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Review Article

# Evaluation of glycated hemoglobin and fasting lipid panels as glucose monitoring markers among nigerian populace with type 2 diabetes and cardiovascular disease

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**Received Date: August 05, 2024**; **Accepted Date: September 16, 2024; Published Date: October 25, 2024**

**Citation:** Ige, I. P, Mokwenye, N. V, Emokpae A. M, Ilesanmi-Ige, I. T. Ugbomoiko, O. D, et al, (2024), Evaluation of glycated hemoglobin and fasting lipid panels as glucose monitoring markers among nigerian populace with type 2 diabetes and cardiovascular disease, *Clinical Trials and Clinical Research*,3(5); **DOI:**10.31579/2834-5126/080



**Abstract**

Glycated hemoglobin (HbA1c) proven its effectiveness as a strong and dependable indicator for long-term glucose control among Nigerian populace with type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD). Its correlation with the incidence and severity of CVD complications emphasizes its crucial role in risk assessment and management. This research work was aimed at providing necessary information, determine the concentration of glycated haemoglobin (HbAic), fasting lipid profile/panel in subjects with type 2 diabetes and cardiovascular disease in comparison with control groups. Data were analyzed using Statistical Package for Social Sciences (SPSS® 20, USA). Descriptive statistics was used to describe the relevant variables and comparisons performed using chi-square test. The average HbAic level in the diabetic patients was 5.98±1.50 while the control was 4.84±0.49 with a p-value <0.001 which was statistically significant, suggestive of a strong relationship between diabetes and elevated HbA1c levels and the impact of diabetes on HbA1c levels, emphasizing the metabolic challenges associated with a substantial risk factor for cardiovascular diseases and stroke among these subjects. The Correlation of lipid profile parameters with Fasting blood sugar in healthy individual was shown that Triglyceride (TG) was moderately raised at (0.48) and (0.49) correlated with FBS and HbAic respectively, but other lipid profile component showed poor correlation. The model was statistically significant which showed that the variables accounts for 53.3% (R2=0.533) of the variance in Type 2 DM status. HbA1c and Total cholesterol are significant predictors of diabetes mellitus status. For each unit increase in HbA1c and total cholesterol, the odds of having diabetes increase by approximately 3.2 and 7.5 times respectively and statistically significant (p = 0.002). Therefore, this study concluded that regular assessment of HbA1c and fasting lipid profile, combined with suitable lifestyle modifications and medical interventions are essential monitoring markers for preventing complications and improving patient outcomes in optimizing diabetes care and preventing CVD complications in the Nigerian population. Future research is necessary in the areas of molecular descriptions of the genetic factors for diagnosing, management and monitoring of type 2 diabetes and cardiovascular diseases among Nigerian populace.

**Keywords:** type 2 diabetes; cholesterol; hemoglobin; glycated; disease

## Introduction

Diabetes is a chronic, metabolic disease categorized by elevated levels of blood glucose (or blood sugar), either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood glucose. Hyperglycaemia, also called raised blood glucose or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels. The mechanism of T2DM is largely understood. It is commonly established that in normal circumstances, there is a feedback loop between insulin action and insulin secretion. When this response is interrupted, the sensitivity to insulin is impaired and insulin secretion is affected, causing irregular blood levels of glucose.4 Insulin resistance (IR) and β-cell dysfunction are the main hallmarks of T2DM. It is clear that an abnormal lipid profile has a close relationship with IR. IR also serves as the major component of other metabolic disorders, in addition to T2DM. For instance, IR has been indicated to be associated with a high level of very-low-density lipoprotein (VLDL), high concentrations of serum triglycerides (TG), and low serum high-density lipoprotein (HDL). Therefore, the lipid profile is emphasized in almost all follow-up programs of T2DM and serves as a serious risk factor. Over a period of time, this can leads to serious damage to the heart, blood vessels, eyes, kidneys and nerves (Saran et al., 2015). The most common is type 2 diabetes (T2D), which is formerly known as adult-onset diabetes since it is usually associated with adults, is a form of diabetes mellitus that is characterized by high blood sugar, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. Type 2 diabetes primarily occurs as a result of obesity and lack of exercise ("Diabetes Fact Sheet No312", 2011). Some people are genetically more at risk than others. Symptoms frequently progresses gradually ("Causes of Diabetes", 2014).

Common symptoms include increased thirst, frequent urination, fatigue and unexplained weight loss, increased hunger, having a sensation of pins and needles, and sores (wounds) that do not heal ("Diagnosis of Diabetes and Prediabetes", 2014). Long-term complications from high blood sugar include heart disease, stroke, diabetes retinopathy which can result in blindness, kidney failure, and poor blood flow in the limbs which may lead to amputations ("Diabetes Fact Sheet No312" 2011). The sudden onset of hyperosmolar hyperglycemi state may occur; however, ketoacidosis is uncommon (Fasanmade et al., 2008; Pasquel and Umpierrez, 2014).

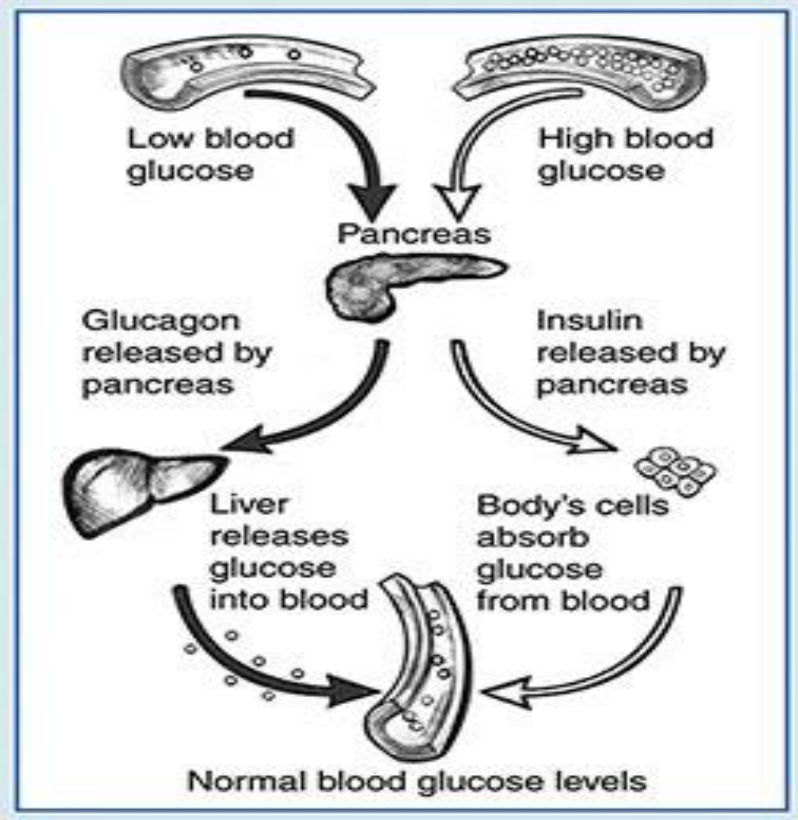


**Figure 1: Glucose metabolism.**

In the past 3 decades the prevalence of type 2 diabetes has risen dramatically in countries of all income levels (Lancet Global Health 2021). The prevalence of diabetes has been steadily increasing for the past 3 decades, reflecting an increase in the prevalence of obesity and overweight people. In particular, the prevalence of diabetes is growing most rapidly in low- and middle-income countries. About 422 million people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.5 million deaths are directly attributed to diabetes each year. Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades. The number of people with diabetes has nearly magnified since 1980. The number of people with diabetes rose from 108 million in 1980 to 422 million in 2014. Prevalence is increasing globally, predominantly in low- and middle-income countries than in high-income countries. Between 2000 and 2019, there was a 3% increase in diabetes mortality rates by age. In 2019, diabetes and kidney disease due to diabetes caused an estimated 2 million deaths (WHO, 2023).

