with diabetes are 2 to 6 times as likely to have the disease, compared with people who have no affected relatives (Harrison *et al.*, 2003). More generally, the sibling of a patient with type 1 has a 15-fold higher risk of developing the disease (6%) than does an unrelated individual (0.4%) (Field, 2002). In type 2, the absolute risk to siblings is 30%–40%, as compared to a population prevalence of 7%, providing a relative risk to siblings of four to six folds (Florez *et al.*, 2003). A significant proportion of the offspring of

Cameroonians with type 2 diabetes have either type 2 diabetes (4%) or IGT (8%) (Mbanya *et al.*, 2000).

2.6.4 Measure of adiposity

Several studies from sub-Saharan Africa have confirmed the association between the prevalence of diabetes and a surrogate of obesity, body mass index (BMI). Relative insulin resistance occurs in obese subjects, perhaps because of down-regulation of insulin receptors due to hyperinsulinaemia (Watkins, 2003). Obese subjects have a considerably increased risk of developing type 2 diabetes. Individuals with diabetes in South Africa have more than 50% rate of obesity (Motala *et al.*, 2008). Lobstein *et al.* (2004), stated that "overweight prevalence is high among the poor in rich countries and high among the rich in poor countries". Reports from Nigeria (Cooper *et al.*, 1997) have shown that the prevalence of diabetes increases with increasing BMI.

2.6.5 Physical activity

There seems to be a significant relationship between physical inactivity and diabetes and obesity (Sobngwi *et al.*, 2002). Physical activity is more common in rural than urban regions of Africa because rural populations rely on walking for transport and often have intense agricultural activities as their major occupation. In sub-Saharan Africa, walking time and pace is drastically reduced in an urban community, as compared with a rural community. The main difference in physical activity between the two types of community, however, is the use of walking in rural areas as a means of transportation.

The reduction in physical activity associated with life in a city partly explains the excess prevalence of obesity in urban areas. Cross-sectional data from 1,417 women aged 15 to 83 years in a rural community and an urban community in Cameroon showed that in all

age groups, fasting blood glucose levels were inversely associated with energy expenditure from walking (Sobngwi *et al.,* 2003). Rural dwellers' higher level of physical activity and related energy expenditure, compared with urban subjects goes far to explain why obesity was found to be at least, four times higher in urban areas than rural (Aspray *et al.,* 2000). Thus, lack of physical activity appears to be a significant risk factor for diabetes mellitus.

2.7 EPIDEMIOLOGY OF DIABETES MELLITUS

The global burden of disease study of the World Health Organization (WHO) estimated that about 177 million people in the world had diabetes in the year 2000 (WHO, 2003). In the second edition of the International Diabetes Federation's *Diabetes Atlas* it was estimated that 194 million people had diabetes in the year 2003, and about two-thirds of these people lived in developing countries (IDF, 2003). Estimates from 2009 by the International Diabetes Federation, suggest that the number of adults with diabetes in the world will expand by 54%, from 284.6 million in 2010 to 438.4 million in 2030. The projected growth for sub-Saharan Africa is 98%, from 12.1 million in 2010 to 23.9 million in 2030 (IDF, 2009).

Communicable diseases still make up the greatest disease burden, but by 2020, non communicable diseases, including hypertension and diabetes, will outstrip communicable diseases as the major cause of death throughout the whole world (Murray and Lopez, 1997). The highest prevalence is found in populations of Indian origin, followed by Black populations and Caucasians. The prevalence in Blacks follows a westernization gradient, with that of rural communities in west and east Africa generally below 3% but

that of urban and peri-urban communities in South Africa between 3 and 10% (Mbanya *et al.,* 2010).

The available evidence suggests that non communicable diseases currently contribute substantially to the burden of mortality and morbidity in adults. Age-specific levels of diabetes and hypertension in many urban areas of sub-Saharan Africa are as high as, or higher than, those in most Western European countries (Aspray *et al.,* 2000). Epidemiological studies carried out in that decade, however, provided evidence of a trend toward increased incidence and prevalence of type 2 diabetes in African populations (Sobngwi *et al.*, 2001).

Type 1 diabetes is considerably rarer than type 2 disease, and large populations need to be surveyed. Elamin and colleagues in the Sudan in 1992 reported a survey of nearly 43,000 school children (age 7 to 11 years) and found a prevalence rate of 0.95 per 1,000 and reported an incidence of 10.1 per 100,000 children per year (Elamin *et al.,* 1992). This rate is comparable to a reported prevalence rate of 0.3 per 1,000 in Nigeria (Afoke *et al.*, 1992) and 1.5 per 100,000 per year in Tanzania (Swai *et al.*, 1993).

Nonetheless, it emerges from careful clinic studies that the behavior of type 1 diabetes is different in sub-Saharan Africa from that in the rest of the world. Studies indicate that the age of onset in South Africa and Ethiopia is later than elsewhere, and the peak age of onset of type 1 diabetes in sub-Saharan Africa is a decade later than in the West (Afoke *et al.,* 1992; Kalk *et al.,* 1993). In addition, it afflicts more females than males. In South Africa it has been reported that the peak age of onset was about 13 years in the white South Africans (similar to Europeans) but about 23 years in the black South Africans

(Kalk *et al.*, 1993). The reasons for this difference are obscure, although it has been suggested that prolonged breastfeeding, which is common in Africa, may be reducing the incidence and delaying the onset of type 1 diabetes.

2.7.1 Some factors associated with type 1 diabetes mellitus

2.7.1.1 Genetic factors

More than 90% of type 1 diabetes subjects in sub-Saharan Africa, as in the rest of the world, have one or both human leukocyte antigens (HLA) DR3 and DR4, while DR 2 is protective against diabetes (Watkins, 2003), however there appears to be specificities in the HLA susceptibility found in certain African populations. Important associations have been seen with HLA-B8, HLA-B14, and HLA-B8/B14, and a negative link has been noted with HLA-BW42. Data from studies in which allele-specific probes were used in several populations from sub-Saharan Africa, indicate that type 1 diabetes is associated positively with alleles *DQB*0201*, *DQB*0302*, *DRB*0301*, and *DRB*0401* and negatively with *DQB*0501* (Levitt, 2008; Motala *et al.*, 2008). There is also association between polymorphism in the insulin gene (INS) and type 1 diabetes (Vafiadis *et al.*, 2001).

2.7.1.2 Immunological factors

Prior to clinical onset, autoimmune type 1 diabetes is characterized by lymphocytic infiltration of the islets cells and circulating autoantibodies against a variety of islet cell antigens (Titty, 2010). The most useful autoimmune markers of immune islet cell attack are islet cell autoantibodies (ICAs), glutamic acid decarboxylase autoantibodies (GADab), insulin autoantibodies (IAAs) and the insulinoma antigen 2 (IA-2) autoantibodies (Schatz and Winter, 1995). These substances are found in most Caucasian

type 1 diabetic patients at diagnosis, but levels gradually decline with time. Interpretation of ICA and GADab levels in type 1 diabetes is dependent on duration of disease. In South Africa, Motala *et al.* (2000) found that 44% of blacks with newly diagnosed type 1 diabetes were positive for GADab. Recently, it was reported that the positivity of ICA and GADab was 29.4% and 17.6% respectively in autoimmune type 1 diabetic patients in Ghana (Titty, 2010). It appears from these preliminary results that the genetic susceptibility and risk factors for type 1 diabetes in sub-Saharan Africa may be different from those in the Western world. It can be speculated that non-autoimmune factors are the major determinants of type 1 diabetes in sub-Saharan Africa. More recently, additional evidence has emerged of an autoimmune basis of type 1 diabetes in indigenous Africans. An association between a polymorphism (C159G) of CTLA4 (cytotoxic T-cell-associated antigen-4, a gene known to encode the T-cell receptor responsible for T-cell proliferation and apoptosis was found in West African children with type 1 diabetes and the presence of at least one islet cell antibody (Osei-Hyiaman *et al.*, 2001). Additionally, Pirie *et al.*, (2005) found an association between type 1 diabetes and intron 3 of the toll-like receptor 3 in subject of Zulu descent.

2.7.1.3 Environmental factors

The association of hyperglycaemia with infection has long been recognized, although the overall magnitude of the problem is still somewhat unclear (Joshi *et al.*, 1999). An environmental "trigger" factor for the onset of type 1 diabetes has long been sought. Its existence is supported by the well-known seasonality of presentation in Europe, and viral infection is considered a likely candidate. A seasonality of type 1 diabetes has been reported in Tanzania (with most cases presenting between August and November) (McLarty *et al.*, 1989). It would therefore seem likely that potential viral triggers operate

also in the rest of Africa. Malnutrition during childhood may also result in malnutrition-related diabetes mellitus (MRDM) exhibited at the time of initial presentation and normally manifest as fibrocalcific pancreatitis (Swai *et al.*, 1992).

2.8 PATHOPHYSIOLOGY OF DIABETES MELLITUS

The pathogenesis of diabetes distinguishes type 2 diabetes, resulting from the interaction between insulin resistance and β-cell dysfunction (Polonsky *et al.*, 1996), from type 1 diabetes, in which the autoimmune destruction of pancreatic β-cells leads to absolute insulin deficiency (Eisenbarth, 1986). As a result of lack of insulin production, type 1 diabetes presents with hyperglycaemia which then presents with the characteristic signs and symptoms of polyuria, weight loss, polydipsia, polyphagia and others. Chronic hyperglycaemia results in long-standing diabetes which is associated with severe complications, such as retinopathy, coronary disease, nephropathy, peripheral vascular disease, peripheral neuropathy and other cardiovascular diseases (Florez *et al.*, 2003).

Type 2 Diabetes mellitus is a heterogeneous syndrome of polygenic origin and involves both defective insulin secretion and peripheral insulin resistance. Once diabetes is established, chronic hyperglycaemia and hyperlipidaemia can exert deleterious effects on β-cell function, respectively, referred to as glucotoxicity and lipotoxicity. Over time, both of these phenomena contribute to the progressive deterioration of glucose homeostasis characteristic of this disease (Poitout and Robertson, 2002).

Considerable evidence has been reported suggesting that chronic hyperglycaemia impairs glucose-induced insulin secretion and insulin gene expression (Robertson *et al.*, 2000). Adverse effects of chronic hyperglycaemia on β-cell function encompass three distinct phenomena: glucose desensitization, β-cell exhaustion, and glucotoxicity (Poitout and Robertson, 2002). Glucose desensitization refers to the rapid and reversible refractoriness of the β-cell exocytotic machinery that occurs after a short exposure to elevated glucose and is a physiological adaptive mechanism that occurs even when insulin secretion is inhibited, thus differentiating it from β-cell exhaustion (Kilpatrick and Robertson, 1998). β-Cell exhaustion refers to depletion of the readily releasable pool of intracellular insulin following prolonged exposure to a secretagogue (Leahy *et al.*, 1994). In contrast, the term glucotoxicity describes the slow and progressively irreversible effects of chronic hyperglycaemia on pancreatic β-cell function, which occurs after prolonged exposure to elevated glucose. In addition to inducing functional changes, chronic hyperglycaemia can also decrease β-cell mass by inducing apoptosis (Pick *et al.*, 1998; Donath *et al.*, 1999). The mechanism of glucotoxicity is that, there is impaired insulin gene expression after prolonged exposure to elevated glucose levels. The generation of reactive oxygen species brings about this leading to chronic oxidative stress (Ihara *et al.*, 1999).

Similar to the paradoxically deleterious effects of chronic hyperglycaemia, fatty acids (FAs) which are essential β-cell fuels in the normal state, become toxic when chronically present in excessive levels. Prolonged exposure of pancreatic β-cells to fatty acids increases basal insulin release but inhibits glucose- induced insulin secretion (McGarry and Dobbins, 1999). In addition, excessive fatty acids inhibit insulin gene expression in the presence of elevated glucose levels (Ritz-Lazer *et al.*, 1999). Finally, excessive fatty

acids induce β-cell death by apoptosis both *in vitro* (Cnop *et al.*, 2001) and in ZDF rat islets (Shimabukuro *et al.*, 1998).

2.9 SIGNS AND SYMPTOMS OF DIABETES MELLITUS

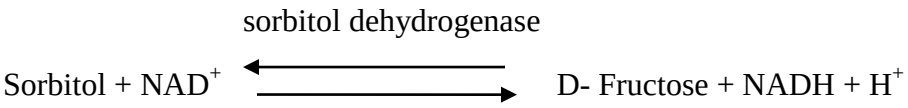
The classical symptoms of diabetes are polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger) (Cooke and Plotnick, 2008). According to International Diabetes Federation (IDF) in addition to the above symptoms, unusual weight loss, increased fatigue, irritability, blurry vision, slow healing wounds and recurrent infections are the "warning signs" of diabetes (IDF, 2007). Symptoms may develop rapidly (weeks or months) in type 1 diabetes while in type 2 diabetes they usually develop much more slowly and may be subtle or absent. The ADA recommends that an individual should see a doctor immediately if one or more of these symptoms are present. Other symptoms significantly associated with type 2 diabetes are erectile/sexual dysfunction, shortness of breath, chest discomfort and other health problems (Clark *et al.*, 2007).

