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The Efficacy of Glycated Hba1c in Diagnosis of Type 2 Diabetes Mellitus and their Association with Dyslipedemia

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Abstract: ***Hemoglobin A1C (HbA1c) has been widely recognized and used as a reliable test for monitoring glycemic control in diabetic patients for around three decades. It offers an estimation of the average blood glucose levels over the past 8-12 weeks. Despite advancements in the development of antidiabetic medications, maintaining optimal glycemic control remains a challenging task. The main objective of the present study was to evaluate the diagnostic value of HbA1c in predicting the presence of dyslipidemia in patients diagnosed with type 2 diabetes. In the current study, a total of 60 participants diagnosed with type 2 diabetes were included. The assessment involved measuring HbA1c levels, fasting blood glucose, and lipid profiles. The mean HbA1c value for males was 7.35±2.31, while for females, it was 9.18±2.59. Based on their glycemic index, the diabetic patients were categorized into two groups: group 1 with HbA1c ≥7.0% and group 2 with HbA1c ≤7.0%. The results revealed a positive correlation between HbA1c levels and lipid parameters, while a negative correlation was observed between HbA1c and HDL cholesterol. Patients in group 1 (diabetic dyslipidemia) exhibited significantly elevated levels of triglycerides, total cholesterol, LDL cholesterol, and fasting blood glucose compared to those in group 2 (good glycemic control). The mean HbA1c value in the diabetic dyslipidemia group was 9.47±2.46, significantly higher than the mean HbA1c of 6.52±0.12 in the group with good glycemic control. Furthermore, the mean triglyceride level in the diabetic dyslipidemia group was 309.27±89.2, whereas in group 2, it was 127.01±37.65. The mean LDL cholesterol in the diabetic dyslipidemia group was 118.12±25.82, compared to 103.8±27.51 in the group with good glycemic control. The mean total cholesterol in group 1 was 215.4±30.78, which was higher than the mean total cholesterol of 165.83±37.3 in group 2. Additionally, the mean HDL cholesterol in the diabetic dyslipidemia group was lower at 39.5±6.84, while in group 2, it was 45.07±7.19. The mean fasting blood glucose in group 1 was higher at 209.26±73.23, whereas group 2 had a mean fasting blood glucose of 115±20.1. These findings indicate that type 2 diabetic patients with dyslipidemia are at an increased risk of cardiovascular diseases. The association between HbA1c and various lipid parameters underscores the importance of achieving good glycemic control to reduce the likelihood of developing diabetic dyslipidemia and other complications associated with diabetes. Monitoring HbA1c levels serves as a convenient, cost-effective, and time-efficient tool for assessing diabetes and its associated dyslipidemia.***

Keywords: HbA1c, Type 2 Diabetes Mellitus, Dyslipidemia, Cardiovascular Risk, Lipid Profile

1.Introduction

Background

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels, known as hyperglycemia. It is a rapidly increasing global epidemic and a significant cause of premature illness and death worldwide [1]. In 2010, the estimated global prevalence of diabetes mellitus was approximately 285 million individuals (6.4%), and it is projected to rise to 1.552 million individuals (7.7%) by 2050 [2] . There are two main types of diabetes mellitus: Type 1 diabetes mellitus (T1DM), which is insulin-dependent and accounts for 5% of cases, and Type 2 diabetes mellitus (T2DM), which is insulin-independent and accounts for 95% of cases [3]. Uncontrolled blood glucose levels in diabetic patients often result in Dyslipidemia, leading to various complications. Chronic Dyslipidemia increases the risk of long-term vascular complications and organ failure [4]. These complications include coronary artery disease, heart attack, stroke, heart failure, diabetic nephropathy (kidney failure), diabetic neuropathy (loss of nerve sensation, especially in the feet), diabetic retinopathy (eye damage), gas gangrene, gastro paresis (delayed stomach emptying), and poor wound healing after surgery [5]. Individuals with Type 2 diabetes mellitus have a higher risk of cardiovascular diseases (CVD). Dyslipidemia, characterized by abnormal lipid profiles, is common in diabetic patients and contributes to the increased risk of cardiovascular-related deaths. Many individuals may have undiagnosed dyslipidemia, resulting in elevated levels of triglycerides (TGs), total cholesterol (TC), low-density lipoproteins (LDL), and decreased levels of high-density lipoproteins (HDL) [6].

Glycated Hemoglobin: (HbA1c)

Diagnosing diabetes has traditionally relied on various glucose tests conducted over several years. The Diabetes Complication and Clinical Trials (DCCT) established Glycated Hemoglobin (HbA1c) as the gold standard method for analyzing a patient's glycemic control status, with levels below 7.0% considered appropriate for reducing the risk of vascular complications. HbA1c is a commonly used marker for long-term glycemic control [7]. Following a World Health Organization (WHO) consultation, HbA1c has been recognized as the most widely used clinical test for diagnosing diabetes mellitus [8]. HbA1c serves as a marker that reflects the average blood glucose levels over a period of 8-12 weeks, representing the previous 2-3 months before the measurement [9]. A cutoff value of 48 mmol/L (6.5%) is used to diagnose diabetes, and levels above this threshold are significantly associated with an increased risk of diabetic complications. Glycated hemoglobinA1c is a variant of hemoglobin that is primarily utilized to assess the average plasma glucose levels over an extended period, typically 4-12 weeks. It is formed through a non-enzymatic process when normal hemoglobin is exposed to elevated levels of glucose in the plasma [10]. HbA1c testing is favored because

it reflects chronic hyperglycemia rather than instantaneous blood glucose levels. HbA1c levels equal to or greater than 7.0% are strongly linked to the development of micro vascular and macro vascular complications [11]. Micro vascular complications of diabetes mellitus include diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy, while macro vascular complications encompass various forms of cardiovascular diseases such as coronary artery disease, heart failure, and stroke. The reference range for a healthy individual is typically around 4%-5.9% [12]. The American Diabetes Association (ADA) has recently recommended HbA1c as a diagnostic test for diabetes once the HbA1c goal of ≤7% has been achieved. This recommendation has significantly elevated the importance of HbA1c as a diagnostic tool for assessing glycemic control adequacy [13].