In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2019, diabetes was the direct cause of 1.5 million deaths and 48% of all deaths due to diabetes occurred before the age of 70 years. Another 460 000 kidney

disease deaths were caused by diabetes, and raised blood glucose causes around 20% of cardiovascular deaths (Global Burden of Disease Collaborative Network, 2020). Between 2000 and 2019, there was a 3% increase in age-standardized mortality rates from diabetes. In lower-middle-

income countries, the mortality rate due to diabetes increased 13%. By contrast, the probability of dying from any one of the four main noncommunicable diseases (cardiovascular diseases, cancer, chronic respiratory diseases or diabetes) between the ages of 30 and 70 decreased by 22% globally between 2000 and 2019 (The Emerging Risk Factors Collaboration, 2010).

The causes are complex, but the rise is due in part to increases in the number of people who are overweight, including an increase in obesity, and in a widespread lack of physical activity. Diabetes of all types can lead to complications in many parts of the body and increase the risk of dying prematurely. In 2012 diabetes was the direct cause of 1.5 million deaths globally. A large proportion of diabetes and its complications can be prevented by a healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use. In April 2016, WHO published the Global report on diabetes, which calls for action to reduce exposure to the known risk factors for type 2 diabetes and to improve access to and quality of care for people with all forms of diabetes (Pasquel and Umpierrez, 2014). For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival. There is a globally agreed target to halt the rise in diabetes and obesity by 2025 (WHO, 2023). A healthy diet, regular physical activity, maintaining a normal body weight and escaping the use of tobacco are the inhibiting techniques to delay the onset of type 2 diabetes. Diabetes can be treated and its consequences can be avoided or delayed with diet, physical activity, medication and regular screening and treatment for complications (Lancet Global Health, 2021).

**Pathophysiology**

Type 2 diabetes is due to inadequate insulin production from beta cells in insulin resistance situation (Gardner et al., 2011). Insulin resistance, which is the failure of cells to respond adequately to standard insulin levels that occurs predominantly inside the muscles, liver, and fat tissue Diabetes Mellitus a Guide to Patient Care. (2007). (Diabetes Mellitus a Guide to Patient Care, 2007). In the liver, insulin routinely overwhelms glucose release. Conversely, in insulin resistance situation, the liver inappropriately releases glucose into the blood (Melmed et al., 2011). The fraction of insulin resistance against beta cell dysfunction varies between individuals, with some consuming principally insulin resistance and only a negligible deficiency in insulin secretion and others with insignificant insulin resistance and predominantly a lack of insulin secretion (Gardner et al., 2011).

Additionally, some important devices associated with type 2 diabetes and insulin resistance embraces increased breakdown of lipids within fat cells, resistance to and lack of incretin, high glucagon levels in the blood, increased retention of salt and water by the kidneys, and unsuitable regulation of metabolism by the central nervous system (Melmed et al., 2011). However, not all individuals with insulin resistance progress to diabetes as long as a damage of insulin secretion by pancreatic beta cells is also necessary (Gardner et al., 2011).

The Hypothalamic cells standardise blood glucose through projections to the autonomic nervous system. Autonomic innervation of liver and muscle cells stimulates an increased uptake of glucose. The control of blood glucose by the autonomic nervous system is frequently irregular in diabetic individuals (Lundqvist et al., 2020). During aging or during exposure to a high-fat diet, Leptin-sensitive cells, glucose regulating neurons become resistant to leptin (leptin-resistance). These leptin-resistant neurons fail to restrain food intake, thereby leading to obesity and elevated blood glucose levels. The explanations for this lowered reaction to leptin are undefined and are part of the mystery of the causes of type 2 diabetes (Salazar et al., 2019).

**Cardiovascular Diseases (Cvds)**

Cardiovascular diseases (CVDs) are a group of disorders encompassing the heart and blood vessels which include: coronary heart disease – a disease of the blood vessels supplying the heart muscle, e.g. angina and heart attack (Mendis et al., 2011); cerebrovascular disease – a disease of the blood vessels supplying the brain; peripheral arterial disease – a disease of blood vessels supplying the arms and legs; rheumatic heart disease – damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria; congenital heart disease – birth defects that affect the normal development and functioning of the heart caused by malformations of the heart structure from birth; and deep vein thrombosis and pulmonary embolism – blood clots in the leg veins, which can dislodge and move to the heart and lungs. (Shanthi et al., 2011). Heart attacks and strokes are usually acute events which are predominantly caused by a blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can be caused by bleeding from a blood vessel in the brain or from blood clots (GBD 2013 Mortality and Causes of Death Collaborators, 2015).

The fundamental devices of CVDs vary depending on the disease. It is estimated that dietary risk factors are associated with 53% of CVD deaths (Petersen and Kris-Etherton, 2021). Coronary artery disease, stroke, and peripheral artery disease involve artherosclerosis, which may be triggered by high blood pressure, smoking, diabetes mellitus, lack of exercise, obesity, high blood cholesterol, poor diet, excessive alcohol consumption, and poor sleeping, among other things (Jackson et al., 2015; Wang et al., 2017). High blood pressure is estimated to account for approximately 13% of CVD deaths, while tobacco accounts for 9%, diabetes 6%, lack of exercise 6%, and obesity 5%. Rheumatic heart disease may follow untreated strep throat (Shanthi et al., 2011).

Cardiovascular diseases (CVDs) are the prominent origin of death worldwide. An expected 17.9 million people died from CVDs in 2019, signifying 32% of all global deaths. Of these deaths, 85% were due to heart attack and stroke. More than three quarters of CVD deaths occur in low- and middle-income countries. Out of the 17 million premature deaths (under the age of 70) due to non-communicable diseases in 2019, 38% were caused by CVDs. Coronary artery disease and stroke account for 80% of CVD deaths in males and 75% of CVD deaths in females (Shanthi et al., 2011). Most cardiovascular diseases can be prevented by addressing behavioural and environmental risk factors like tobacco use, unhealthy diet and obesity, physical inactivity, harmful use of alcohol and air pollution. It is essential to identify cardiovascular disease as early as possible, since it is preventable so that management with counselling and medications can begin (Jackson et al., 2015; Wang et al., 2017; WHO. 2021).

It is estimated that up to 90% of CVD may be preventable (O'Donnell et al., 2016). Prevention of CVD involves improving risk factors through: healthy eating, exercise, avoidance of tobacco smoke and limiting alcohol intake (Shanthi et al., 2011). Treating risk factors, such as high blood pressure, blood lipids and diabetes is also beneficial. Treating people who have strep throat with antibiotics can decrease the risk of rheumatic heart disease (Spinks et al., 2021). The use of aspirin in people who are formerly healthy is of unclear value (Sutcliffe et al., 2013).

Individuals with diabetes are at increased risk of heart and kidney disease, retinopathy, neuropathy, and nonalcoholic fatty liver disease (NAFLD). Routine eye and foot exams, along with blood pressure, lipids, urine albumin-creatinine ratio, creatinine/estimated glomerular filtration rate (eGFR), and liver function testing, are recommended to detect the onset and

monitor progression of these complications (American Diabetes Association Professional Practice Committee. 4, 10 and 11 2023).

Tools for diagnosing diabetes mellitus comprises assessment of fasting plasma glucose (FPG) measurement, oral glucose tolerance tests (OGTT), and standardized hemoglobin A1c (HbA1c) assays. Generally, all 3 tests are equally appropriate for diagnostic screening, although one may be more appropriate than another depending on an individual's characteristics (eg, due to nondiabetic illness or phase of pregnancy) (American Diabetes Association Professional Practice Committee 11 2023).