2.9.1 Biochemical basis of signs and symptoms

2.9.1.1 The polyol (sorbitol) pathway

One of the consequences of hyperglycaemia in human diabetes mellitus is increased metabolism of glucose by the sorbitol pathway. This involves the reduction of glucose to sorbitol catalysed by aldose reductase and the oxidation of sorbitol to fructose by sorbitol dehydrogenase.

$$\text{D-Glucose} + \text{NADPH} + \text{H}^{+} \xrightleftharpoons[\text{Sorbitol dehydrogenase}]{\text{Aldose reductase}} \text{Sorbitol} + \text{NADP}^{+}$$



Aldose reductase is present in human brain, nerves, aorta, muscle, erythrocytes and ocular lens. (Das and Srivastava, 1985). Although the purified enzyme has a low affinity for glucose, it can be activated by glucose 6-phosphate, NADPH and glucose (Das and Srivastava, 1985). Sorbitol is not permeable to cell membranes and tends to accumulate in the cell. At high glucose concentration, the flux through the sorbitol pathway in rabbit lens may account for one-third of glucose metabolism (Gonzalez *et al.*, 1984). In the ocular lens particularly, sorbitol concentrations are grossly elevated in diabetic rats, and this may be related to formation of cataracts, at least of the acute type. The increased metabolism of glucose through the sorbitol pathway may be a contributory factor of cataract formation in the lens of the eye of diabetic patients (Teal and Saggers, 1997). In animal models, the accumulation of sorbitol has been linked with microaneuresym formation which are small vascular dilations that occur in the retina. This results in blurry vision and forms cataracts which are often the first signs of retinopathy (Fowler, 2008).

2.9.1.2 Nonenzymatic glycosylation

Glycosylated proteins are thought to be injurious to cells, at high glucose concentration, it can link covalently to many proteins by non-enzymatic reactions. Non-enzymatic glycosylation brings about formation of advanced glycosylation end products (AGEs). Retinal pericyte loss and formation of microaneuresyms are associated with AGEs and are injurious to the peripheral nerves. This injury may start with burning sensations, tingling and “electrical” pain, but sometimes the individual may experience simple numbness (Fowler, 2008). Glycosylation of apoprotein B causes a reduction of affinity

for the low density lipoprotein receptor (Kesaniemi *et al.*, 1983). Glycosylated collagen displays increased intramolecular cross-linking and this may underlie the decreased small joint mobility of longstanding diabetes. The latter has been claimed to be an indicator for the development of microvascular complications (Rosenbloom *et al.*, 1983). Glycosylated haemoglobin has been suggested as a diagnostic and screening tool for diabetes mellitus in the general population (Rohlfing *et al.*, 2000). In acutely ill patients with random hyperglycaemia at hospital admission, a gylcosylated haemoglobin level >6.0% reliably diagnoses diabetes mellitus, and a glycosylated haemoglobin level <5.2% reliably excludes it (Greci *et al.*, 2003). It has been suggested that, in diabetic patients, management plan should be adjusted to achieve normal or near normal glycaemia with a glycosylated haemoglobin goal of <7% (Stratton *et al.*, 2000).

2.9.1.3 Basement membrane thickening

Thickening of basement membranes is a universal finding in longstanding diabetes. After 5 years of clinical diabetes, basement membranes become thicker than in normal subjects (Osterby *et al.*, 1986). The basement membrane matrix, composed of type IV collagen and laminin, is more permeable in diabetes, and thickening may represent a compensatory change (Rohrbach *et al.*, 1982). The role of collagen glycosylation in the pathogenesis of the basement membrane abnormality remains to be elucidated, but it is clear that basement membrane thickening does not antedate metabolic disturbance. Tight metabolic control can partially reverse basement membrane thickening (Raskin *et al.*, 1983). Glycosylation and subsequent thickening of basement membrane of the capillaries in the kidney glomerulus and retina give rise to ocular and renal problems in diabetics (Teal and Saggers, 1997). Glucose uptake by the retina is insulin-independent, and the

retina depends for its energy supply upon anaerobic glycolysis. Aldose reductase inhibitors prevent loss of retinal capillary pericytes and basement membrane thickening, which are thought to be associated with polyol pathway activation. Retinal pericytes contain aldose reductase and loss of retinal pericytes could induce some of the retinal capillary changes observed in diabetes (Akagi *et al*., 1983).

2.10 COMPLICATIONS OF DIABETES MELLITUS

The major source of worry with diabetes is the development of complications arising from the injurious effect of chronic hyperglycaemia and its metabolic abnormalities.

2.10.1 Acute complications of diabetes mellitus

The three main metabolic complications of diabetes are diabetic ketoacidosis (DKA) hyperosmolar nonketotic coma, and hypoglycaemia. These acute metabolic complications of diabetes were considered to be the cause of death in 26 (3.5%), 25 (3.4%) and 17 (2.3%) of patients respectively, in a hospital admissions (Zargar *et al.,* 2009). Complications related to DKA are the commonest cause of death in children, teenagers and young adults with diabetes; it causes up to a third of all deaths in people with diabetes younger than 24 years (White, 2000). The major contributing factors to such high mortality are the chronic lack of availability of insulin, delays in seeking medical assistance by newly diagnosed type 1 patients presenting with ketoacidosis, misdiagnosis of diabetes, and poor health care in general and diabetic care in particular (Rwiza *et al.*, 1986).

Hyperosmolar nonketotic coma is usually a complication of type 2 diabetes and is less common and accounts for about 10 percent of all hyperglycaemic emergencies in

developing countries. Infection is the leading precipitating factor for both diabetic ketoacidosis and hyperosmolar nonketotic coma, followed by non-compliance with a medical regimen (Zouvanis *et al.*, 1997).

Hypoglycaemia, which is largely preventable, is not an uncommon cause of mortality or major morbidity requiring hospitalisation. Hypoglycaemia is a serious complication of treatment in patients with diabetes and is considered to be the primary or contributory cause of death in up to 3.5% of patients with diabetes (Zargar *et al.*, 2009). Of a total of 51 episodes in 43 patients admitted at the Baragwanath Hospital, Johannesburg, South Africa, 14 cases (33%) were associated with sulfonylurea treatment. The major cause precipitating the event was a missed meal (36%), although alcohol (22%), gastrointestinal upset (20%), and inappropriate treatment (18%) were also important contributory factors (Gill and Huddle, 1993).

2.10.2 Chronic complications of diabetes mellitus

Primarily, the chronic complications have been classified as microvascular (that is, diabetic nephropathy, neuropathy, and retinopathy) and macrovascular (that is, coronary artery disease, peripheral arterial disease, and stroke). The associated complications of diabetes make it very serious which can be disabling, and even fatal. Prevalence studies on complications of diabetes have reported figures ranging from 9 to 16% for cataract, 7 to 52% for retinopathy, 6 to 47% for neuropathy, 6 to 30% for nephropathy, and 1 to 5% for macroangiopathy (Mbanya and Sobngwi, 2003). The prevalence of diabetic retinopathy varies from 13 to 55%, depending on the duration of diabetes and glycaemic control, with severe retinopathy representing 15% of all cases. At diagnosis, 21 to 25% of type 2 patients and 9.5% of type 1 patients have retinopathy (Kalk *et al.*, 1997). It is

stated that retinopathy may begin to develop as early as 7 years before the diagnosis of diabetes in patients with type 2 diabetes (Fong *et al.,* 2004).

The prevalence of nephropathy varies between 32 and 57% after a mean duration of diabetes of 5 to 10 years and between 5 and 28% within the first year following the diagnosis of diabetes (Sobngwi *et al.,* 1999). Diabetic nephropathy also occurs early in the course of diabetes, because between 32 and 57% of diabetic patients with a mean duration of diabetes between 5 and 10 years have microalbuminuria (Kalk *et al.,* 1997; Sobngwi *et al.,* 1999). As many as 7% of patients with type 2 diabetes may already have microalbuminuria at the time they are diagnosed with diabetes (Gross *et al*., 2005). In Africa, diabetes mellitus accounts for a third of all patients who are admitted to dialysis units (Diallo *et al.,* 1997). It appears, therefore, that diabetic end-stage renal failure is the first cause of hospital mortality in diabetic patients in Africa. In South Africa, for example, 50% of all causes of mortality in type 1 diabetic patients may be due to renal failure (Gill *et al.,* 1995).

American Diabetes Association recognizes diabetes neuropathy as the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes (ADA, 2007). Macrovascular complications of diabetes are considered rare in Africa despite a high prevalence of hypertension. More than 80% of amputations occur after foot ulceration or injury, which can result from diabetic neuropathy (Boulton *et al*., 2005). A high proportion of patients have lower-limb arterial disease that contributes to the development of diabetic foot lesions. It is common to see patients with diabetic foot ulcers as the presenting complaint of diabetes. Data from Tanzania have shown that the

vast majority (over 80%) of ulcers are neuropathic in origin and not associated with peripheral vascular disease (Abbas *et al.*, 2000).

Data on cerebrovascular disease are scarce because of the mortality associated with this complication, the low proportion of patients seen in hospitals, and the lack of death certificates or proper records of the cause of death. Recent results from the general population of Tanzania where morbidity and mortality surveillance has been set up, show that stroke mortality was three to six times that of England and Wales and that 4.4% of type 2 diabetic patients presented with stroke at the diagnosis of diabetes (Walker *et al.*, 2000). Coronary heart disease may affect 5 to 8% of type 2 diabetic patients and cardiomyopathy up to 50% of all patients with type 2 diabetes. Close to 15% of patients with stroke have diabetes, and up to 5% of diabetic patients present with cerebrovascular accidents at diagnosis. Peripheral vascular disease prevalence varies across sites from 4% to 28% (Kengne *et al*., 2005).

2.11 MORTALITY ASSOCIATED WITH DIABETES MELLITUS

Long-term diabetes is associated with high mortality and morbidity. Mortality attributable to diabetes in sub-Saharan Africa was estimated, in 2010, at 6% of total mortality, an increase from 2.2 – 2.5% in 2000 (Roglic and Unwin, 2010). The absolute and relative mortality rates are highest in the 20-39 year age-group; that is, the most economically productive population (IDF, 2009). Mortality and morbidity studies in diabetes have revealed that two-thirds to three-quarters of patients with diabetes mellitus will eventually die of CVDs (Bloomgarden, 2003). The main CVDs are stroke and heart disease and are now responsible for 30% of the total deaths worldwide (Tunstall-Pedoe,

2006) and is the second leading cause of death in Africa and leading cause of death in those aged 30 years or older (Gaziano, 2008).

There is some evidence, however, that at least, in some parts of Africa the prognosis of diabetes is improving. Interestingly, although metabolic emergencies were still the major cause of death, the mortality from renal failure was substantial, presumably from diabetic nephropathy and large vessel disease. A cohort of type 1 diabetic patients who were followed up in Soweto, South Africa, has also shown relatively prolonged survival (Gill *et al*., 1995). At follow-up after 10 years, with mean diabetes duration of 14 years, only 16 percent had died. This figure was still in excess of Western rates, although almost all these deaths were due to nephropathy, a complication mostly untreatable in Africa even now.

2.12 TREATMENT AND MANAGEMENT OF DIABETES MELLITUS

Diabetes is a complex disorder which needs life-long management. There are three distinctive aspects in management, each of which requires entirely different approaches. The main aims of treatment are to relieve symptoms of hyperglycaemia and to prevent the development of ketosis in those with type 1 diabetes, to prevent or minimize the long-term macrovascular and microvascular complications of diabetes and to minimize the risks of hypoglycaemia (Jerreat, 1999). The main therapeutic approaches are dietary therapy (combined with exercise if possible), drug therapy (oral hypoglycaemic agents) and insulin therapy (WHO, 1994).

2.13 COST OF DIABETES MELLITUS

The chronic nature of diabetes and its devastating complications make it a very costly disease. The cost of diabetes in the U.S. in 2007 was US$174billion (ADA, 2008). In Tanzania about US$4 million would have been required to take care of all patients with diabetes in 1989/90, which translates to US$138 per patient per year. This sum is equivalent to 8.1 percent of the total budgeted health expenditure for that financial year and well above the allocated per capita health expenditure in Tanzania of US$2 for the year 1989/90 (Chale *et al.*, 1992). Estimates of diabetes care management suggest that a type 1 diabetic patient spends about US$100 per year for the purchase of insulin, and a type 2 patient spends US$25 annually on oral hypoglycemic agents (Vaughan *et al.*, 1989). A study in Thailand found that the average cost of illness of diabetes was US$881.47 in 2008 which was 21% of per capita GDP of Thailand and diabetes complications resulted in about 2.5 times higher cost of illness (Chatterjee, 2010), and in Norway the indirect cost of diabetes were estimated to be 70.1 million EURO in 2005 (Solli *et al.*, 2010). For persons aged 20 to 79 years, the ratio of the cost of care for people with diabetes compared with the cost of care for people without diabetes lies between 2 and 3 for countries with high or moderate incomes (IDF, 2003).