HbA1c Historical Background:

The significance of HbA1c in monitoring blood glucose control in diabetic patients was first proposed by researchers Ceramic and Koenig in 1976 [14]. HbA1c testing is considered a remarkable achievement in the history of diabetes mellitus and is approaching its 50th anniversary. It is the most important and widely accepted diagnostic procedure for assessing average blood glucose control. HbA1c has emerged as a marker of glycemic control and a predictor of cardiovascular complications. It is also used as a screening tool for diagnosing diabetes mellitus [15]. In 1955, researchers from various parts of the world described the heterogeneity of adult hemoglobin, but its significance was not explained until 1969 when Rahbaret al identified the unusual hemoglobin found in diabetic patients as HbA1c [16]. By the late 1970s, the glycation process of HbA1c was elucidated, where glucose molecules covalently bind to the amino terminals of beta-globin chains of hemoglobin [17]. In 1980, HbA1c testing became widely accepted in clinical practice. Glycated HbA1c is a form of hemoglobin that is irreversibly Glycated at one of the N-terminal valines of the beta Hb chains, although additional glycation at other sites of alpha or beta hemoglobin chains is not excluded [18]. In 1962, Heisman and Dozy observed a slight increase in HbA1c fractions in four diabetic patients who were taking the hypoglycemic drug tolbutamide, but they did not characterize this phenomenon in vitro. Five years later, Rah bar et al. described HbA1c as an abnormal hemoglobin in diabetes mellitus after documenting this unusual clinical finding [19]. Rah bar's investigations on diabetic patients with poorly controlled blood glucose led to the discovery of a new component called the diabetic hemoglobin component in red blood cells in 1969. Subsequent studies revealed that this abnormal hemoglobin was identical to the HbA1c fraction, and its levels increased in proportion to the degree of hyperglycemia [20]. The International Expert Committee (IEC) recommended the use of HbA1c for diagnosing diabetes with a reference value of ≥6.5%. However, standardization of HbA1c is crucial, and the Diabetes Control and Complication Trials (DCCT) reference assay and the National Glycohemoglobin Standardization Program (NGSP) certified method are important for achieving standardization [21].

Formation of Glycated HbA1c:

During hyperglycemic conditions, erythrocytes circulate in the blood, and one or both N-terminal valine residues of the beta chain of hemoglobin slowly undergo irreversible non-enzymatic glycation [22]. About 80% of Glycated hemoglobin is formed through this process. The glycation of hemoglobin occurs over the entire lifespan of red blood cells, which is approximately 120 days [23]. There is a specific pattern followed in the formation of glycation. Approximately 25% of glycation occurs in the first two months of erythrocyte lifespan, another 25% occurs in the third month, and the remaining HbA1c is formed during the senescence of the red blood cells, covering the period of 2 months prior to HbA1c measurement. As a result, older or senescent red blood cells have higher concentrations of HbA1c compared to reticulocytes. This process allows HbA1c to represent the average blood glucose concentration over a period of 4-8 weeks [24, 25]. During abnormal glucose metabolism, hyperglycemia leads to the excessive production of early glycation products, which is an acute reversible change. These glycation products are formed both inside and outside the cells. Glucose molecules rapidly attach to the amino group of proteins (Terminals) through a non-enzymatic nucleophilic addition reaction, forming unstable Aldi mine Schiff base adducts. These adducts reach an equilibrium level directly proportional to the blood glucose concentration. Subsequently, the reaction undergoes Amador rearrangement to form a more stable ketamine linkage known as advanced glycation end products (AGEs) [26]. This process reaches equilibrium over a period of 4-12 weeks and is irreversible. Once the hemoglobin molecule is Glycated within erythrocytes, the buildup of Glycated hemoglobin reflects the average blood glucose level to which red blood cells have been exposed during their entire lifespan. Older or senescent red blood cells lose their ability to metabolize glucose, leading to equal concentrations of intracellular and extracellular glucose [27]. The HbA1c assay measures the total glycation of hemoglobin in both younger Glycated and older more Glycated red blood cells. Therefore, the level of HbA1c is directly proportional to the average blood glucose concentration over the previous 4-12 weeks. By measuring Glycated hemoglobin, the effectiveness of therapy can be assessed by monitoring long-term blood glucose control [28].