Monitoring of blood glucose can be implemented by both patients and health care providers, is considered a foundation of diabetes maintenance and the outcomes of monitoring are used to evaluate the effectiveness of therapy and to observe the alterations in medical nutrition therapy (MNT), exercise, and medications to accomplish the paramount potential blood glucose control. The recommendations of the American Diabetes Association on the most commonly used assessments in monitoring the glycemic status of people with diabetes emphasizes on both patient and physician/laboratory-based testing. It does not address tests for diabetes screening and diagnosis ("Tests of Glycemia in Diabetes," 2003).

**Glycated Hemoglobin (Hba1c)**

Blood oligosaccharides are attached to many proteins after translation, forming glycoproteins. Glycosylation is an alteration of enzyme-facilitated process that changes protein function, like their life span or their communications with other proteins (Dalziel et al., 2014). In disparity, glycation is the nonenzymatical attachment of a monosaccharide (usually glucose) to the amino group of a protein. Glycated hemoglobin is formed by the condensation of glucose with special amino acid residues, usually lysine, either the α- or β-chain of hemoglobin (Welsh et al., 2016) in hemoglobin to form an unstable Schiff base (aldimine, pre-HbA1c). The Schiff base may dissociate or may undergo an Amadori rearrangement to form a stable ketoamine. Glycation reaction results to the generation of a heterogeneous group of chemical moieties recognized as advanced glycated end products (AGEs), which play a fundamental role in the pathophysiology of diabetic complications. Advanced glycation end-products (AGEs) are generated in the diabetic milieu, as a result of chronic hyperglycemia and enhanced oxidative stress. These AGEs, via direct and receptor dependent pathways promote the development and progression of cardiovascular disease.

For many years, HbA1c has been extensively integrated into the diagnosis and management of patients with diabetes. It has recommended that improving glycemic control in patients with type 2 diabetes may be more important than treating dyslipidemia for the inhibition of both microvascular and macrovascular complications (Vaag, 2006). An essential feature of HbA1c is the uninterrupted occurrence of glycation over the lifespan of the protein, hence the concentration of the glycated protein replicates the regular blood glucose value over a period of time. This differences with the estimation of blood glucose reveals the glucose concentration at the instant blood is sampled and extremely changed by various issues like hormones, disease, ingested foods, and exercise. HbA1c is the most widely used and studied glycated protein, other glycated proteins that have been evaluated in clinical studies include fructosamine, glycated albumin, and advanced glycation end products (AGEs) (Saudek et al., 2006).

Glycated hemoglobin (HbA1c) is a synthetic product of the natural reaction between hemoglobin and elevated glucose levels in the blood ("Tests of Glycemia in Diabetes," 2003). HbA1c is when glucose is attached to the N-terminal valine residue of each β-chain of hemoglobin A (HbA) (Welsh et al., 2016). It is sometimes called advanced or progressive glycation end products, the most important for clinical diagnosis of diabetes mellitus, and can serve as an alternative to glycemia measurement. For more than 40 years past, glycated haemoglobin (HbA1c) was originally acknowledged as an "uncommon" haemoglobin in patients with diabetes (Bomholt et al., 2021). The degree of glycation in hemoglobin is predisposed by the concentration of glucose in the blood. Since the life span of erythrocytes is ∼120 days, HbA1c replicates the average plasma glucose concentration over the previous eight to twelve weeks (2-3 months). It can be performed at any period of the day and does not require any special preparation like fasting (Nathan et al., 2007). These properties have made it the preferred investigation for evaluating glycaemic control in people with diabetes. Recently, there has been significant concern in using it as a problem-solving (diagnostic) tool for diabetes and as a screening test for persons at high risk of diabetes (WHO, 2011).

Glycated hemoglobin (HbA1c) is a supplementary indicator, apart from the regular glucose and glycemia analyses, which has develop a significant marker in new analytical methods. The determination of HbA1c is substantial for diabetes diagnosis and provides substantial results compared to the simple measurement of glycemia (Amaefule et al., 2020; Kaur et al., 2020). Glycated hemoglobin is an essential biochemical marker that make available more consistent evidences for diabetes mellitus diagnosis than glucose and glycemia measurements (Hirst et al., 2017).

**Glycated Hemoglobin and Other End-Products of Glycation**

HbA1c is a glucose-improved hemoglobin created throughout the spontaneous reaction concerning glucose and N-terminal valine excesses on β chains of hemoglobin-creating β-N-1-deoxy fructosyl. The particular chemical tool of glycosylation is established on the development of a Schiff base then shifting into rearrangement by means of Maillard reactions, eventually providing the final molecule with covalently bound glucose, called the Amadori product, or an advanced glycation end-product (Bergmann and Sypniewska 2016). Once HbA1c is formed, it remains in the blood circulation for quite a long time, typically from two to three months, because of the lifespan of erythrocytes, which is approximately 120 days. The blood level of HbA1c is moderately steady and not thoughtful to time of day, fasting or newly taken food (Buffarini et al., 2016). All the aforementioned facts make HbA1c a good marker for diabetes mellitus, with minimal misdiagnosis due to temporary and non-pathological changes in glycemia (Winston, 2020). Though the evaluation of HbA1c is frequently considered a good way to diagnose diabetes mellitus. Some pathologies like hemolytic anemia, which have emotional impact in the lifespan of erythrocytes, or the manifestation of an abnormal chain in the hemoglobin molecule, as this can cause results falsification (Katwal et al., 2020).

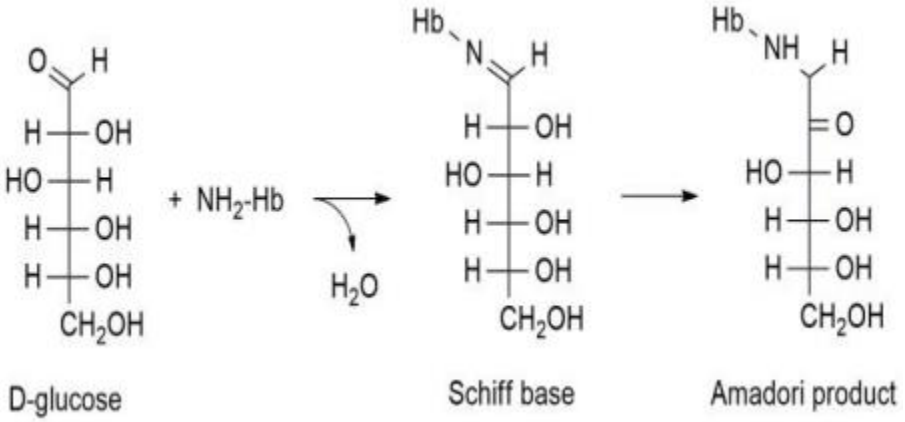


**Figure 2: Structure of Glucose (Yaylayan *et al.*, 1994).**

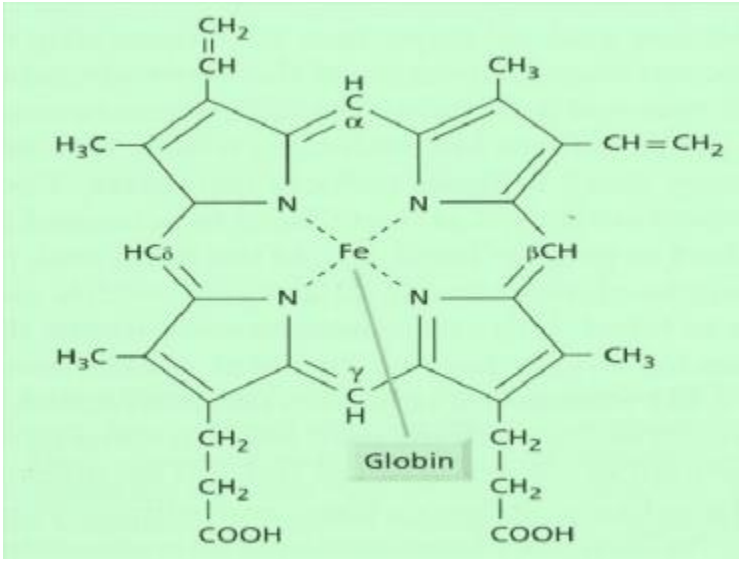


**Figure 3: Structure of Hemoglobin. Yaylayan et al., 1994).**

The ratio of HbA1c against the non-glycated hemoglobin, an aid for the diagnosis of diabetes mellitus. Healthy people have less than approximately 42 mmol/mol of HbA1c compared to the total hemoglobin, representing 6.0%. Suspected diabetes mellitus (prediabetes) fall in the range of 42–47 mmol/mol, signifying 6.0% to 6.4%. The presence of HbA1c above the value of 48 mmol/mol (6.5%) and over, is typical for people suffering from diabetes mellitus (Bancks et al., 2015; Appel et al., 2018).