2.14 STRATEGIES FOR THE CONTROL OF DIABETES MELLITUS

The problems encountered in the management of diabetes in sub-Saharan Africa include diagnosis, medical care, insulin and other drug supplies, monitoring, infections associated with diabetes, dietary advice, diabetes education, and the low priority placed on non

communicable diseases (Mbanya and Ramiaya, 2006). Health care institutions are thus expected to put in strategies to control the above problems. A few of these strategies are;

1. Provision of infrastructure and health care facilities for diabetic patients to access.
2. Provision of education for people with diabetes to ensure effective self-care, starting from the point of diagnosis and remaining as an essential component of diabetes care thereafter.
3. Dietary and lifestyle support for people with diabetes should be provided.
4. Regular supply of insulin and other hypoglycaemic drugs at affordable cost for diabetic patients.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 STUDY DESIGN

This study was a cross-sectional survey that was conducted over a five-month period, from January to May 2012.

3.2 STUDY SITE (AREA)

The study was carried out in the Kassena Nankana District of the Upper East Region of Ghana. The district shares boundaries with Burkina Faso to the North, the Builsa district to the west, the Bolgatanga Municipality to the East and to the south, West Mamprusi district in Northern region. The district lies between latitudes $10^{o}30'$ and $11^{o}00'$ north of the equator and between longitudes $1^{o}00'$ and $1^{o}30'$ west of the zero meridian and covers an area of 1,675 square kilometers along the Ghana-Burkina Faso border. The map of the district is as shown in appendices I and II. The district measures roughly 50 km long and 55 km wide and has an altitude of 200 - 400m above sea level. The total population of the district as at 31st December 2010 was 153,856 people (NDSS, 2010). The inhabitants are mainly rural, except for those living in Navrongo.

Located in the Guinea savanna belt, the district's ecology is typically sahelian (hot and dry), with the vegetation consisting mostly of semi arid grassland, interspersed with short trees. There are two main climatic seasons, a wet and dry seasons. The wet season extends from April/May to October, with the heaviest rainfall mainly occurring between June and October. The mean annual rainfall is 1365 mm but the highest level is recorded in August. Similarly, the dry season is subdivided into the Harmattan (November to mid

February) and the dry hot (mid February to April) seasons. Monthly temperatures range from 20°C to 40°C with the mean minimum and maximum temperatures for 1999 estimated at 22.8°C and 38.4°C respectively (Nyarko *et al.*, 2008).

3.3 STUDY POPULATION

Three hundred and five (305) children and young adults of age 5 to 20 years were recruited into the study. There were 266 children from 5-17 years and 39 young adults of 18-20 years. They were randomly sampled from the Navrongo Demographic Surveillance System (NDSS) of the Navrongo Health Research Centre (NHRC) which contains the list of individuals and compounds in the district. These were apparently healthy volunteers who agreed and consented or gave assent to participate in the study. Out of the 372 individuals who were randomly sampled, 305 met the inclusion criteria and agreed to participate in the study. The sample size was estimated by using a crude prevalence of 7.0% of diabetes mellitus, an error of margin of ±0.03 at a confidence interval of 95% and a non-response rate of 10%.

3.4 SAMPLING PROCEDURE

The population was stratified by age and clusters. The district, through the NDSS is divided into zones; namely, Central, North, South, East and West zones. Each zone is also partitioned into clusters which contained compounds. Six (6) clusters were sampled from the zones and fifty-one (51) participants were randomly selected from each cluster to give the sample size. Moreover, stratifying by age, there were three (4) strata; 5-9

years, 10-13 years, 14-17 years and 18-20 years, and 105, 87, 74 and 39 participants were respectively sampled from the age groups (strata).

3.5 INCLUSION AND EXCLUSION CRITERIA

Individuals who were of the ages of 5 to 20 years, were apparently healthy, who gave consent to participate, were recruited into the study. These individuals had not eaten at the time of taking the samples, and had had an overnight fast of 10 - 12 hours.

Individuals below 5 years and above 20 years were not eligible to participate, severely-ill individuals that could not respond to the questionnaire were excluded from the study.

3.6 PARTICIPANTS RECRUITMENT

A participant was recruited into the study when the subject was randomly sampled from the list of persons from the clusters in the district; that is, the individual's name, as well as the name and number of the compound the selected participant lived. The individual was followed up to the community for the recruitment. When a subject twelve years or older agreed to participate in the study, a written consent was obtained from the individual while for participants below twelve (12) years an assent was obtained from the child and a written consent was obtained from the parents or guardian of the child. An individual, who was selected and could not be found or did not agree to participate in the study, was replaced with another sex- and age-matched individual from the list. Each participant was recruited into the study a day before the blood sample was taken for the biochemical analysis, so the participants were informed to have an overnight fast for the blood sample analysis the next day.

3.7 QUESTIONNAIRE-BASED DATA COLLECTION

Data were collected through the use of a structured questionnaire. The questionnaire was administered by the researcher to the participant and the information collected included the participant's age, sex, educational background, any family history of diabetes and hypertension, participant's or participant's parents' knowledge of diabetes.

3.8 ANTHROPOMETRIC MEASUREMENTS

For all the participants who were recruited into the study, body weight and height were measured using a standard physician's scale and a wall-mounted meter rule, to the nearest 1.0 kg and 0.005m respectively. These measurements were taken when the subjects were without footwear and wearing light clothe or no clothing but an underwear, in the case of children. The body mass indices (BMIs) of the participants were calculated as weight/height^2 (kg/m^2). Waist circumference was measured with a tape measure in a standing position around the navel or level of the umbilicus to the nearest 0.1cm.

3.9 BIOCHEMICAL MEASUREMENTS

The biochemical measurements made were fasting blood glucose levels, triglycerides, total cholesterol, high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) levels in blood. Blood samples were taken from each participant after an overnight fast of 8-10 hours. A ONETOUCH® Select™ glucometer from LifesScan, Inc. (Milpitas, CA, USA) with serial number AW06505402A was used to measure the blood glucose levels from a finger prick of the participant. Individuals with fasting blood glucose levels greater than 5.6 mmol/L had their tests repeated and the

average values were recorded. About 2.0 millilitres (ml) of venous blood sample was taken from each participant and put into vacutainer tubes. The blood samples in the tubes were centrifuged at 3000 rpm for 10 minutes at room temperature. The blood sera were separated into plain separator tubes and stored in a freezer at -20^{o}C. These samples were kept for a period of two (2) to four (4) weeks and transported to Clinical Analysis Laboratory, at the Department of Biochemistry and Biotechnology of KNUST, Kumasi. The levels of total cholesterol (TC), triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) were then determined. The low density lipoprotein cholesterol (LDL-C) levels were obtained by calculation.

3.10 DIAGNOSTIC CRITERIA

Prediabetes is a general term for blood glucose intolerance. According to WHO and IDF, the cut-off point for impaired fasting glucose is ≥110mg/dl (6.1 mmol/L) and <126mg/dl (7.0 mmol/L) (WHO, 2006), but according to ADA the fasting blood glucose levels ≥100mg/dl (5.6 mmol/L) but <126mg/dl (7.0 mmol/L) were considered to be prediabetes (The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2003). Diabetes was diagnosed when fasting blood glucose was 126 mg/dl (7.0 mmol/l) and higher. Individuals from 5-17 years were grouped regarding their weight status according to the age- and gender-specific BMI growth charts (Cole *et al*., 2000). A BMI exceeding the 85th percentile and less than the 95th percentile for age and gender was considered overweight whilst a BMI exceeding the 95th percentile for age and gender was considered obese. Individuals from 18- 20 years were considered as normal weight if the BMI is <25 Kg/m^2, as overweight when the BMI ranges from 25.0-30.0 Kg/m^2 and is considered

obese when BMI is >30.0 Kg/m^2. Dyslipidaemia in the children (5-17 years) was defined if the fasting blood total cholesterol, triglyceride, LDL cholesterol levels were greater than the 95th percentile for age and gender and when the HDL cholesterol was less than the 5th percentile for both age and gender (Klingman *et al.*, 2007). Dyslipidaemia was considered in the young adults when total cholesterol level was ≥5.2 mmol/l, triglyceride level was ≥2.3 mmol/l, LDL-cholesterol level was ≥ 3.4 mmol/l and if HDL-cholesterol level was <1.0 mmol/l in males and <1.30 mmol/l in females according to NCEP ATP III.

3.11 ETHICAL APPROVAL AND INFORMED CONSENT

The ethical approval of the research protocol was granted by two review boards. Firstly, the Committee on Human Research Publication and Ethics of Kwame Nkrumah University of Science and Technology and Komfo Anokye Teaching Hospital (CHRPE-KNUST/KATH) reviewed and approved it and secondly, it was reviewed and approved by the Institutional Review Board of the Navrongo Health Research Centre (IRB-NHRC).

In the process of seeking informed consent, the aims and objectives of the study, as well as the benefits of the proposed study, were explained to the participants, their guardians and the control population. Moreover, the procedure of work, confidentiality of the information collected, voluntariness to participate, costs or compensation to participation, were all explained clearly to the participants and their guardians before their agreement to participate. Written consent or assent was obtained from each subject or parent/guardian and this was signed or thumb-printed by the participant or the guardian, the investigator

and an independent witness. This was done in duplicate and one form was kept by the investigator and the other form given to the participant.

3.12 STATISTICAL ANALYSIS

The Statistical Package for Social Science (SPSS) version 19.0 for windows was used for the statistical analysis of the data. For continuous variables, means and standard deviations (SD) were calculated, while for categorical variables, proportions were determined. Differences between means were assessed by the analysis of variance (ANOVA). The Chi- square (χ^2) test was used to determine the differences in proportions and logistic regression model was used for the computation of odds ratio for each risk factor. A p-value of <0.05 was considered statistically significant.

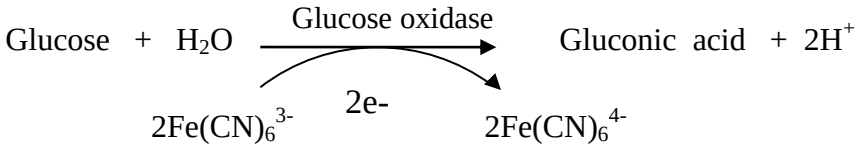
3.13 DETERMINATION OF GLUCOSE

Blood glucose was measured using the Onetouch® select™ glucometer on fresh capillary blood from a finger prick of the participant. The procedure was followed according to the manufacturer's instructions. The glucometer test kit has a control solution. Whenever a new vial of Onetouch® select™ test strips was used it was calibrated with the control solution to make sure it gave reliable results.

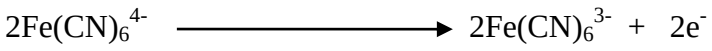
3.13.1 Principle of the determination of glucose using a glucometer.

Glucose can be determined chemically based on its ability to reduce Cu^{2+} ions or alkaline ferricyanide and also through the use of o-toluidine dye. Another method is the enzymatic reaction, like the use of hexokinase, to produce glucose-6-phosphate, which is oxidized by NAD+ to produce NADH, which gives a measure of the amount of glucose present.

The principle used by the Onetouch® select™ glucometer is that the glucose in the blood sample undergoes enzymatic chemical reactions in the test strip. The test area of the test strip is embedded with an enzyme glucose oxidase and other mediators such as hexacyanoferrate III. When blood sample is applied to the test area, the glucose in the blood is enzymatically oxidized by glucose oxidase to gluconic acid, with the release of two moles of electrons, to reduce hexacyanoferrate III ions to hexacyanoferrate II ions.



Subsequently, hexacyanoferrate II ions are oxidized back to hexacyanoferrate III, producing a current which is measured and used to determine the concentration of glucose in the blood sample.



The strength of this current changes with the level of glucose in the blood sample (Hones *et al.,* 2008).

3.14 DETERMINATION OF TOTAL CHOLESTEROL, TRIGLYCERIDES, HDL-C AND LDL-C

Total Cholesterol, HDL cholesterol and triglycerides levels in blood were determined in this study using the Fortress diagnostics reagent kits from FORTRESS DIAGNOSTIC Ltd (Antrim, United Kingdom). The cholesterol reagent kit with product code BXC0261 was used for cholesterol determination, the HDL- C precipitant reagent kit with product code (BXC0422A) was used for LDL precipitation for HDL- C determination and the

triglycerides reagent kit product code BXC0272 was used to determine triglycerides. The instrument used was the Humalyser Junior semi automated chemical analyser manufactured by HUMAN GmbH (Germany) with catalogue number 18050 and serial number 70801. The procedures of work and preparation of the working reagents were as described by the manufacturer. The LDL-C levels were calculated using the Friedewald's formula [LDL-C (mmol/L) = Total Cholesterol (mmol/L) – HDL-C (mmol/L) – Triglyceride/2.2] (Friedewald *et al.*, 1972).