HbA1c Clinical significance: A Useful tool to assess or to predict the risk of Diabetic Complications:

Macro vascular Complications: (Correlation with HbA1c): Today, the global Epidemic of diabetes is a growing concern, with approximately 220 million diagnosed cases worldwide. Type 2 diabetes patients often have an imbalanced lipid profile, increasing their risk of cardiovascular diseases compared to those without diabetes. In fact, around 60% of individuals with type 2 diabetes die from cardiovascular complications [29]. Furthermore, individuals with both diabetes and metabolic syndrome, which includes dyslipidemia, hyperglycemia, and hypertension, have the highest prevalence of cardiovascular disease [30]. Despite advancements in anti-diabetic agents, maintaining tight glycemic control to prevent diabetic complications remains challenging.[31] HbA1c, a marker of

long-term blood glucose levels, is strongly associated with various lipid parameters and a thermogenic ratio. Therefore, it is crucial to maintain tight glycemic control to manage diabetic hyperlipidemia and reduce the risk of cardiovascular diseases [32]. Several efforts have been made to improve HbA1c test results and reduce diabetic dyslipidemia. The DCCT study conducted by the National Institute of Diabetes, Digestive, and kidney diseases in the USA established HbA1c as the gold standard for measuring glycemic control. HbA1c levels of ≤7.0% are considered appropriate to reduce the risk of cardiovascular complications.[33] HbA1c levels have a positive correlation with triglycerides (TGs), low-density lipoproteins (LDL), and total cholesterol, while they have a negative correlation with high-density lipoproteins (HDL). Poorly controlled diabetic patients with HbA1c levels ≥7% tend to have higher values of total cholesterol, LDL cholesterol, and total cholesterol/HDL cholesterol ratios compared to well-controlled diabetic patients with HbA1c values ≤7.0%. Therefore, HbA1c serves as a dual biomarker for assessing both glycemic control and circulating lipids in individuals with type 2 diabetes [34, 35].

Micro vascular Complications:

The clinical significance of HbA1c as a crucial diagnostic tool for assessing the risks of diabetic complications was first proposed in research studies such as the DCCT publications and the United Kingdom Perspective of Diabetic Study (UKPDS). [36, 37] Micro vascular complications of diabetes mellitus (DM) encompass conditions like diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. The UKPDS, conducted in 1988, provided evidence confirming a correlation between HbA1c levels and micro vascular complications. Specifically, an HbA1c level above 6.8% serves as a robust predictor of diabetic retinopathy [38].

HbA1c Vs Blood Glucose Testing:

Fasting Blood Glucose (FBG) and Oral Glucose Tolerance Tests (OGTTs) have been associated with significant practical challenges. Both tests are time-consuming and require specific patient preparation. For an OGTT, patients need to adhere to a strict diet for at least three days and fast overnight. The test itself takes a minimum of three hours and involves collecting three blood samples, which can be labor-intensive. Moreover, diabetic patients who experience symptoms such as vomiting, nausea, delayed gastric emptying, or difficulties with venous access may have poor tolerance for blood glucose tests, leading to potentially invalid results. Consequently, repeat testing may be necessary, further adding to the inconvenience. To overcome these issues, HbA1c has emerged as a superior and more efficient diagnostic tool, eliminating the need for OGTTs. It is less time-consuming and requires no special patient preparation.[39] In Australia, a recommended HbA1c value of 48mmol/l (6.5%) or higher has been established for the diagnosis of diabetes, aligning with the guidelines of the National Health and Medical Research Council for the treatment and management of diabetes. The Australian Diabetes Society (ADS) has also submitted a proposal to Medicare to accept HbA1c measurement for diagnosis, although it is currently under review [40].

Diagnosis of Diabetes:

The diagnosis of diabetes is confirmed when the HbA1c value is ≥6.5% on two separate occasions in an asymptomatic individual. This means that if an individual does not exhibit symptoms, it is necessary to have a second elevated HbA1c value to confirm the diagnosis, with both values being equal to or greater than 6.5% (>48mmol/L). However, if a person is symptomatic, a single HbA1c test showing a value above 48mmol/L is sufficient for diagnosis. In the range of 42-47mmol/mol (5.7-6.4%), individuals are classified as having pre-diabetes. For such patients, it is recommended to have annual HbA1c testing. A red code C11ys is used to indicate pre-diabetes, while the temporary code EMISNQPR215 was assigned by EMIS [41].

Table 1: Diagnostic Criteria for Diabetes Mellitus with normal an abnormal Glucose Tolerance [41]

	Fasting plasma glucose mmol/L	2 hours glucose mmol/L	Random glucose mmol/L	HbA1c mmol/L
Normal	<6.0	<7.8	_	<42mmol/L <6.0
Impaired fasting glucose	6.1-6.9	<7.8	_	_
Impaired glucose Tolerance	>7.0	7.8 – 11.0	_	_
Pre diabetes	_	_	_	42-47mmol/L 5.7-6.4%
Diabetes Mellitus	>7.0	>11.1	>11.1	48mmol/L >6.5%

Correlation between HbA1c and Mean Plasma Glucose:

The relationship between HbA1c and plasma glucose levels is quite complex. Elevated HbA1c levels are typically found in diabetic patients with consistently high blood glucose levels. However, diabetic patients who maintain tight glycemic control may still have HbA1c levels within or close to the reference range. The recommended HbA1c values vary between different guidelines. IDFACE recommends values below 6.5%, while ADA recommends values below 7.0% for most diabetic patients. On average, an HbA1c of 6% corresponds to a mean plasma glucose level of 135mg/dl [42].