**Mechanisms of Hemoglobin Destruction**

Glycated hemoglobin causes an elevation of extremely reactive free radicals inside blood cells, to alter the cell membranes properties, thereby leading to aggregation of blood cell and intensified blood viscosity, resulting in damaged blood flow. A different technique glycated hemoglobin cause impairment is through inflammation, resulting to the formation of atherosclerotic plaque (atheroma). Build-up of Free-radical promotes the excitation of Fe2+-hemoglobin through Fe3+-Hb into abnormal ferryl hemoglobin (Fe4+-Hb). Fe4+ is unsteady and which reacts with specific amino acids in hemoglobin to regain its Fe3+ oxidative state. Hemoglobin molecules cluster together through cross-linking reactions, and these hemoglobin clumps (multimers) promote cell damage and the release of Fe4+-hemoglobin into the matrix of innermost layers (subendothelium) of arteries and veins. This results into an elevated penetrability of internal surface (endothelium) of blood vessels and formation of pro-inflammatory monocyte adhesion proteins, which support accumulation of macrophages in the surface of blood vessel, and eventually leading to harmful plaques in these vessels. This total disintegration of blood cells also releases heme from them. Loose heme can cause oxidation of endothelial and LDL proteins bring about plaques formation (Saleh, 2015).

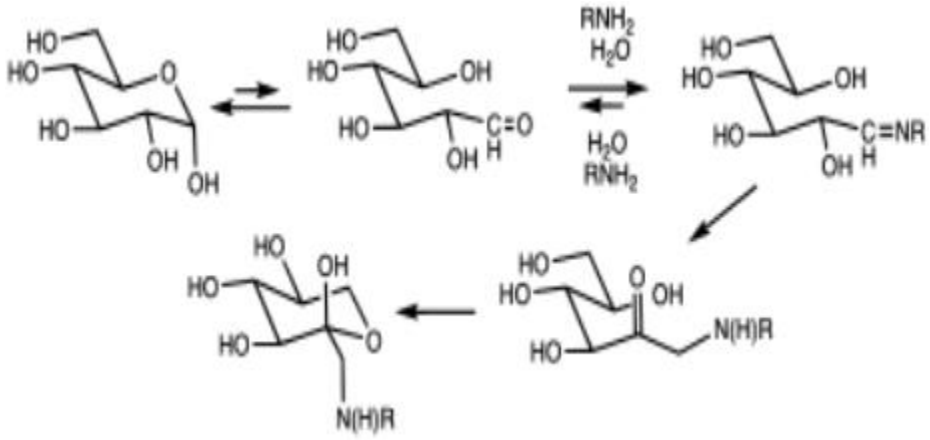


**Figure 4: Glycation pathway via Amadori rearrangement (in HbA1c, R is typically N-terminal valine) (Yaylayan et al., 1994).**

**Implication of Glycated Haemoglobin**

The International Diabetes Federation and the American College of Endocrinology recommend HbA1c level below 48 mmol/mol (6.5%): Diabetes Control and Complications Trial (DCCT) (DCCT %), while the American Diabetes Association recommends HbA1c below 53 mmol/mol (7.0 DCCT %) for most patients ("Executive Summary: Standards of Medical Care in Diabetes--2009," 2008).

Laboratory values might fluctuate based on the biological difference amongst individuals, diagnostic method adopted and the age

of the subject. Advanced levels of HbA1c are found in people with insistently raised blood sugar, which is diabetes mellitus. The goals of diabetic patient treatment vary because many of them embrace a objective choice of laboratory HbA1c results. A diabetic person with considerable glucose control has an HbA1c values that is related to or within the reference range.

Persistent rises in blood sugar (and, therefore, HbA1c) elevate the possibility of long-term vascular complications of diabetes, such as heart failure, kidney failure, blindness, coronary disease, heart attack, stroke, erectile dysfunction, neuropathy (loss of sensation, especially in the feet), gangrene and gastroparesis (slowed emptying of the stomach). Poor blood glucose control also elevate the risk of short-term complications of surgery such as poor wound healing. All-cause mortality is elevated above 8.0% HbA1c as well as lower than 6.0% in diabetic patients, and above 6% as well as below 5.0% in non-diabetic individuals, demonstrating the possibilities of hyperglycemia and hypoglycaemia respectively. Comparable danger results are also perceived for cardiovascular disease (Cavero-Redondo et al., 2017).

The American Diabetes Association, European Association for the Study of Diabetes, International Diabetes Federation, and World Health Organization has recently inculcated HbA1c as a diagnostic criterion for diabetes ("Presidents' Statement on WHO Recommendation on HbA1c for Diabetes Diagnosis," 2011). Immunoassays and high-performance liquid chromatography (HPLC) are the two most commonly used methods in the U.S. and many other developed countries, affinity chromatography, capillary electrophoresis, and enzymatic assays. Until recently when clover is adopted. Standardization of methods by the NGSP (formerly called the National Glycohemoglobin Standardization Program) and the International Federation of Clinical Chemistry and Laboratory Medicine has generated exceedingly reliable HbA1c results for a blood sample, irrespective of the technique adopted (provided the method is certified by NGSP). (Welsh et al., 2016).

**Factors Affecting Glcated Hemoglobin (Hba1c) Results**

There are numerous published reports of conditions that change HbA1c independent of glucose. Based on the nature of the interference, these can be conveniently divided into two groups: conditions that influence interpretation (i.e., change HbA1c concentration in ways unrelated to changes in glucose) and conditions that interfere with HbA1c measurement (i.e., analytic interferences) (Welsh et al., 2016).

**1. In Erythropoiesis**

A change in erythrocyte survival alters HbA1c. For example, assume HbA1c is 7.0% (53 mmol/mol), with a normal erythrocyte life span of 120 days. If the red blood cell life span is 10 days shorter or longer, the corresponding HbA1c values would be 6.4% (46 mmol/mol) and 7.6% (60 mmol/mol), respectively. Iron, vitamin B12 deficiency and decreased erythropoiesis increases HbA1c, while erythropoietin administration, iron, vitamin B12, reticulocytosis, and chronic liver disease decreases HbA1c. HbA1c does not accurately reflect average blood glucose concentration if erythrocyte survival is significantly altered, as in, for example, hemolytic anemia or severe β-thalassemia (Welsh et al., 2016).

**2. In Haemoglobin Alteration**

Over 1,200 hemoglobin variants have been identified; the β gene is involved in ~70% of these. While the vast majority are uncommon or rare, certain hemoglobin variants, particularly HbAS, HbAC, HbAD, and HbAE, occur at relatively high frequencies in some populations. One cannot measure HbA1c in individuals who are homozygous for these common variants or who have HbSC disease since they have no HbA. Haemoglobinopathies, HbF, methaemoglobin, may increase or decrease HbA1c due to genetic or chemical alterations in haemoglobin (Weykamp et al., 2015; Welsh et al., 2016)

**3. In Glycation Process**

There has been speculation that the rate of deglycation (i.e., the removal of glucose from HbA1c) might vary among individuals, resulting in different HbA1c concentrations despite similar average glycemia. Although at least three groups of deglycating enzymes have been identified, only one, fructosamine 3-kinase, is found in humans. Importantly, fructosamine 3-kinase has no effect on valine-1 of the β-chain of hemoglobin (Welsh et al., 2016). Increased HbA1c are due to alcoholism, chronic renal failure, decreased intra-erythrocyte pH, while decreased HbA1c are as results of aspirin administration, vitamin C and E, certain haemoglobinopathies, increased intra-erythrocyte pH. But genetic determinants causes' variable HbA1c values (Weykamp et al., 2015).