3.14.1 Principle of the determination of total cholesterol.

Cholesterol is present in blood serum as cholesterol esters and free cholesterol. In this method of analysis; the cholesterol esters are hydrolysed by cholesterol esterase (CE) and the cholesterol is then measured by oxidizing with cholesterol oxidase (CO) to form hydrogen peroxide. The hydrogen peroxide in the presence of a peroxidase (POD) in turn, reacts with phenol and 4- aminoantipyrine to form the red quinoneimine dye.

$$\text{Cholesterol Esters} + H_2O \xrightarrow{CE} \text{Cholesterol} + \text{Fatty acids}$$

$$\text{Cholesterol} + O_2 \xrightarrow{CO} \text{Cholest-4-ene-3-one} + H_2O_2$$

$$2H_2O_2 + \text{4-Aminoantipyrine} + \text{Phenol} \xrightarrow{POD} \text{Quinoneimine} + 4H_2O$$

The intensity of the red dye formed is directly proportional to the level of total cholesterol present in the sample. The concentration of total cholesterol in the sample was measure digitally by the Humalyser Junior in millimole per litre (mmol/L).

3.14.2 Principle of the determination of triglycerides.

Triglycerides are enzymatically hydrolysed by lipases to glycerol and fatty acids. Glycerol is phosphorylated to glycerol-3-phosphate by adenosine triphosphate (ATP) in a reaction catalysed by glycerol kinase (GK). The resulting glycerol-3-phosphate is then oxidized in the presence of glycerol phosphate oxidase (GPO) to yield hydrogen peroxide and dihydroxyacetone phosphate. The hydrogen peroxide produced reacts with 4-aminoantipyrine and 4-chlorophenol, in a reaction catalysed by peroxidase (POD) to produce a red dye, quinoneimine.

$$\text{Triglyceride} + H_2O \xrightarrow{\text{lipases}} \text{Glycerol} + \text{Fatty acids}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{GK , Mg2+}} \text{Glycerol-3-phosphate} + \text{ADP}$$

$$\text{Glycerol-3-phosphate} + O_2 \xrightarrow{\text{GPO}} \text{Dihydroxyacetone phosphate} + H_2O_2$$

$$2H_2O_2 + \text{4-aminoantypyrine} + \text{4-chlorophenol} \xrightarrow{\text{POD}} \text{Quinoneimine} + 4H_2O + HCl$$

The intensity of the colour of the red quinoneimine dye is proportional to the concentration of triglyceride in the sample. The concentration of the triglyceride in the sample was measured using the Humalyser Junior in mmol/l.

3.14.3 Principle of the determination of HDL-C.

This method involves two steps. Firstly, the LDL, VLDL and chylomicrons are selectively precipitated by the addition of phosphotungstic acid in the presence of magnesium ions. This prevents them from participating in subsequent reactions. In the second step, the resulting mixture is centrifuged and the HDL fractions remaining in the supernatant reacts with cholesterol esterase (CE) to produce cholesterol which in turn,

become oxidised by cholesterol oxidase to release hydrogen peroxide. The resulting hydrogen peroxide reacts with 4-aminoantipyrine and phenol in the presence of peroxidase (POD) to form the coloured dye, quinoneimine.

Initial step;

$$\text{LDL, VLDL, Chylomicrons} \xrightarrow{\text{precipitant}} \text{precipitate + HDL}$$

$$\text{HDL- C} \xrightarrow{\text{CE}} \text{cholesterol + fatty acids}$$

$$\text{Cholesterol + } O_2 \xrightarrow{\text{CO}} \text{Cholest-4-ene-3-one + } H_2O_2$$

$$2H_2O_2 + \text{4-aminoantipyrine +phenol} \xrightarrow{\text{POD}} \text{Quinoneimine + } 4H_2O$$

The intensity of the dye is proportional to the concentration of HDL-C in the sample. The concentration of HDL-C was recorded digitally by the Humalyser Junior in mmol/l.

3.15 QUALITY CONTROL

To verify the performance of the analysis; for both performance of the reagent and the instrument in the determination, normal and abnormal reference control sera were used. These were the Fortress normal bovine assayed control Catalogue number BCX0313A, Fortress abnormal bovine assayed control Catalogue number BXC0313B, Fortress normal human assayed control Catalogue number BXC0312A and Fortress abnormal human assayed control Catalogue number BXC0312B (Antrim, United Kingdom). All results obtained fell within the specified ranges.

CHAPTER FOUR

4.0 RESULTS

4.1 CHARACTERISTICS OF PARTICIPANTS

The total number of individuals recruited into the study was 305 and this comprised of 147 (48.2%) males and 158 (51.8%) females. Out of this number, 266 (87.2%) were children of 5-17 years and 39 (12.8%) were young adults of 18-20 years. The distribution of male and female between the children and young adults is shown in table 4.1. Among these participants, 57 (18.7%) had no formal education or had not started schooling, whilst 248 (81.3%) were in school or have had some formal education. Thirty-three (10.8%) of the participants were in the pre-primary level, 114 (37.4%) were in the primary level whilst the remaining 101 (33.1%) were in the high school or had gone through high school (Table 4.1).

The mean age of the children was 11.03 ± 3.43 (±S.D.) years and that of the young adults was 18.90 ±0.94. There were 105 (39.5%) of the children from 5-9 years, 87 (32.7%) from 10-13 years and 74 (27.8%) from 14-17 years. There were 138 (51.9%) children from the urban settlements, whilst 128 (48.1%) were resident in the rural communities. The number of males and female children from the urban communities were 73 (23.9%) and 82 (26.9%) respectively and the male and female respondents from the rural settlements were 74 (24.3%) and 76 (24.9%) respectively.The mean BMI of the study population was 18.13 ± 3.6 (±S.D.) kg/m^2. The male and female respondents recorded mean BMI of 17.9 ± 3.4 and 18.33 ± 3.7 respectively. The mean BMI of the children and young adults were 17.52 ± 3.21 and 22.30 ± 3.15 respectively. Females on the average,

recorded a higher BMI than the males, though there is no significant difference between their mean BMI values (p=0.322).

Table 4.1: Baseline characteristics of study participants

	All (n=305)	Children (n=266)	Young adults (n=39)
Age (years)			
Mean	12.04 ± 4.15	11.03 ± 3.41	18.90 ± 0.94
Gender			
Male	147 (48.2%)	130 (48.9%)	17 (43.6%)
Female	158 (51.8%)	136 (51.1%)	22 (56.4%)
Educational Status			
No education	57 (18.7%)	46 (17.3%)	11 (28.2%)
Preprimary	33 10.8%)	33 (12.4%)	0 (0%)
Primary	114(37.4%)	114 (42.9%)	0 (0%)
High School	101 (33.1%)	73 (27.4%)	28 (71.8%)
BMI (Kg/m^2)			
Mean	18.13 ± 3.60	17.52 ± 3.21	22.30 ± 3.15
<85th percentile	275 (90.2%)	244 (91.7%)	31 (79.5%)
85th-95th percentile	24 (7.9%	17 (6.4%)	7 (17.9%)
≥95th percentile	6 (2.0%)	5 (1.9%)	1 (2.6%)
WC (cm)			
Mean	63.3 ± 8.0	61.82 ± 7.15	72.69 ± 5.77

<60	110 (36.1%)	109 (40.9%)	1 (2.6%)
60-80	191 (62.6%)	155 (58.3%)	36 (92.3%)
>80	4 (1.3%)	2 (0.8%)	2 (5.1%)

WC= Waist circumference

It was seen that 244 (91.7%) children were of normal weight (BMI <85th percentile), 17 (6.4%) were overweight (BMI ≥85th percentile and < 95th percentile) and 5 (1.9%) of them were obese (BMI ≥95th percentile) whilst in the young adults, 31 (79.5%), 7 (17.9%) and 1 (2.6%) of them were of normal weight, overweight and obese respectively (Table 4.1).

The lowest and highest waist circumference values of the subjects were 44.0 and 89.5 cm respectively in all the participants. In males the waist circumference values ranged from 48 to 78 cm with a mean value of 62.1 ± 7.16 cm and the range in females was from 44.0 to 89.5 cm with a mean value of 64.5 ± 8.54. It was observed that no male participant had central obesity or had a waist circumference of >104 cm, but 1 (0.63%) of the females had central obesity or had a waist circumference >88 cm.

The levels of fasting blood glucose in all the participants ranged from 3.0 to 6.6 mmol/l, with a mean value of 4.96 ± 0.51 mmol/l. In the children, the mean fasting blood glucose was 4.98 ± 0.52 mmol/l and was 4.83 ± 0.49 in the young adults (Table 4.2). As many as 174 (57.0%) of the participants had low fasting blood glucose level of <5.0 mmol/l, 96 (31.5%) of the participants had normal fasting blood glucose of 5.0 to 5.6 mmol/l. According to the ADA criteria of diagnosis, 35 (11.5%) participants had an impaired

fasting glucose level of 5.6 to 6.9 mmol/l, which comprised of 32 (12.0%) children and 3 (7.7%) young adults, but according to the WHO criteria of diagnosis, 10 (3.3%) of all the participants [comprising of 9 (3.4%) children and 1 (2.6%) of the young adults] had impaired fasting glucose of 6.1 to 6.9 mmol/L and none of the participants had high (diabetic) fasting blood glucose level of >7.0 mmol/l.

From the mean fasting blood glucose levels, according to age groups, the 10-13 years group had the highest mean glucose levels of 5.12 mmol/L, followed by the 5-9 years age group with a mean glucose of 4.93 mmol/l, then the 14-17 years age group with a mean glucose of 4.88 mmol/l and the age group with the lowest mean glucose of 4.83 mmol/L was 18-20 years. These differences were statistically significant (p=0.004).

The levels of total cholesterol in blood ranged from 1.10 to 8.60 mmol/L with a mean value of 3.76 ± 1.14 mmol/l. The mean value in the males of 3.69 ± 0.98 mmol/l was lower than the female value of 3.82 ± 1.28 mmol/l, but the difference is not of statistical significance (p=0.307). The mean total cholesterol for the children and young adults was 3.79 ± 1.19 and 3.64 ± 0.88 mmol/l respectively.

The lowest triglycerides level was 0.18 mmol/L whilst the highest value was 3.65 mmol/L, with a mean value of 0.81 ± 0.51 mmol/l (Table 4.2). The mean levels of triglycerides in the males and females were of 0.82 ± 0.54 mmol/l and 0.79 ± 0.48 mmol/l respectively and they are statistically not different from each other (p=0.568). There was no statistical difference between the mean triglyceride levels of the children and young adults (p= 0.782). It was observed that 9 (3.0%) of the subjects had hypertriglyceridaemia (triglyceride $\geq 95^{th}$ percentile) according to the guidelines for diagnosis of dyslipidaemia

in children (Klingman *et al.*, 2007)). Six (4.1%) of the male population had hypertriglyceridaemia and 3 (1.9%) of the female population were hypertriglyceridaemic.

In the males, the HDL cholesterol levels ranged from 0.31 to 2.40 mmol/L with a mean value of 1.10 ± 0.34 and those in the females were from 0.26 to 2.2 mmol/L and with a mean value of 1.11 ± 0.37 mmol/l (Table 4.6).

Table 4.2: Mean levels and categories of FBG and some lipid profile parameters

	All (n=305)	**Children (n=266)**	**Young adults (n=39)**
FBG (mmol/l)			
Mean	4.96 ± 0.51	4.98 ± 0.52	4.83 ± 0.49
<5.0	174(57.0%)	149 (56.0%)	25 (64.1%)
5.0-5.6	96 (31.5%)	85 (32.0%)	11 (28.2%)
*5.6-6.9	35 (11.5%)	32 (12.0%)	3 (7.7%)
**6.1-6.9	10 (3.3%)	9 (3.4%)	1 (2.6%)
≥7.0	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total Cholesterol (mmol/l)			
Mean	3.76 ± 1.14	3.79 ± 1.19	3.64 ± 0.88
≥5.2	36 (11.8%)	34 (12.8%)	2 (5.1%)
<5.2	269(88.2%)	232 (87.2%)	37 (94.9%)
Triglycerides (mmol/l)			
Mean	0.81 ± 0.51	0.81 ± 0.53	0.81 ± 0.42
≥2.30	9 (3.0%)	9 (3.4%)	0 (0.0%)
<2.30	296(97.0%)	257 (96.6%)	39 (100.0%)

HDL-Cholesterol (mmol/l)			
Mean	1.11 ± 0.36	1.10 ± 0.36	1.14 ± 0.31
<1.00 in males	40 (13.1%)	37 (13.9%)	3 (7.7%)
<1.30 in females	95 (31.1%)	80 (30.1%)	15 (38.5%)
≥1.00 in males	107(35.1%)	93 (35.0%)	14 (35.9%)
≥1.30 in females	63 (20.7%)	56 (21.0%)	7 (17.9%)
LDL-Cholesterol (mmol/l)			
Mean	2.29 ± 0.94	2.32 ± 0.96	2.14 ± 0.81
≥3.40	39 (12.8%)	35 (13.2%)	4 (10.3%)
<3.40	266(87.2%)	231 (86.8%)	35 (89.3%)

*ADA cut-off point for prediabetes

**WHO/IDF cut-off point for prediabetes

The mean HDL level in the children and young adults was 1.10 ± 0.36 and 1.14 ± 0.31 mmol/l respectively. In all, 135 (44.3%) of the total number of participants were with low HDL cholesterol levels. The mean level of HDL cholesterol among the urban dwellers was higher than the level among rural settlers (1.28 versus 0.93 mmol/L) [p=0.000].