For every 1% increase in HbA1c, the mean plasma glucose increases by 35mg/dl. In non-diabetic individuals, the recommended HbA1c range is 3.5%-5.5%. For individuals with diabetes, a value of 6.5% is considered good glycemic control. Although HbA1c is often considered an indicator of mean plasma glucose levels over the past weeks to months, it does not truly reflect glycemic control for the entire 2–3-month period as claimed. Instead, it reflects more recent weeks [43]. The measurement of HbA1c covers approximately 50% of the mean plasma glucose in the month preceding the measurement, while the following 30-60 days

contribute another 25%. The remaining 25% is contributed by mean plasma glucose levels during the 60–120-day lifespan of red blood cells prior to the measurement. Different HbA1c levels corresponding to various blood glucose levels can be found in a table. An approximate mapping between HbA1c and Estimated Average Glucose (EAG) measurements can be represented by the following master equation:

EAG (mg/dl) = 28.7 × HbA1c - 46.7 or
EAG (mg/dl) = 1.59 × HbA1c - 2.59.

If the HbA1c level exceeds 6.5%, drug treatment for diabetes is typically recommended [44].

Table 2: Correlation between HbA1c level and Mean Plasma Glucose levels

HbA1C%	6	7	8	9	10	11	12
MPG	135	170	205	240	275	310	354

MPG=Mean Plasma Glucose

Factors Affecting HbA1c Results:

Several clinical conditions can impact the accuracy of HbA1c tests, leading to falsely elevated results and potentially influencing a patient's diagnosis. Factors that contribute to inaccurate HbA1c values include increased lifespan or turnover rate of circulating erythrocytes (red blood cells), decreased red cell survival, hemoglobinopathies, alcoholism, iron deficiency, renal failure, and hyperbilirubinemia. The HbA1c level is influenced by the lifespan of red blood cells, so a longer circulation time of erythrocytes can result in falsely elevated HbA1c levels. Additionally, exposure of hemoglobin molecules to higher blood glucose levels in older red blood cells can lead to unexpected elevation of HbA1c results.[45]

Abnormal hemoglobin can also interfere with HbA1c measurements. When abnormal hemoglobin is present, the formation of HbA1c from adult HbA1o may be disrupted, resulting in falsely increased HbA1c levels. Iron deficiency is another known cause of increased HbA1c levels, which can be reversed by providing iron supplements [46]. Conversely, falsely decreased HbA1c levels may be observed in cases of hemolytic anemia. Certain factors such as children under 18 years of age, patients undergoing acute pancreatic surgery, and medications that increase blood glucose levels can also affect HbA1c levels. During pregnancy, HbA1c levels may either falsely increase or decrease. Therefore, HbA1c estimation is generally not performed for diagnosing gestational diabetes. It's important to consider these factors when interpreting HbA1c results to ensure accurate diagnosis and appropriate management.[47]

2.Review of Literature

In 1992 Daniel Singer and colleagues conducted a cross-sectional study involving 1045 patients to explore the in-order relationship between HbA1c and dyslipidemia. The study aimed to investigate the potential correlation between HbA1c and lipid parameters. Notably, the study revealed a significant positive correlation between HbA1c and lipid parameters. The results indicated that HbA1c levels were notably correlated with cardiovascular diseases among women, but this association was not observed in men. The findings suggested that HbA1c may serve as a valuable indicator for cardiovascular risk assessment in women specifically. [48].

In 2002 Curt Rohlfing et al., established a relationship between HbA1c and plasma glucose levels. The study involved analyzing the data of 1439 subjects, and a linear regression analysis was performed on the mean plasma glucose (MPG) and HbA1c levels. Through the analysis, a relationship between MPG (mmol/L) and HbA1c was determined for all the participants. The relationship was calculated to be equal to 1.98% HbA1c for the morning time gaps, including pre breakfast, post-breakfast, pre-lunch periods. To estimate MPG, the capillary blood glucose was multiplied by a factor of 1.11.[49]

In 2004 Leve R, et al., conducted a study involving 100 pregnant women in early pregnancy who did not have gestational diabetes. The aim of the study was to examine HbA1c levels during pregnancy and compare them to a control group of 145 healthy non pregnant women, with an average age of 30years. The results of the study indicated that HbA1c levels were significantly lower in early pregnancy compared to the control group of non-pregnant women. Additionally, the study found a further decrease in HbA1c levels in late pregnancy compared to both early pregnancy and the non-pregnant control group. The normal HbA1c range in non-pregnant women was reported as 4.7-6.3%. In early pregnancy, the HbA1c range was 4.5-5.7%, which represented a decrease from the normal range. Furthermore, in late pregnancy, HbA1c levels decreased even further to a range of 4.4-5.6%. It can be concluded from the study that HbA1c levels decrease during pregnancy, with a more pronounced decrease observed in late pregnancy compared to early pregnancy. The findings suggest that HbA1c levels in pregnant women may differ from those in non-pregnant women, and this should be taken into consideration when interpreting HbA1c results during pregnancy. [50].

In 2006, C.J.O. Sullivan, Haynes et al., the researchers investigated the correlation between plasma HbA1c levels and increased morbidity and mortality in the patients who had undergone vascular surgery procedures. The study included a total of 165 consecutive patients, who were divided into different groups based on their plasma HbA1c levels. The first group consisted of patients with HbA1c levels between 6% and 7%, while the second group included patients with suboptimal HbA1c levels above 7%. It is important note that patient in the second group with HbA1c levels above 7% were also examined for undiagnosed diabetes. The study found that 58% of patients with suboptimal HbA1c levels above 7% did not have prior diabetes diagnosis. Among the patients with suboptimal HbA1c levels between 6% and 7% there was higher prevalence of overall 30- day morbidity compared to patients with HbA1c levels below 6%. These results indicate that suboptimal HbA1c levels above 7% have prognostic significance in patients without diabetes who have undergone vascular surgery. [51]