**4. In Erythrocyte Destruction**

Increase in erythrocyte life span (Splenectomy) will elevate HbA1c and decrease in erythrocyte life span like haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone will decreased HbA1c (Welsh et al., 2016).

**5. Assays**

Hyperbilirubinaemia, carbamylated haemoglobin, alcoholism, large doses of aspirin, chronic opiate use increases HbA1c while hypertriglyceridaemia decreased HbA1c but haemoglobinopathies show a variable HbA1c (Gallagher et al., 2009).

**6. Chronic Renal Failure**

Chronic renal failure (CRF) is a common complication of diabetes, and diabetes is the leading cause of end-stage renal disease. Since red blood cell existence is reduced in CRF, thereby reducing HbA1c, and consequently the HbA1c concentration in patients with diabetes and with CRF may not accurately indicate glycemic control (Tuttle et al., 2014).

**7. Physiological Factors**

HbA1c concentrations rise by ~0.1% per decade after 30 years of age. It is not clear whether this steady elevation replicates an effect of age on the relationship of mean glycemia to HbA1c or basically the greater incidence of prediabetes and diabetes with aging (a true increase in mean glycemia) (Pani et al., 2008).

**8. Iron-eficiency Anemia**

Studies have concluded that there was no statistically significant difference in HbA1c measured by HPLC in the manifestation of iron deficiency or iron-deficiency anemia (Cavagnolli et al., 2015). On the other hand, another assessment determined that iron deficiency, with or without anemia, increased HbA1c. This inconsistency is possibly due to the alterations in the studies selected and the method of analysis (English et al., 2015).

**9. Uremia**

Isocyanic acid, imitated from urea, is covalently attached to proteins. The nonenzymatic process, termed carbamylation, increases when blood urea concentrations are high, yielding increased carbamylation of circulating proteins, including on lysine or arginine residues of the N-terminus of hemoglobin. Carbamylated hemoglobin altered HbA1c values in some early methods but uremia has no significant effect on HbA1c analysis with most contemporary methods (Cavagnolli et al., 2015; Zhao et al., 2015)

**10. Medications**

Drugs like dapsone and antiretroviral alter HbA1c level the concentration (Welsh et al., 2016).

**Lipid Profile/Panel**

A lipid panel/profile is a summary of blood assessment that measures the amount of certain fat molecules called lipids in your blood. It is used to screen, evaluate and monitor the risk of cardiovascular diseases like heart disease, heart attack (myocardial infarction) and stroke. Other common names for lipid panel include: Lipid profile, Lipid test, Cholesterol panel, Cholesterol risk panel and Fasting lipid panel or non-fasting lipid panel.

**Components**

1. **Total Cholesterol:** This is your overall cholesterol level — the combination of low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and high density lipoprotein cholesterol (HDL-C).
2. **Low-Density Lipoprotein (LDL) Cholesterol:** This is the type of cholesterol that's known as "bad cholesterol." It can collect in your blood vessels and increase your risk of cardiovascular disease.
3. **High-Density Lipoprotein (HDL) Cholesterol:** This is the type of cholesterol that's known as "good cholesterol." It helps decrease the buildup of LDL in your blood vessels.
4. **Triglycerides:** This is a variety of fat from the nutrients we eat. Excess amounts of triglycerides in your blood are associated with cardiovascular disease and pancreatic inflammation.
5. **Very Low-Density Lipoprotein (VLDL) Cholesterol:** This is a type of cholesterol that's usually present in very low amounts when the blood sample is a fasting sample since is mostly comes from food we recently eaten. An increase in this type of cholesterol in a fasting sample may be a sign of abnormal lipid metabolism. VLDL is the total cholesterol that are neither HDL nor LDL. With that definition, Friedewald's equation yields: VLDL = **Triglycerides/5** (Friedewald et al., 1972; Lee and Siddiqui 2023).

Type 2 diabetes mellitus (T2DM) is the greatest collective metabolic condition, regarded internationally as a global health threat (Huang et al., 2020). The 2015 International Diabetes Federation report shows that nearly one out of 11 adults had diabetes mellitus in year 2017 and the predominance is probably be increase to 642 million by 2040 (Zheng et al., 2018). It was estimated that T2DM account for approximately 6.8% of worldwide death in adults aged 20–79 years in 2010 (Roglic and Unwin, 2010).

**Lipids**

Lipids are also commonly known as fats, they are organic compounds principally composed of carbon and hydrogen; Lipids may be defined as compounds which are hydrophobic molecules that do not dissolve with water. That is relatively insoluble in water, but freely soluble in nonpolar organic solvents like benzene, chloroform, ether, hot alcohol, acetone, etc. They may sometimes contain limited quantities of oxygen, nitrogen, sulphur, and phosphorous. Lipids serve various and diverse purposes in the structure and functions of organisms. They can be a source of nutrients, a storage form for carbon, energy-storage molecules, and structural components of membranes, and function as hormones, pharmaceuticals, fragrances, and pigments and also involved in chemical signalling and communication (Fahy et al., 2009). Lipids embrace a comprehensive class of many chemically different combinations which include fats, waxes, monoglycerides, diglycerides, triglycerides, phospholipids, steroids, isoprenoids, fat-soluble vitamins like vitamins A, D, E and K and others (Mashaghi et al., 2013).

**Relationship between Glycated Hemoglobin Lipid Panel and Type 2 Diabetes**

Type 2 diabetes is related with plasma lipids and the group of lipoprotein defects, which include a preponderance of small dense LDL particles, elevated triglycerides and reduced HDL cholesterol (ADA, 2003). These variations are also a distinguishing features of insulin resistance syndrome also called metabolic syndrome, triggering several cases of type 2 diabetes. Regardless of this normal LDL cholesterol levels, these irregularities still happen in various patients. The association between LDL size or density and coronary artery disease (CAD) have been validated in various studies (CAD) (Krauss, 2004). It is evidence based that each features of dyslipidemia is interconnected with increased risk of cardiovascular disease, which is the primary source of death in patients with type 2 diabetes. Additionally, current

reports have also point out that elevated levels of LDL cholesterol concentrations are prognostic of coronary artery events, and that this is self-determinant of different risk factors of coronary disease (St-Pierre et al., 2003).

It is well recognized that dropped HDL cholesterol levels are connected with an amplified risk of coronary heart disease (CHD). Different roles of HDL units may possibly add directly to cardioprotective properties, including promotion of cellular cholesterol efflux and direct antioxidative and anti-inflammatory properties. In addition, reduced HDL cholesterol levels are constantly complemented by raised triglyceride levels, and the mixture has been powerfully related with an elevated chance of CHD. Nicotinic acid (niacin) considerably decreases serum triglyceride levels, elevates HDL levels, and raises LDL particle size and buoyancy, thereby improving the atherogenic lipoprotein profile. Niacin reduces fatty acid excreted from adipose tissue and suppresses hepatic production of VLDL. In turn, these effects decrease triglyceride levels and reduce the number of small dense LDL particles. Current studies demonstrated that the HDL-raising influence of niacin is potentiated by an increase in the active half-life of HDL as a result of condensed uptake by the receptor in charge of intrahepatic degradation of HDL (Kamanna and Kashyap 2000; Krauss, 2004). The American Diabetes Association guidelines specified that glycemic control can be established on self-monitoring of blood glucose (SMBG) and glycosylated hemoglobin (HbA1c) levels. Clinically, the long-term glycemic (HbA1c) levels of < 7.0 is regarded as glycemic control (Silvio et al., 2015; Wang et al., 2020).