In the males, the LDL cholesterol values ranged from 0.23 to 4.99 mmol/l with a mean value of 2.21 ± 0.80 mmol/l, whilst these values ranged from 0.16 to 6.86 mmol/l with a mean value 2.35 ± 1.04 mmol/l in the females. The mean LDL cholesterol value in children was higher than that of the young adults but it was not statistically significant (Table 4.2). High LDL cholesterol values (i.e. ≥ 95^{th} percentile) were recorded in 39 (12.8%) of the total number of the participants, of which 15(38.5%) were males and the

24 (61.5%) were females. There were 35 (13.2%) of children and 4 (10.3%) of the young adults were with high LDL.

4.2 ASSOCIATED RISK FACTORS OF DIABETES MELLITUS IN THE SUBJECTS

Out of the 305 subjects who were screened, 182 (59.7%) of them and their parents or guardians did not have any knowledge of diabetes, whilst the remaining subjects (123) had some general knowledge of what diabetes is. Among the children, 160 (60.2%) of them did not have any knowledge of diabetes whilst 106 (39.8%) had some knowledge of diabetes. Twenty-two (56.4%) of the young adults did not also have any knowledge of diabetes. As many as 106 (86.2%) of all those who had knowledge of diabetes said it was a "sugar disease", mainly caused by eating too much sugar. Eleven respondents (8.9%) said it was an inherited disease that one could acquire from one's parents. The remaining 6 (4.9%) subjects said it was a disease realised when ants gather around an individual's urine. Out of the 123 persons who had knowledge of diabetes, 12 (9.8%) of them were in the pre-primary level of education, 44 (35.8%) of them were in primary school, whilst the remaining 67 (54.5%) were in the high school or had gone through high school. Moreover, out of the 248 individuals who had formal education, 133 (53.6%) of them did not have any knowledge of diabetes, whilst the remaining 115 (46.4%) had knowledge of diabetes. Taking into account the place of residence, out of the number with knowledge of diabetes, 69 (56.1%) were from the urban communities while 54 (43.9%) were from the rural areas. Among the 182 who did not have any knowledge of the disease, 86 (47.3%) were from the urban areas while 96 (52.7%) were from the rural areas.The participants' information on diabetes were from different sources, the most common

being from neighbours, followed by the media (mainly television and radio), from their studies or learnt it in school, from healthcare professionals and from relatives or family members (Fig 4.1).

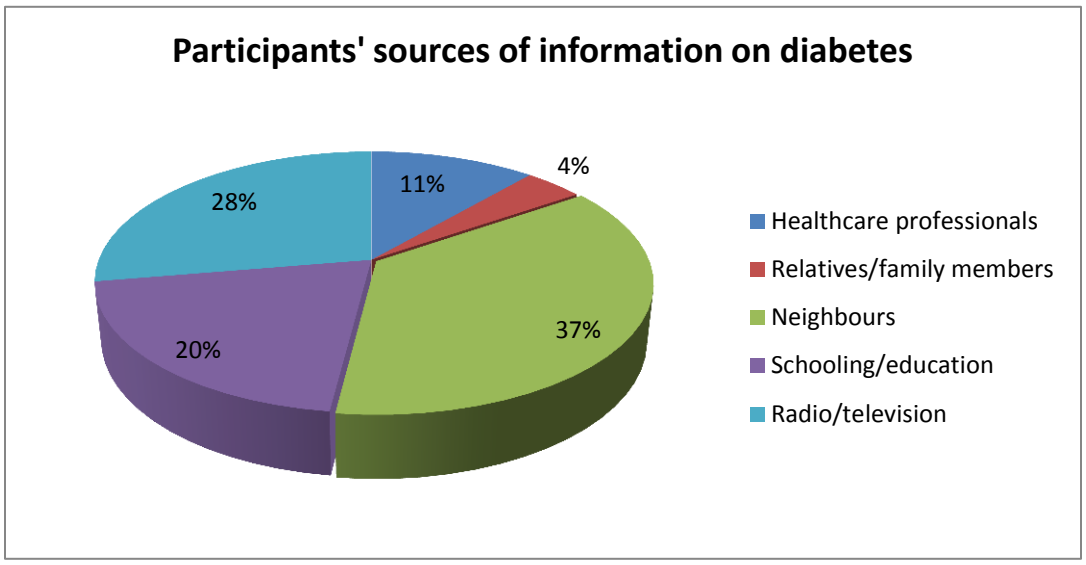


Figure 4.1: Participants' sources of information on diabetes

A positive family history of diabetes and hypertension was observed in 23 (7.5%) and 73 (23.9%) of the participants respectively. Out of those with a positive family history of diabetes 7 (30.4%) of them had a positive parental history of diabetes, 14 (60.9%) of them had their grandparents affected with diabetes whilst the remaining 2 (8.7%) of the respondents had other members of their family with diabetes. The female members of the family with diabetes were 14 (60.9%) individuals and this was higher than the male members of the family with diabetes, 9 (39.1%). It was observed that out of the participants with a positive family history of hypertension, 20 (27.4%) of them had positive parental history of hypertension, 43 (58.9%) of them had their grandparents affected with hypertension and 10 (13.7%) of the participants had other relatives with

hypertension (Table 4.3). More members of the families with hypertension were females, 54 out 73, representing 74%.

Table 4.3: Some risk factors associated with hyperglycaemia

Risk factor	**Hyperglycaemia (n=35)**	**Normoglycaemia (n=270)**	**Significance**
Knowledge of DM			Odds Ratio=0.860
Yes	13 (37.1%)	110 (40.7%)	[95%CI=0.415-1.779]
No	22 (62.9%)	160 (59.3%)	p=0.683
			X^2= 0.167
Family history of DM			
Yes	3 (8.6%)	20 (7.4%)	Odds Ratio=1.172
Parent	1 (2.9%)	6 (2.2%)	[95%CI=0.330-4.165]
Grandparent	2 (5.7%)	12 (4.5%)	p=0.806
Other relative	0 (0%)	2 (0.7%)	X^2= 0.060
No	32 (91.4%)	250 (92.6%)	
Family history of HPT			
Yes	12 (34.3%)	61 (22.6%)	Odds ratio=1.789
Parent	0 (0%)	20 (7.4%)	[95%CI= 0.840-3.802]
Grandparent	8 (22.9%)	35 (13.0%)	p=0.127
Other relative	4 (11.4%)	6 (2.2%)	X^2=2.327
No	23 (65.7%)	209 (77.4%)	

HPT=Hypertension, DM=Diabetes Mellitus, X^2= Pearson's Chi Square

Considering the participants with impaired fasting glucose, 13 (37.1%) of them had knowledge of diabetes whilst 22 (62.9%) did not know anything about diabetes (table 4.3). There was no difference between knowledge of diabetes in the impaired fasting glucose and normoglycaemic subjects (p=0.683). It was also observed that 3 (8.6%) of subjects with impaired fasting glucose had a positive family history of diabetes. For one of them it was the parent who had diabetes, whereas for two of them it was their grandparents. It was also found that 12 (34.3%) of the participants also had a positive family history of hypertension, whereas grandparents with hypertension was observed in 8 (22.9%) participants and 4 (11.4%) observed hypertension in other members of their families. Positive family history of diabetes is similar (p=0.806) in the impaired fasting glucose and normoglycaemic subjects, and a positive family history of hypertension is also similar in both the impaired fasting glucose and normoglycaemic subjects (p=0.127).

Impaired fasting glucose was most prevalent in participants in the age group 10-13 years as 22 (62.9%) of the impaired fasting glucose subjects were in this age group. The mean fasting glucose levels in the normoglycaemic and impaired fasting glucose subjects are statistically not different (p=0.873) from each other. The proportions of males and females with impaired fasting glucose are also not different from each other but the mean total cholesterol levels in subjects with impaired fasting glucose (4.53 mmol/L) is higher than that of the subjects with impaired fasting glucose, which was 3.72 mmol/L (p=0.006). Participants with impaired fasting glucose had higher mean levels of LDL-C than their normoglycaemic counterparts (2.89 mmol/L vrs 2.25 mmol/L) [p=0.008].

Table 4.4: Biochemical characteristics of normoglycaemic and hyperglycaemic subjects

Characteristics	Hyperglycaemic (n= 35)	Normoglycaemic (n=270)	P-value
Age (years)			
Mean	11.9 ± 3.0	12.0 ± 4.3	
5 - 9	6 (17.1%)	99 (36.7%)	
10 - 13	22 (62.9%)	65 (24.1%)	p=0.873
14 - 17	4 (11.4%)	70 (25.9%)	
18 - 20	3 (8.6%)	36 (13.3%)	
Gender			
Male	16 (45.7%)	131 (48.5%)	p=0.755
Female	19 (54.3%)	139 (51.5%)	
BMI (Kg/m^2)			
Mean	18.7 ± 3.3	18.1 ± 3.6	p=0.618
Overweight & obese	4 (11.4%)	26 (9.6%)	
Normal weight	31 (88.6%)	244 (90.4%)	
Total chol. (mmol/l)			
Mean	4.53 ± 1.50	3.72 ± 1.11	p=0.006
≥5.2	7 (20.0%)	29 (10.7%)	
<5.2	28 (80.0%)	241 (89.3%)	
HDL-C (mmol/l)			
Mean	1.22 ± 0.34	1.10 ± 0.36	p=0.208

<1.00 in male	5 (14.3%)	35 (12.9%)	
<1.30 in female	9 (25.7%)	86 (31.9%)	
≥1.00 in male	11 (31.4%)	96 (35.6%)	
≥1.30 in female	10 (28.6%)	53 (19.6%)	
Triglycerides (mmol/l)			
Mean	0.92 ± 0.66	0.80 ± 0.50	p=0.359
≥2.3	2 (5.7%)	7 (2.6%)	
<2.3	33 (94.3%)	263 (97.4%)	
LDL cholesterol (mmol/l)			
Mean	2.89 ± 1.17	2.25 ± 0.91	p=0.008
≥3.4	7 (20.0%)	32 (11.9%)	
<3.4	28 (80.0%)	238 (88.1%)	

On the other hand, there is no statistically significant difference observed in the mean HDL-C levels between the subjects with impaired fasting glucose and normoglycaemic subjects (Table 4.4). There was no difference in the mean triglyceride levels in the participants with impaired fasting glucose and those who were with normoglycaemia (p=0.359).

From table 4.5, the mean fasting blood glucose of participants from the urban and rural communities are statistically not different (p=0.392). The same was realised for the mean fasting blood glucose of the children and the young adults. Furthermore, the mean BMI values of the urban and rural subjects are similar, but the number of subjects who were overweight and obese in the urban communities is higher than those from the rural

communities (19 vrs 11), but the difference is not significant (p=0.588). Though the mean waist circumference of participants from the urban communities was higher than that from the rural communities, there is no statistical difference between them (p=0.123).

Table 4.5: Biochemical characteristics of the rural and urban communities in the children (n=266) and young adults (n= 39)

Characteristics	**5-17 years (n=266)**		**18-20 years (n=39)**	
	Urban	**Rural**	**Urban**	**Rural**
FBG (mmol/l				
Mean	4.95 ± 0.59	5.00 ± 0.42	4.75 ± 0.48	4.88 ± 0.51
≥5.6	17 (12.3%)	15 (11.7%)	1 (5.9%)	2 (9.1%)
<5.6	121 (87.7%)	113 (88.3%)	16 (94.1%)	20 (90.9%)
BMI (Kg/m^2)				
Mean	17.7 ± 3.7	17.4 ± 2.6	21.7 ± 3.3	22.7 ± 3.1
Overweight & obese	15 (10.9%)	7 (4.5%)	3 (17.6%)	4 (18.2%)
Normal	123 (89.1%)	121 (94.5%)	14 (82.4%)	18 (81.8%)
WC (cm)				
Mean	62.7 ± 7.7	60.9 ± 6.4	73.3 ± 5.3	72.2 ± 6.2
>88	0 (0%)	0 (0%)	1 (5.9%)	0 (0%)
≤88	138 (100%)	128 (100%)	16 (94.1%)	22 (100%)
Total Chol. (mmol/l)				
Mean	4.32 ± 1.17	3.22 ± 0.93	3.93 ±1.07	3.41 ± 0.64

≥5.2	29 (21.0%)	5 (3.9%)	2 (11.8%)	0 (0%)
<5.2	109 (79.0%)	123 (96.1%)	15 (88.2%)	22 (100%)
HDL-C (mmol/l)				
Mean	1.28 ± 0.26	0.91 ± 0.36	1.25 ± 0.20	1.06 ± 0.36
<1.00 (men)	8 (5.8%)	30 (23.4%)	0 (0%)	2 (9.1%)
≥1.00 (Men)	58 (42.1%)	34 (26.6%)	7 (41.2%)	8 (36.4%)
<1.30 (Women)	30 (21.7%)	50 (39.1%)	8 (47.1%)	7 (31.8%)
≥1.30 (Women)	42 (30.4%)	14 (10.9%)	2 (11.7%)	5 (22.7%)
Triglyceride (mmol/l)				
Mean	0.63 ± 0.29	1.00 ± 0.65	0.68 ± 0.27	0.91 ± 0.49
≥2.3	0 (0%)	9 (7.0%)	0 (0%)	0 (0%)
<2.3	138 (100%)	119 (93.0%)	17 (100%)	22 (100%)
LDL-C (mmol/l)				
Mean	2.74 ± 0.95	1.85 ± 0.74	2.41 ± 0.91	1.94 ± 0.67
≥3.4	30 (21.7%)	5 (3.9%)	4 (23.5%)	0 (0%)
<3.4	108 (78.3%)	123 (96.1%)	13 (76.5%)	22 (100%)

WC=Waist circumference, FBG= Fasting Blood Glucose

According to table 4.5, participants from the urban communities had a higher mean total cholesterol value than their rural counterparts in both the children group and the young adults group (p=0.000) and more than 90% of participants with hypercholesterolaemia (cholesterol ≥95th percentile) were from the urban communities. Similarly, mean LDL-C in urban subjects was 2.70 mmol/L and this was higher than that of the rural subjects

which was 1.86 mmol/L (p=0.000), and out of the number of participants with high LDL-C values, 34 (87.2%) of them were urban subjects.