In 2008 Lydie N Pani, Leslie Korenda at al., studied the effect of aging on HbA1c levels in individuals without diabetes. Across sectional survey examining HbA1c levels in non-diabetic patients across different age groups was conducted using data from the from Framingham off spring study (FOS) and National health &Nutritional Examination survey (NHAHES). The study aimed to investigate the relationship between age and HbA1C levels while adjusting for factors such as BMI, Sex, Age and fasting glucose through a multivariate analysis. The result of the analysis revealed a positive association between HbA1C levels and age in non-diabetic subjects. After adjusting for confounding variables, the study found that approx.97% of non-diabetic individuals <40 years had HbA1c level of 6.0% or lower, while it was 5.6% for same age group and in NHANES survey 6.6% and 6.2% for aged >70 years with a peak value of 0.001 (P <0.001). Since HbA1c association with age was similar in both the age groups therefore this study leads to conclusion that HbA1c levels are positively associated with age in non-diabetic subjects [52].

In 2009Amar Rashid and Iqbal Haider did a cross-sectional study which was conducted on 100 patients with type-2 Diabetes to assess their serum lipid profiles in controlled and uncontrolled type-2 diabetes? The study identified statistically significant differences in serum lipid profile between the genders within the diabetic population. Among the participants, 72% were males and 28% were females. The study found that total cholesterol (TC) and LDL cholesterol levels were significantly higher in the uncontrolled diabetes group (group 2) compared to the controlled diabetes (group 1). On the other hand, HDL cholesterol levels were significantly lower in group 1 compared to group 2. These findings lead to the conclusion that diabetic patients with good glycemic control have a lower risk of cardiovascular diseases compared to those with poor glycemic control [53].

In 2010, Chandrasekhar M. Sultanpur and colleagues presented a comprehensive review on HbA1c and its limitations, while HbA1c is widely accepted as the primary biomarker for diagnosing diabetes mellitus. It is crucial to understand the potential interferences or limitations of HbA1c results. The review highlighted various pathological conditions that can interfere with HbA1c measurements, including Hemoglobinopathies or abnormal hemoglobin variants as well as abnormalities in erythrocyte turnover rates. Additionally, the use of certain drugs in the treatment of malignancies can also impact HbA1c levels. It was noted that approx. 700 Hemoglobin variants can cause mutations in globin genes, leading to amino acid substitutions. This in turn can result in falsely high or low HbA1c results. These interferences caused by hemoglobin variants can provide inaccurate measurements when the HbA1c is measured using the standard method. Therefore, the review recommended modifying the measurement method to ensure the most accurate HbA1c results. By addressing the interference caused by hemoglobin variants, it is possible to improve the reliability and accuracy of HbA1c measurements for the diagnosis and management of diabetes mellitus.[54]

In 2011, Iftekhar Ahmad, Asim Syed shed light on standardization of glycosylated HbA1c measurements. Different laboratories use various assays to measure glycosylated hemoglobin in the same sample, leading to a lack of standardization and wide variation in HbA1c results. To address this issue, international federation of clinical chemistry and laboratory medicine (IFCC) developed a new reference method that is now used worldwide to measure HbA1c values in mmol/mol. Additionally, the national Glycohemoglobin standardization program (NGSP) derived HbA1c units in percentages using the IFCC master equation. As a result, HbA1c results can now be expressed in both percentage and mmol/L, providing a standardized approach for interpretation.[55]

In 2012Ikhlas K. Hameed et al., conducted a study to analyze the role of HbA1c as a diagnostic biomarker for predicting diabetic dyslipidemia in patients with type 2- diabetes. The study employed high performance liquid chromatography (HPLC) to estimate Glycosylated HbA1c levels. Blood serum was analyzed for Total Cholesterol, HDL, LDL and Triglycerides. Statistical analysis of the data, based on a population of 450 diabetic patients, revealed a positive correlation between HbA1clevels and various lipid parameters. Specifically a significant positive correlation was observed between HbA1c and Total Cholesterol (p=0.000), LDL cholesterol (p=0.000), and the ratio of LDL to HDL Cholesterol (p=0.0001) furthermore, the study found that Patients with HbA1c values >7.0% were at a high risk of developing cardiovascular diseases these findings suggest that HbA1c can serve as a valuable biomarker for predicting and assessing diabetic dyslipidemia, with higher HbA1c levels indicating an increased risk of cardiovascular complications. [56]

In 2013, Raja Reddy, Jayarama N and colleagues conducted a study to evaluate the relationship between HbA1c and lipid parameters in a total of 750 subjects with type-2 Diabetes. The study included 493 males and 257 female diabetic patients. Statistical analysis was performed to assess the results. The findings of the study indicated that 9.81% of the female diabetic patients exhibited increased values of fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), and LDL cholesterol, while their HDL levels were decreased. These results suggested a higher risk of cardio vascular diseases in diabetic females when compared to diabetic males [57].

In 2014 Yuthika Agarwal, Vipin Goyal, et al., conducted a study to determine the influence of diabetic dyslipidemia in a population of 100 individuals with type-2 diabetes and 100 non- diabetic individuals from the Haryana region of India. The study aimed to compare various parameters between the two groups. The results of the study revealed significant difference Fasting blood glucose (FBG), Total cholesterol (TC), and triglycerides (TG) levels between the diabetic and control groups, with higher levels observed in individuals with diabetes. Furthermore, the levels of high-density lipoproteins (HDL), low density lipoproteins (LDL), triglycerides (TG) were significantly different between diabetic males and diabetic females. Among the diabetic population, the most common dyslipidemia observed was high TG, which was present in 56% of the cases.