Earlier research revealed that lipid profiles, glycated hemoglobin and glycemic levels are worthy control of lipid profiles and glycemic levels can effectively prevent complications like cardiovascular disease, diabetic nephropathy and diabetic retinopathy (Catapano et al., 2016). Clinically, lipid profiles speak of lipids in plasma, which comprises of triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL), and low density lipoprotein (LDL) (Alalwan et al., 2020). For patients with cardiovascular disease and T2D, lipid profiles should be strictly controlled to reduce mortality and complications (Basu, 2019). Numerous researches have long-established the association between glycemic control and lipid profiles in patients with T2D, the results are quite changeable (Laverdy et al., 2015). Khan HA et al. stated that the level of HbA1c was positively correlated with TG, TC, and LDL-C, but negatively correlated with HDL-C (Wang et al., 2020). However, a cross-sectional study in Eastern Sudan showed that poor glycemic control was not associated with TG but was associated with high TC levels (Omar et al., 2018). Furthermore, some studies showed that HbA1c was associated with TG and TC, rather than LDL-C and HDL-C (Zhu et al., 2019). Earlier studies have indicated that HbA1c was used as a pointer of glycemic control. HbA1c used as a pointer of glycemic control in earlier studies (Bergenstal et al., 2017) and also an established indicator of glycemic control, since it revealed an average glycemic level of approximately three months and did not show glycemic inconsistency over a period of time (American Diabetes Association, 2017). Fasting plasma glucose (FPG) is a reasonable and essential indicator for the diagnosis and glycemic variability of T2D. Few studies have shown the relationship between FPG control and lipid profiles (Silvio et al., 2015). It is certain that the relationship between glycemic control and lipid profiles in T2D patients is a major concern that necessitate urgent attention (wang et al., 2020).

## 2.0 Materials and Methods

### 2.1 Study Site/Area

This study was conducted at some selected health institutions in Ondo State: General Hospital, Ile-Oluji; University of Medical Science Teaching Hospital, Ondo and Federal Medical Center, Owo, all in Ondo State.

### 2.2 Duration of the Research Study:

This study was conducted between January to August, 2023.

### 2.3 Study Population

The subjects were recruited among type 2 diabetes mellitus with or without cardiovascular disease and normal subjects. The normal subjects were categorized as neither cardiovascular nor type 2 diabetes attending clinic at the above selected health institutions. The age limit for this study were between 30 to 75 years and both male and female genders were recruited.

Study Instruments OR Questionnaire: A structured questionnaire bothering on biodata and socioeconomic information medical histories and drug use was administered to respondents before collection of specimen.

**2.4 Study design:** Case study/control

### 2.5 Study size

The sample size was determined by Leslie Fisher's formula based on the frequency of Type 2 diabetes mellitus) in Nigeria (Kirkwood, 2010). A total of 140 participants were recruited for this research study. One hundred and three (103) were subjects with T2DM (with or without cardiovascular diseases) were randomly enrolled into the study. Seventy-four (74) were subjects with T2DM, twenty-nine (29) were subjects with T2DM and hypertention, while thirty-seven (37) subjects were recruited as control.

### 2.6 Collection and Preparation of Samples:

A total number of 140 samples were taken (57 were males and 83 were females); 74 were T2DM subjects, 29 were T2DM and hypertensive subjects and 37 were normal subjects (17 were males and 20 were females). A 9-12hours fasting samples was used for this study.

### 2.7 Inclusion Criteria

Adult and elderly patients with age range of 30-70 years old with recent diagnosis of T2DM, based on the World Health Organization criteria, were included in this study. Therefore, patients were considered to have T2DM if they fulfilled one of the following criteria: "HbA1c ≥ 6.5%, Fasting Plasma Glucose (FPG) ≥ 117 mg/dL (6.5 mmol/L),

### 2.8 Exclusion Criteria

Patients who were taking lipid-lowering therapy or those with cardiovascular diseases, endocrinal conditions, liver function impairment, or renal problems were excluded from the study. Furthermore, patients with mental problems were also excluded from the study.

### 2.9 Study Variables

The lipid profile of the diabetic patients, including total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein-cholesterol (LDL-c), and triglycerides (TG), represent the dependent variables of our study, whereas the independent variables included the HbA1c levels of the diabetic patients. The other additional features of the patients, including age, educational level, occupation, marital status, blood pressure, and body mass index (BMI).

### 2.10 Ethical clearance

Ethical approval was obtained from the ethical committee of Federal Medical Centre, Owo and University of Medical Sciences, both in Ondo State, Nigeria.

Ethical approvals were requested for and obtained from the Ethical Committee of University of Medical Sciences (UNIMED), under Ondo State Ministry of Health, Akure and Federal Medical Centre, Owo, Ondo State, Nigeria. Informed consent were obtained from the study participants prior to enrolment in the study. Structured questionnaire were used to collect socio-demographic data, medical history of the study participants were obtained from the medical records department.

**2.11 Collection of Blood Specimen**

After 12 hours of fasting, which must be between the hours of 7 and 10 am; 8mL of blood sample was taken from each participant; 5mL was dispensed into Ethylenediamine tetraacetic acid (EDTA) bottle (in ice pack) for glycated hemoglobin (HbA1c) and fasting lipid profile (FLP) assays. The remaining 3mL was dispensed into fluoride oxalate bottle for fasting blood glucose. Glycated hemoglobin (HbA1c) was analysed from EDTA bottle same day the blood samples were collected. The rest samples were prepared by separating them into plain bottles for different parameters

Both EDTA and fluoride oxalate samples was centrifuged at 1000g for 5 minutes and the supernatants (plasma) was separated into the corresponding plain containers respectively. The plasma from the EDTA bottles was used to assay for FLP, HbA1c, while the plasma from the fluoride oxalate bottles was used to assay for fasting blood glucose. A structured questionnaire bothering on bio-data and socioeconomic information medical histories and drug use was administered to respondents before collection of specimen.

Enzymatic method was adopted estimating fasting blood glucose, total cholesterol, HDL-cholesterol and triglyceride using Spectrophotometry assay, and Friedewald's formula was adopted for LDL-cholesterol. Boronate affinity method was adopted to determine the percentage (%) of A1c hemoglobin (HbA1c) in whole blood using reflection spectrometry (Clover A1c Self Analyser), fully automated.

**2.12 Statistical Analysis**

The data was entered and analyzed by the Statistical Package of Social Science SPSS, version 20. Descriptive statistics, such as frequencies and percentages, were calculated to summarize nominal and ordinal data, whereas the mean, median, and standard deviation or range were calculated to describe numerical variables. The correlation coefficient was calculated for the targeted association. The t-test was used if the independent variable was dichotomized during analysis. The chi-squared test was used to evaluate the association between categorical determinants and the outcome variables. Regression analysis was used to estimate adjusted odds ratios. Any p-value $< 0.05$ was considered as an indication of a statistically significant association or difference. We performed several standard tests to ascertain that the dataset satisfied the multiple linear regression analysis requirement. Four separate regression models were run with continuous variables of cholesterol level (mmol/L), triglyceride level (mmol/L), HDL-c level (mmol/L), LDL-c level (mmol/L) as dependent variables (DVs), and gender, age, nationality, habits, marital status, occupation, education, BMI (kg/m2), systolic blood pressure, diastolic blood pressure, glucose level (mmol/L), and HBA1C (%) were independent variables (IVs).