On the other hand, from table 4.5, triglyceride levels were higher in the rural subjects than their urban counterparts (p=0.000), and all participants with higher levels of triglycerides (triglyceride ≥95th percentile) were from rural communities.

Table 4.6: Comparism of characteristics between males and females of the study participants

	Male (n=147)		Female (n=158)		
			Mean		P-value
Characteristics	**Mean (SD)**	**C.I.**	**(SD)**	**C.I.**	
Age (years)	11.94 (4.3)	5.0 - 20.0	12.13 (4.0)	6.0 - 20.0	0.693
Waist Circ. (cm)	62.1 (7.2)	48.0 - 78.0	64.4 (8.5)	44.0 - 89.5	0.1
BMI (Kg/m^2)	17.9 (3.4)	11.5 -37.8	18.3 (3.7)	9.7 - 30.1	0.322
FBG (mmol/l)	4.9 (0.52)	3.0 - 6.6	5.0 (0.50)	3.6 - 6.6	0.551
Total chol. (mmol/l)	3.69 (1.00)	1.59 - 6.74	3.82 (1.27)	1.11- 8.60	0.307
HDL-chol. (mmol/l)	1.10 (0.34)	0.31 - 2.4	1.11 (0.37)	0.26 - 2.20	0.862
Triglycerides (mmol/l)	0.82 (0.54)	0.18 - 3.65	0.79 (0.48)	0.19 - 3.02	0.568
LDL-chol. (mmol/l)	2.21 (0.80)	0.23 - 4.99	2.35 (1.04)	0.16 - 6.86	0.186

Circ.= circumference, chol.= cholesterol, C.I.= Confidence Interval

CHAPTER FIVE

5.0 DISCUSSION

5.1 BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS

The total number of people enrolled into this study was 305 respondents made up of 266 children of 5-17 years of age and 39 young adults of 18-20 years old. The percentage of the subjects that were males (48.2) and that of females (51.8), giving a male to female ratio of 1: 1.08, is consistent with the 47.8% and 52.2% of males and females respectively in the Kassena Nankana District, as at December 2010 when the study was carried out (NDSS, 2010). This is also consistent with the national percentages of 48.8 and 51.2 for males and females, respectively.

The largest proportion of the respondents (37.4%) had their highest level of education to be the primary school, followed by 33.1% in high school. The distribution of the level of education of the respondents was as a result of the age range of the study population, as most of them were in an age bracket for enrolment to primary school. As many as 57 (18.7%) of the respondents had no formal education, and a larger proportion of this group, 41 (71.9%) were from the rural communities. This is an indication that although there is Free Compulsory Universal Basic Education (FCUBE) policy in Ghana, a good number of the children of school going age in the rural communities are not enrolled in schools and that could be due to lack of educational facilities for children of school going age in the rural communities, as compared to the urban communities.

The mean body mass index (18.1 Kg/m^2) of the all study participants is similar to a BMI of 17.9 kg/m^2 in type 1 diabetic patients of 9 – 16 years (Hamad and Qureshi, 2008). The children had a mean BMI of 17.5 Kg/m^2 and the young adults had a mean BMI of 22.3

Kg/m^2 The mean BMI of the young adults was similar to the mean BMI of 24.2 kg/m^2 reported by (Gyamfi, 2010), in a general population, and 23.1 kg/m^2 in type 1 diabetic patients in a study by Rosario *et al*. (2005). Lobstein *et al.* (2004) have reported that BMI or obesity increases with age so the low overall mean BMI of the study participants was not surprising because a higher percentage (87.2) of the study population were children.

The study recorded 30 (9.8%) of all the participants to be overweight and obese (BMI > 85^{th} percentile) specific for age and gender (Table 4.4) whilst the number of children and young adults to be overweight and obese to be 22 (8.3%) and 8 (20.5%) respectively. The prevalence of overweight in children is similar to the estimated prevalence of 9.8% of overweight in schoolchildren in the Tamale metropolis in Ghana reported by Amidu *et al.,* 2013. There were more females than males who were overweight and obese (22 versus 8), and several researchers have documented higher obesity in females than males (Armstrong *et al.,* 2006; Acquah *et al.,* 2011). The number of participants who were overweight or obese was greater in the urban communities than rural settlements (17 versus 13). Four of the 35 subjects with impaired fasting glucose (11.4%) were overweight or obese and this is inconsistent with findings of other researchers who demonstrated a high number of individuals with impaired fasting glucose who were overweight or obese (Olatunbosun and Bella, 2000; Hillier and Pedula, 2001).

5.2 BIOCHEMICAL INDICES

Out of the 305 participants studied, 35 (11.5%) respondents had impaired fasting blood glucose, otherwise termed as prediabetes, using the ADA cut-off point of ≥5.6 to 6.9 mmol/l and none of the respondents was with high fasting blood glucose in the diabetic

range. IFG was rather low among the participants (3.3%) when the WHO/IDF cut-off point of ≥6.1 to 6.9 mmol/l of fasting blood glucose was considered. The prevalence of prediabetes was lower than 15.7% recorded by WHO (2006), but higher than 2.1% of impaired fasting glycaemia recorded by Oyegbade *et al.* (2007) in Nigeria. The difference in prevalence might be as a result of the type of population studied. This study dealt with an age bracket of 5-20 years; that is, children and young adults, whilst the other studies dealt with the general or whole population. It is reported that the prevalence of prediabetes differs by age and gender, being more common in females than in males and increasing with advancing age (Shaw *et al.,* 1999; Nathan *et al.,* 2007). The prevalence of prediabetes in this study is higher than the finding made by The Expert Committee on Non-communicable Disease (1997) in Nigeria, which gave a prevalence of 2.2%, but is closer to a prevalence of 7.8% in 2004 in Jordan (Ajlouni *et al*., 2008). The reported prevalence of prediabetes varies from study to study as a result of the different definitions and cut-off points of prediabetes and also as a result of the different populations studied with differing ethnic backgrounds.

The similarity in mean glucose levels for males and females (p=0.551, Table 4.7), is not in conformity with findings documented by a previous study that females recorded higher fasting blood glucose than males (WHO, 2006) and Amoah (2003), who rather reported that fasting blood glucose was higher in males than females.

The mean preprandial (fasting) glucose values of the various age categories are significantly different from each other (p=0.003). The trend of glucose levels within the age groups documented by this study is different from the trend of increasing blood glucose with age found by previous studies (Ko *et al.,* 2006; Gyamfi, 2010). The highest

mean blood glucose was observed in the age category of 10 – 13 years, and this conforms with majority of population studies which have demonstrated high levels of blood glucose with some ages in type 1 diabetes, occurring most at 10-13 years of age (Spencer and Cudworth, 1983). It has been reported that physical activity in children decreases as they grow up to adolescence, resulting in an increase in blood sugar levels up to adolescence. Beyond adolescence, age from 18-20 years, there is increasing energy and nutrient needs, leading to low glucose levels. After this period these needs decrease (Lobstein *et al*., 2004) resulting in elevated blood glucose levels again. Sexual maturation has an influence on body fat, as fat gain occurs in both sexes early in adolescence, then ceases and may even temporarily reverse in boys but continues throughout adolescence in girls (Lobstein *et al.,* 2004).

The similarity in the mean fasting glucose value (p=0.392) for the urban and rural communities (Table 4.5) contrasts the findings of Adediran and colleagues who reported high prevalence of elevated fasting blood glucose in urban settlers, compared to their age-matched rural counterparts with similar genetic background (Adediran *et al.,* 2012). On the contrary, researchers from Benin observed that the prevalence of high fasting glucose concentration was significantly lower in urban dwellers than in semi-urban or rural counterparts (Ntandou *et al*., 2009).

From this study, overweight and obese subjects had a higher mean preprandial glucose levels than the non-obese, thus supporting other studies that reported high fasting glucose in respondents with increasing BMI. Olatunbosun and colleagues observed that high BMI was associated with increased blood glucose in their study in Ibadan, Nigeria. (Olatunbosun *et al.,* 1998) and Hillier and Pedula also observed that obesity was a

continuous risk rather than a threshold risk for diabetes onset (Hillier and Pedula, 2001). Individuals who are obese would tend to have insulin resistance and insulin insensitivity, resulting in high blood glucose levels.

The proportion of the study subjects who were overweight or obese (9.8%), was lower compared to previous studies which recorded increased obesity in the respondents (Gyamfi, 2010) and this could be as a result of good nutritional habit among the study subjects. A WHO report, has explained that the global epidemic of obesity has resulted mainly from societal factors that promote sedentary lifestyles and the consumption of high-fat, energy-dense diets, coupled with physical inactivity (WHO, 2000). The rapid rise in obesity prevalence has occurred because of emerging social trends like increased sedentary recreation, increase in the use of motorized transport, increased watching of television, rising use of soft drinks to replace water and other factors (Lobstein *et al.*, 2004). Playing computer/video games and eating food at a school canteen were other factors associated with increased prevalence of overweight and obesity in school children in a Metropolitan set-up (Amidu, *et al*., 2013). A decrease in the occurrence of these factors can substantially reduce the prevalence of obesity in individuals.

Dyslipidaemia is a major risk factor to the development of cardiovascular diseases and diabetes in an adult population, as well as children and young adults, so studies have shown that cardiovascular risk factors traditionally applied to the adult population are apparent in children and young adults, making them prone to the development of atherosclerotic disease (Troiano and Flegal, 1998; Daniels *et al.*, 2005).

The mean total cholesterol levels was similar in both male and females (3.82 versus 3.69; p=0.307), (Table 4.7). The proportion of individuals with high cholesterol levels was 11.8%, with about two-thirds of them being females. This is similar to an observation made by Yip and colleagues that the prevalence of hypercholesterolaemia is more in females, compared to males (Yip *et al*., 2006). The prevalence of hypercholesterolaemia in this study is similar to a study by Yip *et al*. (2006) who recorded a prevalence of 5-11% in different age groups in a paediatric population. It was also observed that there was gradual rise in cholesterol levels across the age groups in the females but the reverse was rather found for the male counterparts. According to one report, sexual maturation decreases levels of serum lipids, which often are more pronounced in boys than girls (Wennlof *et al.*, 2005). During the adolescence and pubertal age, there is accumulation of fats, largely through an increase in the number of adipocytes, without significant change in fat cell volume (Wabitsch, 2002).

The female subjects had significantly higher (p=0.006) mean cholesterol levels in both the normoglycaemic and hyperglycaemic subjects than their male counterparts. This finding is in agreement with Dirisamer *et al*. (2006) who reported higher total cholesterol, LDL-C and triglycerides in females, as compared to males in the age group 3-18 years. In contrast to this result, a study in South Africa documented no significant difference in the cholesterol levels between males and females (Smith, 2010).

Children in the rural communities had a mean total cholesterol level of 3.22 mmol/L which was significantly lower (p=0.000) than the mean cholesterol levels (4.32 mmol/L) of children from the urban communities (Table 4.5), the same trend was seen in the young adults though that was not statistically significant (p=0.068). This shows that place

of residence (rural/urban) has an effect on cholesterol or other lipid levels. This goes to emphasize that lifestyle changes as a result of urbanization and westernization, characterised by changes in dietary habits, involving an increase in the consumption of refined sugars and saturated fat and a reduction in fibre intake (Mennen *et al.*, 2000) result in abnormal lipid levels.

There is no significant difference (p=0.187) between the mean cholesterol levels in the normal weight, overweight and obese subjects in this study and this is inconsistent with a study in Iran which reported high levels of total cholesterol in overweight and obese children and adolescents. (Ghergerehchi, 2009). The accumulation of fat in the adipose tissue, results in the secretion of free fatty acids from the fat cells, which may stimulate hepatic triglyceride and very low density lipoprotein cholesterol production in the youth and adults (Kahn and Flier, 2000; Bacha *et al.*, 2004).