Additionally, HDL alone accounted 27% of most common dyslipidemia in diabetic subjects. These findings highlight the impact of diabetic dyslipidemia on lipid profiles in individuals with type 2 diabetes, with elevated levels of FBG, TC, and TG compared to nondiabetic individuals. Moreover, the study suggests a gender difference in lipid parameters among diabetic patients, with variation in HDL, LDL and TG levels. [58].

In 2015 Syed Waseem Pasha, Faseeh K.M et al., conducted a study to examine the pattern of dyslipidemia among patients with type-2 diabetes mellitus in the Mangalore region of India. The study included a total 905 subjects who had dyslipidemia. The findings of the study revealed that 84% of the subjects with dyslipidemia has low levels of high-density lipoprotein (HDL) cholesterol. Additionally, 7.0% of the participants exhibited reduced HDL levels. The most common pattern of dyslipidemia observed in the study was low HDL cholesterol levels, followed by elevated triglycerides (TG) levels. These results highlight the prevalence of dyslipidemia among patients with type 2 diabetes mellitus in the Mangalore region of India. The study emphasizes the significance of low HDL cholesterol as the primary pattern of dyslipidemia in this population, followed by elevated TG levels. [59].

In 2017, a research study conducted by Arshad Hussain, Iftekhar ali, and colleagues examined the relationship between HbA1c levels and serum lipid profile in a group of Afghan patients diagnosed with type 2 diabetes (T2DM). This study included 401 participants with T2DM, consisting of 175 men and 226 women, with a mean age of 51.29 yrs. The average age ± standard deviation for male patients was 51.71 ± 11.70 yrs, while for female patients, it was 50.97 ± 10.23 yrs. The finding of the study revealed several significant correlations. HbA1c showed a positive correlation with total cholesterol (TC), Triglycerides (TG), LDL-C, and the ratio of LDL-C to HDL-C. However, the correlation between HbA1c and HDL-C was negative and not statistically significant. Additionally, through linear regression analysis, HbA1c was identified as a predictor of hypercholesterolemia, LDL-C, and TG. Furthermore, the study observed that patients with an HbA1c value greater than 7.0% had significantly higher levels of cholesterol, LDL-C, and the LDL-C/ HDL-C ratio compared to those with HbA1c values below 7.0%.[60]

In 2019, Sami Hamdan alzahrani, Mukhtiar Baig, and their colleagues conducted a study to explore the relationship between Glycated hemoglobin (HbA1c) and lipid profile in patients with T2DM at a tertiary care hospital in Jeddah, Saudi Arabia. The data collected from the participants were analyzed separately for males and females. The study found that females had significantly higher values for body BMI, HbA1c, TG, HDL-C and LDL-C compared to males. These differences were statistically significant, with P-vales of 0.002, 0.009, < 0.001, 0.002, and < 0.001, respectively. The participants were categorized into 2 groups based on their HbA1c levels: Good glycemic control (HbA1c < 7%) and poor glycemic control (HbA1c > 7%). No significant differences were observed between the 2 groups except for TGs (p=0.020) and HbA1c (p < 0.001). The correlation analysis between HbA1c and other variables revealed a significant correlation with TGs (r= 0.16. p=0.020), while no significant correlations were found with the other parameters. Linear regression analysis indicated that HbA1c levels were independently associated with TGs and were not influenced by age, BMI, TC, LDL-C, HDL-C are fasting plasma glucose (FPG) levels. Based on these findings, the researchers concluded that glycated HbA1c levels were associated with TGs but did not show significant associations with age, BMI, TC, HDL-C, LDL-C, or FPG levels [61]

In 2021, a retrospective cross-sectional study was conducted by Hussain A al ghadeer, mohammad al Baqri, and their colleagues at the King Faisal university (KFU) health center in eastern region of Saudi Arabia. The study included a total of 191 patients diagnosed with T2DM, of which 137 (71.7%) were Saudi Arabian and 54 (28.3%) were from other countries. The age of patients ranged from 21 to 100 years, with a mean age of ± 11.8 years. Among the participants, 107 (56%) were females. The cholesterol levels observed in the study ranged from 102 to 300 mg/dl, with a mean value of 187.3 mg/dl [62]

In 2022, Ravirala Tagore, Ayesha Jabeen and their colleagues conducted a study on the association between HbA1c and dyslipidemia in patients with T2DM. The study included 162 patients, consisting of 100 males and 62 females. The participant's sera were analyzed for various parameters, including HbA1c, FBS, TC, TG, HDL and LDL levels. The study found significant positive correlation between HbA1c and FBS (r=0.504), PPBS (r=0.628), TC (r=0.557), TG (r=0.517) and LDL (r=0.592). Additionally, a significant negative correlation was observed between HbA1c and HDL (r=0.449). Patients with good glycemic control exhibited lower mean values of HbA1c, FBS, PPBS, TC, TG, and LDL, as well as higher mean values of HDL, compared to those found minimal variations in HbA1c, FBS, PPBS, and lipid profile parameters between males and female diabetic patients. Based on these findings, the researchers concluded that HbA1c can serve as a potential biomarker for predicting dyslipidemia in patients with T2DM, in addition to its role in assessing glycemic control. [63]

3.Objective of the Study

1) To study Glycated Hemoglobin levels (HbA1c) in type 2 Diabetic patients.
2) To establish the link between HbA1c and hyperlipidemia.
3) To Compare and Correlate Glycated Hemoglobin levels with their lipid levels in type 2 Diabetic patients and in normal subjects.
4) To evaluate the association between Glycated Hemoglobin (HbA1c) and various lipid profile Parameters with type 2 Diabetes Mellitus.