## Results

| Variables | Groups | Control n (%) | Case n (%) |
|---|---|---|---|
| Sex | Females | 20 (54.1) | 63 (61.2) |
| | Males | 17 (45.9) | 40 (38.8) |
| Age | ≤40 | 7 (18.9) | 8 (7.8) |
| | 41-60 | 20 (54.1) | 62 (60.20 |
| | 61-80 | 10 (27.0) | 33 (32.0) |
| | **Total** | **37 (100)** | **103 (100)** |

**Table 1: Sociodemography.**

The distribution table presents demographic characteristics of participants categorized by sex and age groups in both control and case groups. These are attributes of a population, such as age, sex, income, education, etc. Data was divided based on gender (male, female) and age ranges (e.g., 18-24, 25-34).

| Variables | Groups | N | Mean±SD | t-value | p-value |
|---|---|---|---|---|---|
| HbAic (%) | Control | 37 | 4.84±0.49 | 4.55 | <0.001 |
| | DM | 103 | 5.98±1.50 | | |

**Table 2: HbAic Level in the DM 2 and the Control subjects.**

The average HbAic level in the diabetic patients was 5.98±1.50 while the control was 4.84±0.49. The comparison of the means showed that the average HbAic in the DM patient was significantly higher that the control subjects.

| Variables | Control (n=37) | Case (n=103) | t-value | p-value |
|---|---|---|---|---|
| TC | 3.78±0.62 | 4.74±0.75 | 7.05 | <0.001 |
| TG | 0.95±0.33 | 1.14±0.48 | 2.14 | 0.03 |
| LDL | 2.79±0.41 | 3.37±0.6 | 6.38 | <0.001 |
| HDL | 1.42±0.26 | 1.49±0.28 | 1.36 | 0.17 |

**Table 3: Lipid Profile level in the DM 2 and the control subjects.**

The lipid profile level between the Control group and the DM patient was depicted in the table above. The table showed that the mean of TC, TG and LDL of the DM type 2 patients was significantly higher than the controls. The level HDL in the Control (1.42) was less than the type 2 DM, the measure of mean difference was statistically significant (p>0.05).

| Variable | FBS | HbAic (%) | TC | TG | LDL | HDL |
|---|---|---|---|---|---|---|
| **FBS** | 1 | | | | | |
| **HbAic** | .87** | 1 | | | | |
| **TC** | 0.04 | 0.05 | 1 | | | |
| **TG** | .48** | .49** | .48** | 1 | | |
| **LDL** | -0.01 | -0.12 | .40* | .33* | 1 | |
| **HDL** | -0.06 | -0.05 | 0.14 | 0.26 | 0.19 | 1 |

**Table 4: Association between Lipid profile parameters and the FBS in control.**

The Correlation of lipid profile parameter with Fasting blood sugar of the apparently healthy individual was shown in the table above. The result showed that Triglyceride (TG) was and moderately positively at (0.48) and (0.49) correlated with FBS and HbAic respectively. Other lipid profile element showed poor correlation.

| Variable | FBS | HbAic | TC | TG | LDL | HDL |
|---|---|---|---|---|---|---|
| **FBS** | 1 | | | | | |
| **HbAic** | .95** | 1 | | | | |
| **TC** | .48** | .46** | 1 | | | |
| **TG** | 0.16 | 0.13 | .538** | 1 | | |
| **LDL** | .36** | .322** | .678** | .296** | 1 | |
| **HDL** | .25* | .195* | .281** | -0.043 | .387** | 1 |

**Table 5: Association between Lipid profile parameters and the FBS in case.**

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

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

The correlation analysis of lipid profile parameters with FBS indicated that TC had a moderately positive correlation with both FBS and HbA1c. In contrast, LDL and HDL exhibited a weakly positive correlation with FBS and HbA1c. These relationships were statistically significant, with p-values less than 0.05 ($p < 0.05$).

| Variables | B | p-values | OR (95% CI) |
|---|---|---|---|
| HbAic (%) | 1.11 | 0.002 | 3.203 (1.48 - 6.21) |
| TC | 2.01 | 0.001 | 7.46 (2.41 - 23.12) |
| TG | -1.55 | 0.06 | 0.21 (0.04 - 1.06) |
| LDL | 1.31 | 0.04 | 3.69 (1.04 - 13.06) |
| HDL | -0.83 | 0.39 | 0.44 (0.07 - 2.93) |
| Age | -0.008 | 0.74 | 0.99 (0.95 - 1.04) |
| Sex (Male) | -0.21 | 0.70 | 0.82 (0.29 - 2.31) |

**Table 6: Logistics regression analysis.**

The table showed the multivariate analysis of the Diabetics mellitus associated variables. Age and gender being important biological factors was added into the model. The model was statistically significant. The result showed that the variables accounts for the 53.3% (R2=0.533) of the variance in Type 2 DM status. Each variable showed independent association while other variables were held constant. HbA1c is a significant predictor of diabetes mellitus status. For each unit increase in HbA1c, the odds of having diabetes increase by approximately 3.2 times. This result is statistically significant ($p = 0.002$). Total cholesterol is a significant predictor of diabetes mellitus status. For each unit increase in total cholesterol, the odds of having diabetes increase by approximately 7.5 times. Sex (being male) is not a statistically significant predictor of diabetes mellitus status ($p = 0.7$). The odds ratio suggests that males may have slightly lower odds of having diabetes compared to females, but this result is not statistically significant and has a wide confidence interval.

## Discussion

The average HbAic level in the diabetic patients was 5.98±1.50 while the control was 4.84±0.49. The comparison of mean HbA1c levels revealed a significantly higher value among DM patients compared to control subjects in compliance to the work of Smith et al, (2023). These findings emphasize the importance of glycemic control in managing diabetes mellitus and the clinical implications of the higher HbA1c levels in DM patients (Smith et al., 2023). This is shown in Table 1 above.

The average HbA1c level among diabetic patients was found to be significantly higher than that of the control group. Specifically, diabetic patients had an average HbA1c of 5.98 ± 1.50, compared to 4.84 ± 0.49 in control subjects with a p-value of less than 0.001. This alteration was statistically significant, suggestive of a strong relationship between diabetes and elevated HbA1c levels and the impact of diabetes on HbA1c levels, emphasizing the metabolic challenges associated with the condition which has been acknowledged as a substantial risk factor for cardiovascular diseases and stroke in subjects with type 2 diabetes who may have diabetes (Martín-Timón et al., 2014). More studies have showed that nondiabetic patients found that raised HbA1c level was intensely associated with the risk of cardiovascular disease and mortality. High levels of HbA1c were connected with an increased risk of relapse of atrial tachyarrhythmia in patients with type 2 DM and paroxysmal atrial fibrillation go through catheter ablation (Lu et al., 2015). A slight elevation of 1% in HbA1c concentration was correspond to nearly 30% rise in all-cause mortality and

40% rise in cardiovascular or ischemic heart disease mortality as a diabetes complications, among patients living with diabetes. But decreasing the HbA1c level by 0.2% could lower the mortality by 10%. It has also be suggested that improving glycemic control in patients with type 2 diabetes

may be more important than treating dyslipidemia for the prevention of both microvascular and macrovascular complications (Sherwani et al., 2016).

The Correlation of lipid profile parameter with Fasting blood sugar of the apparently healthy individual was shown in the table above. The result showed that Triglyceride (TG) was and moderately positively at (0.48) and (0.49) correlated with FBS and HbAic respectively. Other lipid profile element showed poor correlation.