From Table 4.5, there was lower level of mean triglycerides in the urban populations than their rural counterparts in both the children and young adults groups (p= 0.000) and hypertriglycaeridaemia was present among the rural dwellers (6.0%) but absent in their urban counterparts. This, however, contrasts results from a study in Nigeria which showed hypertriglycaeridaemia was commoner in the urban settlers than their rural counterparts (Adediran *et al*., 2012). High levels of triglycerides in the rural subjects may be as a result of the consumption of energy-dense diets high in fats, especially saturated fats and low in unrefined carbohydrates, which among other factors, is the principal cause of hypertriglycaeridaemia in children. Individuals with impaired fasting glucose had higher triglyceride values than the normoglycaemic subjects (0.92 versus 0.80). Similarly, male subjects with impaired fasting glucose had higher triglyceride levels than

male normoglycaemic subjects and the same was realised in the females (p=0.000). This is supported by previous studies which emphasised high triglycerides levels in subjects with impaired fasting glucose and subjects with poor glycaemic control (Titty, 2010).

There is a reported increase in the occurrence of obesity epidemic in children and adolescents (Fagot-Campagna *et al*., 2000; Daniels *et al.,* 2005), and childhood obesity is commonly associated with dyslipidaemia (Goran *et al.,* 1998). Nonetheless, in this study, the triglyceride levels in the underweight and normal subjects were similar to those of the overweight and obese (p=0.291). This could be attributable to the lower number of the overweight and obese individuals.

HDL cholesterol was generally low in the subjects and this study further shows that low HDL-C was commoner among the females than the males, (95 versus 40). (Table 4.5). A similar finding was made in the study by Adediran and colleagues (2012), where 39.7% of males and 54.5% of the females had low HDL-C values. It is also worrying that a high percentage of participants were with low HDL-C levels. HDL-C is a cardioprotective lipoprotein, exerting its effect through different mechanisms such as reverse cholesterol transport, anti-inflammatory activity and scavenging toxic by-products of LDL-C oxidation (Mooradian *et al.*, 2006). Low HDL-C and elevated triglyceride were more common in the rural dwellers, who are supposed to have less exposure to modern dietary pattern and lifestyle, as compared to their urban counterparts. This could be attributed to prenatal and childhood nutritional deficiency, which has a link to metabolic dysfunction and disease in later life (Prentices and Moore, 2005). Decreased HDL-C levels are most often as a result of the catabolism of the triglycerides, resulting in a reduction in HDL particle size and increase in HDL-C clearance (Boyd *et al.,* 2005). Nutrition transition in

the rural areas, characterized by a shift from undernutrition to overnutrition problems could be the cause of low HDL-C and elevated triglycerides in these environments.

The number of individuals with high LDL-C levels was 39 (12.8%) of the study subjects, which were made up 35 (13.2%) children and 4 (10.3%) young adults. High levels of LDL-C was significantly (p=0.000) commoner in the urban dwellers, especially the females than their rural counterparts, similar to the report by Adediran *et al.* (2012) that dyslipidaemia is associated with urbanization. The subjects with impaired fasting glucose had a mean LDL-C value of 2.89 mmol/L, which differs significantly (p=0.008) from the mean LDL-C of the normoglycaemic subjects (2.25mmol/L), showing a strong association between impaired fasting glucose and elevated LDL-C levels in this study. The female subjects presenting with impaired fasting glucose had higher LDL-C than their female counterparts with normoglycaemia. This emphasizes that the females had higher LDL-C levels than males. LDL cholesterol typically makes up 60-70% of the total serum cholesterol and it is the major atherogenic lipoprotein and has long been identified by NCEP as the primary target of cholesterol-lowering therapy (Expert Panel on Detection, Evaluation and Treatment, 2001). Excess fat has often been associated with elevated LDL-C and triglycerides levels, and reduced HDL-C values (Eisenmann *et al.*, 2001). Consumption of trans-fatty acids or hydrogenated fat-enriched diets increase LDL-C levels, and either decrease or have no effect on HDL-C and apo A-1 level (Judd *et al.,* 2002)

5.3 KNOWLEDGE ABOUT DIABETES AND OTHER RISK FACTORS

There was a low knowledge of diabetes among the children and young adults (Table 4.6). Although a higher percentage (81.3%) of the respondents had some formal education (pre-primary, primary and high school), more than half (59.7%) of the respondents did not have any knowledge of diabetes. Majority of the participants who had some formal education had lower level of education (pre-primary, primary and junior high school) and that could explain why there was a decreased knowledge of diabetes. Previous studies had shown that there is a good association between the level of education and an increase in the knowledge of diabetes (Caliskan *et al*., 2006; Al Shafaee *et al.,* 2008). Approximately, three-quarters of the participants and their caregivers had a misconception that diabetes is caused by eating too much sugar or sugary foods and they also had the belief that diabetes can be cured. This points out that health education should be intensified to the general population on non-communicable diseases, especially diabetes. There is the advocacy that the greatest weapon in the fight against diabetes mellitus is knowledge (The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997). Information can help people assess their risk of acquiring diabetes, motivate them to seek proper treatment and care, and inspire them to take charge of their disease for their lifetime (Zimmerman and Walker, 1999). This is similar to a report by Clarke (2003) who also indicated that individuals with unrecognized diabetes had a limited understanding of diabetes before diagnosis. After diagnosis, knowledge of diabetes is accessed in order to reduce the development of complications.

It can be deduced that the persons in the general population do not worry about a disease or disorder unless they are affected by the disease. Understanding what diabetes means to

the newly diagnosed individual will assist in the accessing of literature and education programmes to promote informed approaches on prevention of complications, through treatment and lifestyle modifications.

This study has shown similar general knowledge of diabetes in the rural and urban communities (p=0.130), though previous researchers have reported the lack of knowledge of diabetes among rural dwellers (King, 2001; Moodley and Rambiritch, 2007). This could be attributable to the springing up of so many FM radio stations that people can listen to acquire education on health issues like diabetes. Another good source of information is health facilities in the rural communities as well as the urban communities, where children or young adults can obtain information.

The knowledge of diabetes among healthy participants in this study decreased with increasing age (data not shown) and it is consistent with the report of West and Goldberg (2002) who showed a decrease of 3% in the knowledge score of diabetic patients for every 10-year increase in age.

According to Figure 4.1, obtaining information through interaction with people (neighbours) represented the highest proportion, followed by the media (radio and television), but healthcare professionals represented a low percentage of 11.4%. A similar percentage of 17.8 was reported by Sabra *et al.* (2010) from Eastern Saudi Arabia and in support of this, other authors claimed that "there is a serious gap in the provision of basic educational services to the majority of people with diabetes in the region". Primary health care (PHC) is the first level of professional contact in the community and forms the cornerstone strategy for the attainment of level of health, that will permit socially and economically productive life (Oparah and Arigbe-Osula, 2002; Al-Rubeaan, 2003) and it

thus highlights the need for more efforts on educating the general population about diabetes within the PHC.

There is strong evidence from literature that generally, diabetes is commoner among first degree relatives of affected individuals (Olatunbosum *et al*., 1998; Field, 2002). This study shows a low (7.5%) positive family history of diabetes among the participants where children showed an 8.3% and young adults showed a 2.6% of a positive family history of diabetes. In addition, there is weak association between impaired fasting glucose and positive family history of diabetes among the subjects (Odds ratio = 0.853, 95% CI= 0.240-3.033). Findings from recent studies from various countries have reported that individuals with positive family history of diabetes had two to six times the risk of diabetes, compared to individuals without a positive family history of the disease (Harrison *et al.*, 2003; Oyegbade *et al*., 2007). The weak association from this study could be as a result of the low prevalence of first-degree relatives having a family history of diabetes. Nonetheless it is imperative that individuals with a close relative with diabetes should seek health screening for diabetes.

A positive family history of hypertension was reported in 23.9% of all the respondents, whiles it was 25.6% and 20.5% in the children and young adults respectively. Similarly, there was a positive association between impaired fasting glucose and positive family history of hypertension. Thus, an individual with a positive family history of hypertension has about two-fold increase in the risk of developing elevated fasting blood glucose (Odd ratio= 1.988, 95% CI = 0.697-5.672), compared to those with no positive family history of hypertension. From a previous study (Dekkers *et al.*, 2003), family history of hypertension was associated with an increase in the prevalence and incidence

of hypertension and further supported by Fava *et al.* (2004) that both genetic and environmental factors appear to contribute to an association between family history and hypertension.

5.4 SOME LIMITATIONS IN THE STUDY

This study had the following limitations;

Since the study was undertaken in one district, there is some element of bias, making the generalization of the findings difficult. The cross sectional nature of the study could not ensure reproducibility of results. Another limitation was the inability to repeat the tests for all the subjects, due to limited resources and time constraints. Moreover, the reference ranges used for the study were not locally generated data, but data from the developed world.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

This study assessed the prevalence of prediabetes and diabetes and some risk factors associated with diabetes and the levels of lipids such as total cholesterol, triglycerides, HDL-C and LDL-C in children in the Kassena Nankana District of Upper East Region of Ghana. The hypothesis that some children in the Kassena Nankana District suffer from prediabetes or have the risk of developing diabetes has been proven.

The study has shown the overall prevalence of impaired fasting glucose otherwise termed as prediabetes to be 3.3% and 11.5% using the WHO/IDF and ADA criteria of classification respectively, whilst none was with diabetes (FBG > 7.0 mmol/L) in the the study participants in the district. The prevalence of prediabetes in the children was 3.4% and 12.0%, whilst the prevalence of prediabetes in the young adults was 2.6% and 7.7% using the WHO/IDF and ADA criteria respectively. The small sample size of the young adults, makes it less statistically representative. Putting the two groups together does not unduly alter the determined overall prevalence of 3.3% and 11.5% by the WHO/IDF and ADA criteria of classification respectively. Prediabetes or impaired fasting glucose occurred equally in both males and females, and in rural and urban communities in this study. Age of the individual, obesity and family history of hypertension were clearly associated with prediabetes in this study. There was however a weak association between prediabetes and family history of diabetes.

The study has indicated that more than half of the respondents (59.7%) and their guardians did not have any knowledge of diabetes mellitus. This level of unawareness is

serious, especially among the young and more efforts should be made so that the level of awareness will increase considerably in both rural and urban communities.

6.2 RECOMMENDATIONS

Following the key findings from the study, it is suggested that;

1. There is the need for follow-up tests on the individuals with hyperglycaemia and those with the associated risk factors so that they adopt appropriate lifestyle modifications as a primary prevention measure.
2. More efforts should be made to increase the knowledge of diabetes, its associated risk factors and associated complications among the younger population and the general population as a whole.
3. Further research should be carried out on a larger population of children and the general population in the District and other Districts including high risk individuals.
4. There should be establishment of health facility-based screening programmmes in the District and sub-district hospitals or clinics for early detection of asymptomatic diabetic individuals.
5. Individuals, especially children should be educated to adhere to taking healthy diets such as diets high in fruit and vegetables, whole grains, beans, fish and lean meat and a reduction in consumption of saturated and trans-fatty acids, cholesterol and refined sugar.
6. The dietary pattern modification should be coupled with a reduction in sedentary lifestyle but increased physical activity.