4.Materials and Methods

The Study was conducted at Metropolis laboratory Baghat Barzulla, Srinagar, in the department of Biochemistry. A total of 60 subjects participated in the study (28 male and 32 female) participants with a minimum ≤4 year history of diabetes and maximum ≥4 year history of diabetes were

recruited for the study. The study was completed covering the period of 3 months from (January 05 to April 05-2023). Patients were selected from indoor and outdoor patient department. The age group selected was from 20– 83 years. Majority of the patients were stabilized on drugs and few were insulin dependent. All the 3 parameters i.e. HbA1c, blood glucose and lipid profile was estimation was performed on Pentra C-400 (by Horiba) and Tosoh HLC-723GX Automated Glycohemoglobin Analyzer.

HbA1c levels were determined by using (HLC-723GX) fully automatic HbA1c analyzer which is based on the principle of Cation exchange HPLC. It gives quick and accurate results. Analysis time 2.2minute/sample.

Blood glucose in the venous blood was determined by using (Pentra C-400) fully automatic biochemistry analyzer based on the principle of Spectrophotometry.
Lipid profile levels viz.; serum triglyceride, total cholesterol and HDL- cholesterol were determined by using (Pentra C-400) a fully automatic biochemistry analyzer. The main advantage of analyzer is that it processes 340 samples per hour and has integrated barcode reader and calculations.

Selection of patients:

Type- 2 Diabetic Patients were selected on the following criteria,

- Duration of diabetes. Diabetic Patients having either maximum ≥ 4 history of diabetes or minimum≤ 4 year history of diabetes.
- Drug dependent or insulin dependent.

Specimen collection and preparation for analysis:

Blood Collection- Fasting blood samples were collected from patients in the indoor and outdoor patient department of the concerned laboratory from 7 .00 am to 1.00 pm. Approx. 5ml blood was taken from the patients for estimation of 3 biochemical parameters: HbA1c, blood glucose and Lipid profile. Therefore, separate Vacutainer tubes were required for each test at the time of collection. One for HbA1c test (EDTA) and one for Lipid Profile (Gel top) and another blood glucose (sodium fluoride grey top) estimation.

Figure 1: Sample collection requirements

Figure 2: EDTA samples for HbA1c

Figure 3: Grey and gel Vacutainer for

BSF and lipid profile

Serum separation:

Serum was separated from blood into the centrifuge and was later used for analysis of blood glucose and lipid profile estimation.

In case of HbA1c testing Whole blood sample was used for estimation.

Figure 4: Centrifuge

Autoanalyzer: Pentra C-400 (By Horiba)

Procedure, sampling, reagent delivery, mixing, processing were automatically performed by analyzer.

Its main advantage is that it processes 340 samples per hour.
It has integrated barcode reader and calculations.
It has multiple sample checks using crash, level and clot detection.
It has high performance mixer design for optimal mixing in minimum time without cross contamination.
It has mono and bi reagent cassettes for reagents. ABX Pentra reagents are used (liquid based – ready to use).
It has westgard multi rule QC procedure with up to 3 default controls.
It has full QC Program: up to 12-month control history, Levy – Jennings chart and statistics.

Figure 5: Fully Automatic Bio Chemistry Analyzer& loaded rack with samples

5.Methodology

TOSOH HLC-723 GX analyzer

The Tosoh HLC-723 GX HbA1c analyzer utilizes high performance liquid chromatography (HPLC) to measure Glycated hemoglobin (HbA1c) levels in blood samples. The working principle involves several steps;

Figure 6: Fully automatic HbA1c Analyzer

Sample Preparation: Blood samples are collected using EDTA anticoagulant tubes. The samples are then prepared by undergoing hemolysis, which involves breaking down the red blood cells to release hemoglobin.

HPLC Separation: The analyzer employs a specialized high-pressure liquid chromatography column designed to separate different forms of hemoglobin in the sample. This column effectively separates HbA1c from other hemoglobin fractions, such as unmodified hemoglobin (HbA0) and variant hemoglobin's.

Elution and Detection: The separated hemoglobin fractions are eluted from the column and pass through a detector, typically a spectrophotometric detector. This detector measures the absorbance of each fraction at a specific wavelength.

Quantification: The absorbance data acquired from the detector is processed by the instrument's software. Using this data, the software calculates the HbA1c percentage by determining the ratio of the HbA1c peak area to the total hemoglobin peak area.

Calibration and Quality Control: The instrument necessitates regular calibration using certified reference materials that have known HbA1c values. Additionally, quality control samples with predetermined HbA1c values are periodically analyzed to ensure the accuracy and reliability of the instrument's measurements.

Result Reporting: Once the analysis is completed, the instrument generates a comprehensive report that includes the HbA1c results for each sample. These results are typically expressed as a percentage of total hemoglobin.

By automating sample handling, preparation, separation, detection, and result calculation, the TOSOH HLC-723 GX HbA1c Analyzer offers precise and efficient analysis of HbA1c levels in clinical samples.

REAGENTS:

Gx Elution buffers: The elution buffer is a solvent or buffer solution that flows through the column and aids in the elution of the separated components.