The comparison of lipid profile levels between the control group and patients with Type 2 diabetes mellitus (DM) highlighted significant differences. The averages of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) were notably higher in Type 2 DM patients compared to the control group. In support of our findings, study conducted by Johansen, et al (2023) how triglyceride content increases while cholesterol content decreases in HDL and LDL+IDL fractions following normal meals: the Copenhagen General Population Study of 25,656 individuals, which suggested that TG is higher and HDL was dropped in type 2 diabetes but contrarily suggested diminished LDL and triglycerides; and another study reported that reduced triglyceride content and increased cholesterol content in HDL and LDL fractions following oral fat tolerance tests (Johansen et al., 2023). Also, in a long-term population-based study, it was showed that low high-density lipoprotein (HDL) cholesterol was suggested as an established indicator of raised plasma triglycerides and triglyceride-rich remnant lipoproteins, like high HbA1c exists as a stable symbol of elevated plasma glucose (Langsted et al., 2020); this is in line with the modifications in HDL cholesterol observed in this present study (Johansen et al., 2023).

Previous research has consistently demonstrated that individuals with type 2 diabetes mellitus (T2DM) exhibit significantly elevated levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) cholesterol compared to non-diabetic controls. The level HDL in the Control (1.42) was less than the type 2 DM suggests that HDL levels in the control group were lower than in the type 2 diabetes group. The measure of mean difference was statistically significant ($p>0.05$) indicates that there was no significant difference between the two groups. A p-value greater than 0.05 typically denotes a non-significant result. On the contrary, the high-density lipoprotein (HDL) level was higher in Type 2 DM patients than in controls, with the control group having an HDL level of 1.42. However, this difference in HDL levels was not statistically significant with a p-value of 0.17 ($p > 0.05$). This conformed to the study conducted by Farbstein and Levy (2012), suggesting that diabetes is associated with quantitative modifications in the amount of circulating lipids; remarkably an increase in triglycerides, elevated LDL and a reduction in HDL. An unhealthy lifestyle is the most common cause of high "bad" LDL cholesterol or low "good" HDL cholesterol. However, inherited genes from parents, other medical conditions, and some medications may also raise LDL cholesterol levels or lower "good" HDL cholesterol levels. The combination of high triglycerides and low high-density lipoprotein (HDL) cholesterol can arise from physical inactivity, drinking too much alcohol, and obesity. It can lead to serious health problems, such as high blood pressure and atherosclerosis. Like other lipoproteins, HDL also undergoes significant qualitative changes in diabetes, in both structure and function. However, since dyslipidemia may be present several years before the onset of diabetes, it is hard to determine which of these changes are related to the pathognomonic features of the disease, and which precede and accelerate its progression (Farbstein and Levy 2012). Though the findings of research conducted by Parhofer (2015) showed a significant differences between rodent and human lipoprotein metabolism which may similarly assist to explain the interaction of HDL and glucose metabolism in humans (Parhofer, 2015). As indicated in Table 1, the lipid profile of Type 2 DM patients differed significantly from the control group. Mean values for TC, TG, and LDL-C were notably higher in the DM group compared to controls ($p < 0.05$). Conversely, HDL-C levels were lower in the control group than in the DM group, although this difference did not reach statistical significance value ($p > 0.05$).

For more than 4 decades, HbA1c of 6.5% has been identified as an "unusual" haemoglobin in patients with diabetes and recommended as the cut point for diabetes diagnosis. Though a value lesser than 6.5% does not disregard diabetes diagnosed using glucose tests. Therefore HbA1c is a significant predictor of diabetes mellitus status in addition to increased blood glucose concentration. Several research studies has implicated that HbA1c concentration of 6.5% as a significant predictor of diabetes mellitus status. These works include "Studies of an unusual hemoglobin in patients with diabetes mellitus" by Rahbar et al., (1969); "Changing targets in the treatment of type 2 diabetes" by Massi-Benedetti, (2006); "Relationship between glycated haemoglobin levels and mean glucose levels over time" by Nathan et al., (2007); "Translating the A1C assay into estimated average glucose values" by Nathan et al., (2008); and the "International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes", (2009), which are in conformity with the present study (Rahbar et al., 1969; Nathan et al., 2007; Nathan et al., 2008; Massi-Benedetti, 2006; International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes, 2009).

Studies have indicated that blood glucose concentrations are positively associated with TG and LDL-C levels, but others have found no association (Laverdy et al., 2015; Omar et al., 2018). In recent times, a study reported that fasting plasma glucose is related to HDL and TC but not to LDL or TG (Wang et al., 2020). In the interim, an investigation conducted in Eastern Sudan establish that poor glycemic control was not correlated to TG but was connected to raise TC (Omar et al., 2018). Considerable heterogeneity in the study population, design, and variable definition, or an insufficient modification for medical challenging may clarify the inconsistency. In addition, several factors affect the blood glucose levels and lipid profiles of people with T2DM. For instance, diet is a substantial feature affecting them together (Hernandez-rodas et al., 2015), and eating arrangements of individuals may contribute to different associations between blood glucose levels and lipid profiles (Abdelhamid et al., 2020; Ulven et al., 2016). Consequently, triglyceride in the triglyceride-FBG index leads to a predictive significance in distinguishing pre-diabetes, diabetes and diabetes complications (Wang et al., 2022).

Total cholesterol include triglyceride, LDL-cholesterol and HDL-cholesterol levels. Since, this our present study point out that Total cholesterol is a significant predictor of diabetes mellitus status with odd ratio of 7.46 (p-value 0.001), and showed further that raised triglyceride, raised LDL-cholesterol and low HDL-cholesterol concentrations alone or in integrated with fasting blood glucose index in the triglyceride-FBG index, is considered a significant interpreter of prediabetes and diabetes. In line with these findings, previous studies also revealed that triglyceride had elevated levels in prediabetics and T2DM patients, and their positive association with the risk of developing cardiovascular diseases was markedly recognized (Alexopoulos et al., 2019; Nichols et al., 2018; Upadhyay et al., 2015).

Additionally, a link between high serum levels of triglyceride and over-secretion of insulin in apparently healthy individuals has been reported.

Hypertriglyceridemia may have a causal relationship with insulin resistance, and reducing levels of triglyceride serum in the individuals with hypertriglyceridemia was associated with a decline in the levels of serum insulin and low incidence of T2DM (Jasim et al., 2022). The current study also indicated that assessing the triglyceride-FBG index may be more important in forecasting pre-diabetes and diabetes than triglyceride alone since this index is closely related to diabetes to recognize early insulin resistance without measuring insulin. Insulin resistance is considered a condition with an impaired biological response to insulin stimulation, resulting in reducing the disposal of glucose and hyperinsulinemia. Hyperglycemia, visceral adiposity hypertension, dyslipidemia, and up-regulated levels of inflammatory indicators are all metabolic consequences of insulin resistance, associated to a raised risk of T2DM and cardiovascular disease (Lim et al., 2019).

## Conclusion

This present study demonstrated a strong association between elevated HbA1c levels and dyslipidemia as increased risk of myocardial infarction and stroke as complications in Nigerian patients with T2DM. While fasting lipid panels provided valuable information on cardiovascular risk, they did not independently predict glycemic control. Therefore, this study concluded that regular HbA1c monitoring, combined with fasting lipid profile assessment, is essential for optimizing diabetes care and preventing CVD complications in this population. HbA1c and fasting lipid panels are essential implements for managing type 2 diabetes and cardiovascular disease in the Nigerian population. Regular monitoring of these markers, combined with suitable lifestyle modifications and medical interventions, is essential for preventing complications and improving patient outcomes. Future research is necessary in the areas of molecular descriptions of the genetic factors for diagnosing, management and monitoring of type 2 diabetes and cardiovascular diseases among Nigerian populace.

## Ethics

All studies were performed in compliance with the rules and regulations of the Federal Republic of Nigeria. Ethical Committee of Federal Medical Cental, Owo, and University of Medical Science (UNIMED), Ondo, all in Ondo State, Nigeria.

**Funding:** Authors disclose no external funding sources.

**Competing Interests:** The authors declare that they have no potential conflict of interest.

## Acknowledgment

The authors would like to appreciate the Chemical Pathology Laboratory Unit of Achievers University, Owo, Ondo State and Igbinedion University, Okada, Edo State, Nigeria.

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