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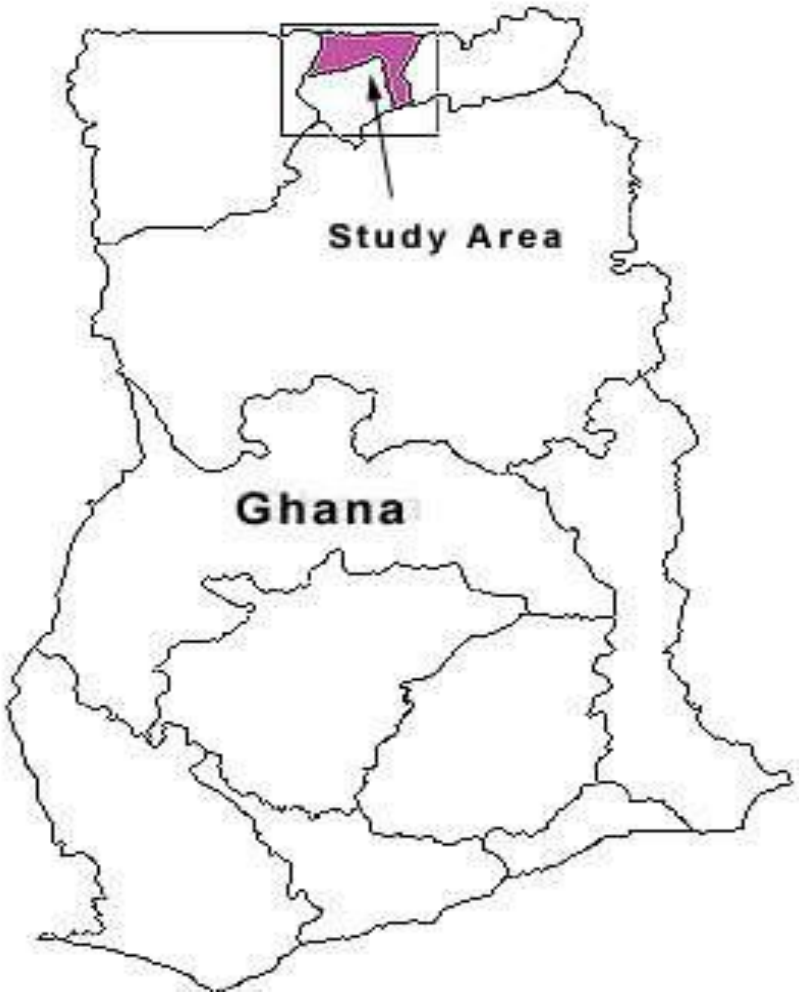
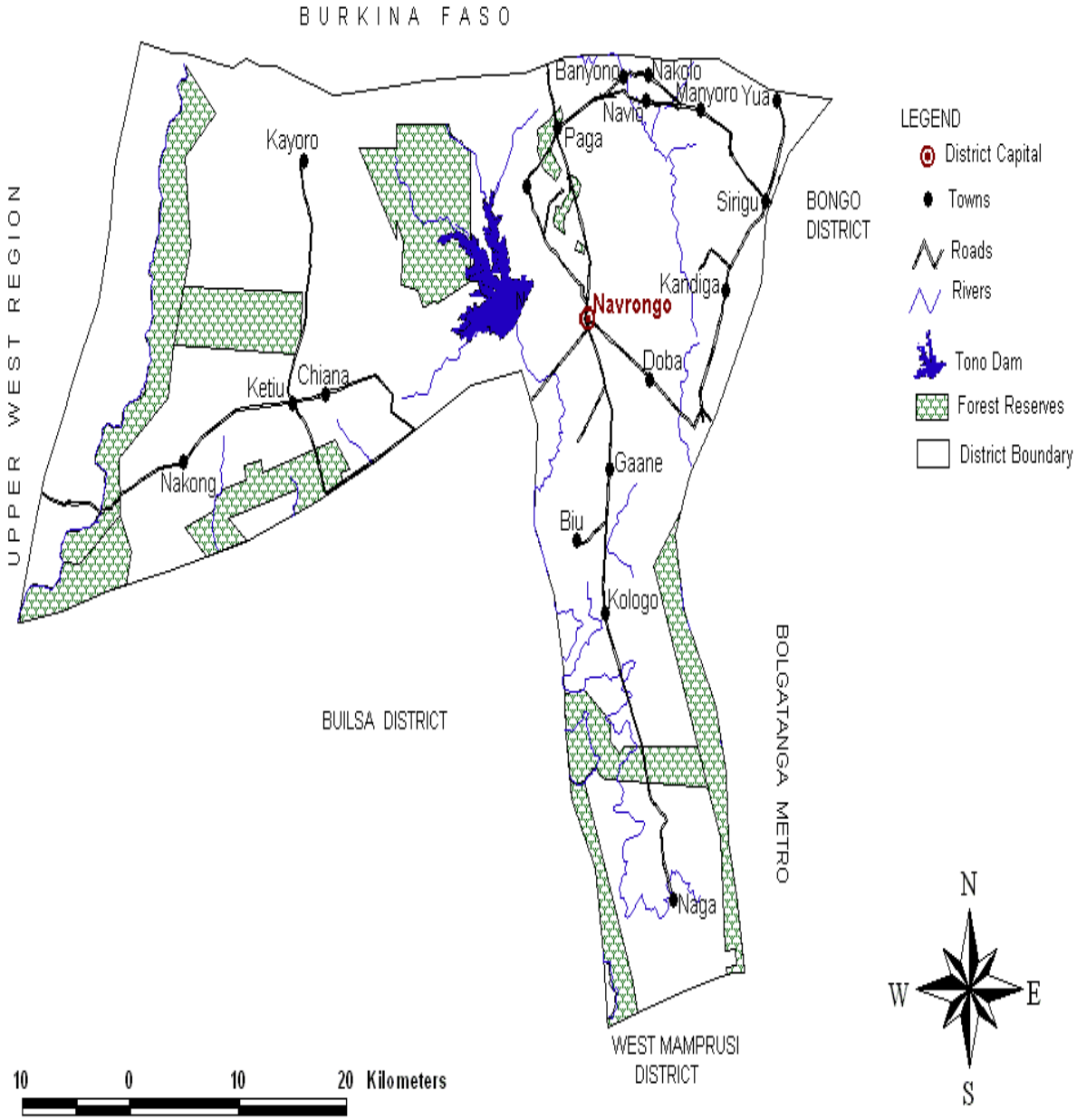
APPENDICES

APPENDIX I: MAP OF GHANA SHOWING KASSENA NANKANA DISTRICT (STUDY AREA)



Source: Adapted from Adokiya, (2010).

APPENDIX II: MAP OF KASSENA NANKANA DISTRICT



Source: Adapted from Adokiya, (2010).

APPENDIX III: QUESTIONNAIRE FOR DATA COLLECTION.

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY,
COLLEGE OF SCIENCE,
DEPARTMENT OF BIOCHEMISTRY AND BIOTECHNOLOGY

PREVALENCE OF PREDIABETES AND DIABETES MELLITUS IN CHILDREN AND YOUNG ADULTS IN THE KASSENA NANKANA DISTRICTS OF GHANA.

QUESTIONNAIRE:

1. Serial number……. 2. Age……

3. Weight …… 4. Height……

5. Sex…… 6. Waist circumference ……

7. Educational Status: No Educ. ☐ Preprimary ☐ Primary ☐ High sch. ☐

8. What do you know of diabetes? .....

9. Where and when did you hear of it? ……

10. How did you get your information on the condition? ……

11.Is any of your family members suffering from diabetes? YES ☐ NO ☐

12. If **yes,** how are you related to the person? .....

13. Do you usually feel thirsty often? YES ☐ NO ☐

14. Do you have constant hunger or get hungry often? YES ☐ NO ☐

15. Do you always urinate often? YES ☐ NO ☐

16. If **YES**, how often in a day? .....

17. Do you readily feel tired always even without working? YES ☐ NO ☐

18. Do you usually have any abnormal heart beats? YES ☐ NO ☐

19. Do you feel chest pains on exertion? YES ☐ NO ☐

20. Have you had chest pains even at rest? YES ☐ NO ☐

21. Do you have a relation who is hypertensive? YES ☐ NO ☐

22. If **YES**, how are you related to the person? ……

APPENDIX IV: PARTICIPANT CONSENT AND INFORMATION FORM

<u>This leaflet must be given to all prospective participants to enable them know enough about the research before deciding to or not to participate</u>

Title of Research
Prevalence of Prediabetes and Diabetes Mellitus in Children and young adults in the Kassena Nankana Districts of Ghana.

Name(s) and affiliation(s) of researcher(s):
This study is being conducted by Samuel Sunyazi Sunwiale of Department of Biochemistry and Biotechnology, Kwame Nkrumah University of Science and Technology, Kumasi, supervised by Kwabena Nsiah of Department of Biochemistry and Biotechnology, KNUST Kumasi and Co-supervised by Prof. Opare-Sem O. of School of Medical Sciences, KNUST, Kumasi and Dr. Abudulai A. Forgor of War Memorial Hospital, Navrongo

Background:
Diabetes mellitus has been established as a chronic disease affecting people all over the world. It is known to commonly affect people at middle age and above, but literature has shown that it also affects people of the lower age. The study is therefore, to find out the prevalence of prediabetes and diabetes in children and young adults in the study area.

Purpose(s) of research:
The main purpose of the research is to find out the blood glucose levels in children and young adults as well as their lipid profile. From the blood glucose levels, the subjects can be classified as normal, prediabetic or diabetic. The pattern of the anthropometric indices and the lipid profile would be correlated to the glycaemic states of the participants.

Procedure of the research, what shall be required of each participant and approximate total number of participants that would be involved in the research:
About Three hundred (300) participants (healthy volunteers) of 5-20 years of age would be enrolled at the health centre or hospital upon obtaining their consent. In addition, fifty (50) diabetic patients would also be enrolled as control subjects. Your weight, height, waist circumference and other parameters would be taken. You and your caregivers would be educated on diabetes. About 30 minutes of your time will be needed to administer a questionnaire and to take your blood. 5.0 millilitres of each your blood sample would be taken and tested, to find the level of blood glucose and the lipid profile of the participants. Your participation is only two days; today and the day your blood will be taken.

Risk(s)
It is painful and discomforting when your venous blood sample is taken but this is for a few seconds. It can sometimes swell but not at all times. You can be infected, but this will be prevented by using one sterile needle and syringe for each participant. The

technician will also wear surgical gloves when taking the blood samples. All risks involved will be minimal or prevented as much as possible.

Benefit(s):
After this study, information on the prevalence of prediabetes and diabetes or the risk of developing these conditions in children and young adults in the study area would be available. We will also find out how weight and BMI affects blood glucose and lipid levels. You and your caregivers or parents will also receive education on diabetes mellitus. High risk individuals or those with diabetes would be referred to a medical doctor or advised appropriately.

Confidentiality:
All the information collected about you would be coded and made confidential; Code numbers are to be assigned to all samples taken from you for the analyses. In the research write-up or report, your name shall not be used.

Voluntariness:
Your participation in this research is voluntary; you have the right to accept or not to accept to be part of the study. You are not obliged to be part of the study.

Alternatives to participation:
If you choose not to participate, this will not affect your treatment in this hospital/institution in any way. You would not be blamed by anybody for not taking part in the study.

Withdrawal from the research:
If you choose to withdraw from the research at anytime you don't have to explain yourself. You may also choose not to answer any question you find uncomfortable or private.

Consequence of Withdrawal:
There will be no consequence, loss of benefit or care to you if you choose to withdraw from the study. Please note however, that some of the information that may have been obtained from you without identifiers (name, etc), before you chose to withdraw, may have been modified or used in analysis reports and publications. These cannot be removed anymore. We do promise to make good faith effort to comply with your wishes, as much as practicable.

Costs/Compensation: For your time and inconvenience, we will provide you with fruits (one or two oranges and some banana) to show our appreciation for your participation.

Contacts:
If you have any question concerning this study, please do not hesitate to contact Mr. Sunyazi on 0242642543, Dr. Abdulai , the Medical Superintendent of War Memorial Hospital, Navrongo on 03821 22662/22647 or Dr. K. Nsiah on 0200237253.

Further, if you have any concern about the conduct of this study, your welfare or your rights as a research participant, you may contact:

The Office of the Chairman	**The Chairman**
CHRPE	**NHRC-IRB**
Kumasi	**Navrongo**
Tel: 03220 63248 or 020 5453785	**Tel: 03821 22348 or 0244564120**

CONSENT FORM

Statement of person obtaining informed consent:

I have fully explained this research to _____ and have given sufficient information about the study, including that on procedures, risks and benefits, to enable the prospective participant make an informed decision to or not to participate.

DATE: _____ NAME: _____

Statement of person giving consent:

I have read the information on this study/research or have had it translated into a language I understand. I have also talked it over with the interviewer to my satisfaction.

I understand that my participation is voluntary (not compulsory).

I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it.

I understand that I may freely stop being part of this study at any time without having to explain myself.

I have received a copy of this information leaflet and consent form to keep for myself.

NAME:_____

DATE: _____ SIGNATURE/THUMB PRINT: _____

Statement of person witnessing consent (Process for Non-Literate Participants):

I _____ (Name of Witness) certify that information given to

_____ (Name of Participant), in the local language, is a true reflection of what l have read from the study Participant Information Leaflet, attached.

INDEPENDENT LITERATE WITNESS' SIGNATURE: _____

PARENT'S SIGNATURE/THUMB PRINT:_____

PARENT'S NAME: _____

APPENDIX V: ASSENT FORM (minor participants)

PREVALENCE OF PREDIABETES AND DIABETES IN CHILDREN AND YOUNG ADULTS IN KASSENA NANKANA DISTRICTS OF GHANA.

My name is Samuel Sunyazi Sunwiale and a student of Kwame Nkrumah University of Science and Technology, Kumasi.

I am asking you to take part in a study which is to find the number of children and young people of the ages of 5 to 20 years who have diabetes or are at risk of getting diabetes. Diabetes is affecting many people this days especially adults but can now be found in children too, so I want find the number of children who have it in the district.

If you agree to be part of the study, we need you for only two days; today and the next day. Your name will be written and a number given to you. The next day, you will be taken to the health centre and you will be asked some questions and your weight and height will be taken. 5.0 ml of your venous blood will be taken by a qualified person. It may be painful during the blood taking but we will be careful not to cause unnecessary pain. All these will take not more than 30 minutes.

You can choose not to be part of the study, nobody will be angry at you if you decide not to be part of the study. If you start, you can even stop later if you want. Your name will not be used for any discussion in the study and we will tell nobody what you said in the study.

Signing here means that you have read this form or have had it read to you and you have understood it and willing to take part in the study.

If you have any question concerning this study, please do not hesitate to contact Mr. Sunyazi on 0242642543, Dr. Abdulai , the Medical Superintendent of War Memorial Hospital, Navrongo on 03821 22662/22647 or Dr. K. Nsiah on 0200237253.
Further, if you have any concern about the conduct of this study, your welfare or your rights as a research participant, you may contact: The Chairman, NHRC-IRB
Tel: 03821 22348/0244564120

Name of participant_____

Signature/Thumb print of participant_____

Signature of investigator_____

Date_____