During the separation process, the different hemoglobin fractions, including HbA1c, are eluted from the column and passed through a detector, typically a spectrophotometric detector, which measures the absorbance of each fraction at a specific wavelength. The absorbance data is then processed by the instrument's software for quantification and result reporting.

Figure 7: Elution buffers

GX hemolysis & wash Solution:

The Tosoh HLC 723 GX analyzer utilizes specific hemolysis and wash solutions to facilitate the sample preparation and system cleaning processes.

Hemolysis Solution:

The TOSOH HLC-723 GX Analyzer employs a hemolysis solution in the following manner:

Sample Preparation: Blood samples collected in tubes containing the anticoagulant EDTA are introduced into the analyzer.

Hemolysis Process: The hemolysis solution is added to the blood sample, leading to the rupture (hemolysis) of red blood cells and the release of hemoglobin.

Hemoglobin Release: The breakdown of red blood cells causes the hemoglobin to be released into the solution, making it available for subsequent analysis.

The purpose of the hemolysis solution is to facilitate the liberation of hemoglobin from red blood cells, ensuring accurate separation and analysis of the different hemoglobin fractions in subsequent steps.

Wash Solution:

The TOSOH HLC-723 GX Analyzer employs a wash solution to perform system cleaning and maintenance:

1) **System Cleaning**: The wash solution is used to clean various components of the analyzer, including the chromatography column, detector, and other relevant parts.

2) **Removal of Residues**: The wash solution is circulated through the system, effectively removing any residual sample components or contaminants that may remain from previous analyses.

3) **Preventing Carryover**: Thorough cleaning with the wash solution helps prevent carryover and cross-contamination between samples, ensuring accurate and reliable results.

Figure 8: Wash solution

Table 3: Reference range

HbA1c:

Range	Remarks
4-5.7%	Normal (Non Diabetes).
5.7-6.4%	Pre diabetes (Pre Diabetes).
6.5%	good control
>=6.5 % >= 7.0%	Diabetes
	Diabetic complications

Lipid profile:

Test	Normal Range
Cholesterol	<200 mg/Dl
Triglycerides	<150mg/Dl
HDL cholesterol	>=60mg/dL
LDL cholesterol	<100mg/Dl
VLDL cholesterol	<30 md/Dl

Blood sugar fasting:

Range	Remarks
70-99mg/Dl	Normal
100-125mg/Dl	Impaired tolerance
>=126, g/dL	Diabetes mellitus

6.Results

A total of 60 individuals were enrolled in the research study. The demographic profile of the participants (n=60) consisted of 32 females and 28 males. The age range of the participants varied from 20 to 83 years. In the initial phase of the study, the subjects were categorized based on different HbA1c cutoff values. Among the 60 participants, 42 were identified as having both diabetes and dyslipidemia, 4 were diagnosed with diabetes only, 6 were classified as pre-diabetic, and 8 individuals exhibited normal glucose regulation.

In the second phase of the study, all 60 subjects were divided into two groups based on their HbA1c cutoff value: ≥ 7.0% and ≤ 7.0%.

Group 1 consisted of patients with HbA1c ≥ 7.0%, indicating poor control of diabetes, and they were referred to as diabetic dyslipidemia.

On the other hand, Group 2 comprised patients with HbA1c ≤ 7.0%, indicating good glycemic control.

The results of the study revealed a positive association between HbA1c levels and lipid parameters as well as fasting blood glucose (FBG). However, a negative correlation was observed between HbA1c and HDL cholesterol.

Specifically, patients with poor control of diabetes exhibited decreased levels of HDL cholesterol, while those with good glycemic control demonstrated higher levels of HDL cholesterol.

Out of the 42 individuals diagnosed with diabetic dyslipidemia, 15 were male, while the remaining 27 were females. The mean age and standard deviation of the male and female participants were 49.46 ± 15.42 and 46.28 ± 13.21, respectively.

In terms of HbA1c levels, females had a slightly higher mean of 9.18 ± 2.59 compared to males with a mean of 7.35 ± 2.31.

Females also exhibited higher mean fasting blood glucose (FBG) levels of 197.76 ± 76.85, whereas males had a mean FBG level of 157.03 ± 68.61.

The mean total cholesterol (TC) level in females was 215.12 ± 29.57, surpassing the male average of 181.75 ± 42.45.

Among females, the average triglyceride (TG) level was significantly higher at 281.86 ± 98.15 compared to males, who had an average TG level of 219.08 ± 120.22.

Furthermore, females had higher mean levels of low-density lipoprotein (LDL) with values of 119.87 ± 19.30, while males had lower LDL levels. Lastly, females showed slightly higher mean levels of high-density lipoprotein (HDL) compared to males. (Table)

Table 4: Assessment and comparison of lipid profile parameters and HbA1c results in male and female participants (n=60)

Total no. of patients (n=60)	**Males (n=28)**	**Females (n=32)**
	Mean ±SD	Mean ±SD
Age (yrs.)	49.46 ± 15.42	46.28 ± 13.21
HbA1c (%)	7.35 ± 2.31	9.18 ± 2.59
T.G (mg/dl)	219.08 ± 120.2	281.86 ± 98.15
T. chol (mg/dl)	181.75 ± 42.45	215.12 ± 29.57
HDL (mg/dl)	41.27 ± 7.26	40.85 ± 7.53
LDL (mg/dl)	107.47 ± 32.19	119.87 ± 19.30
FBG (mg/dl)	157.03 ± 68.61	197.76 ± 76.85

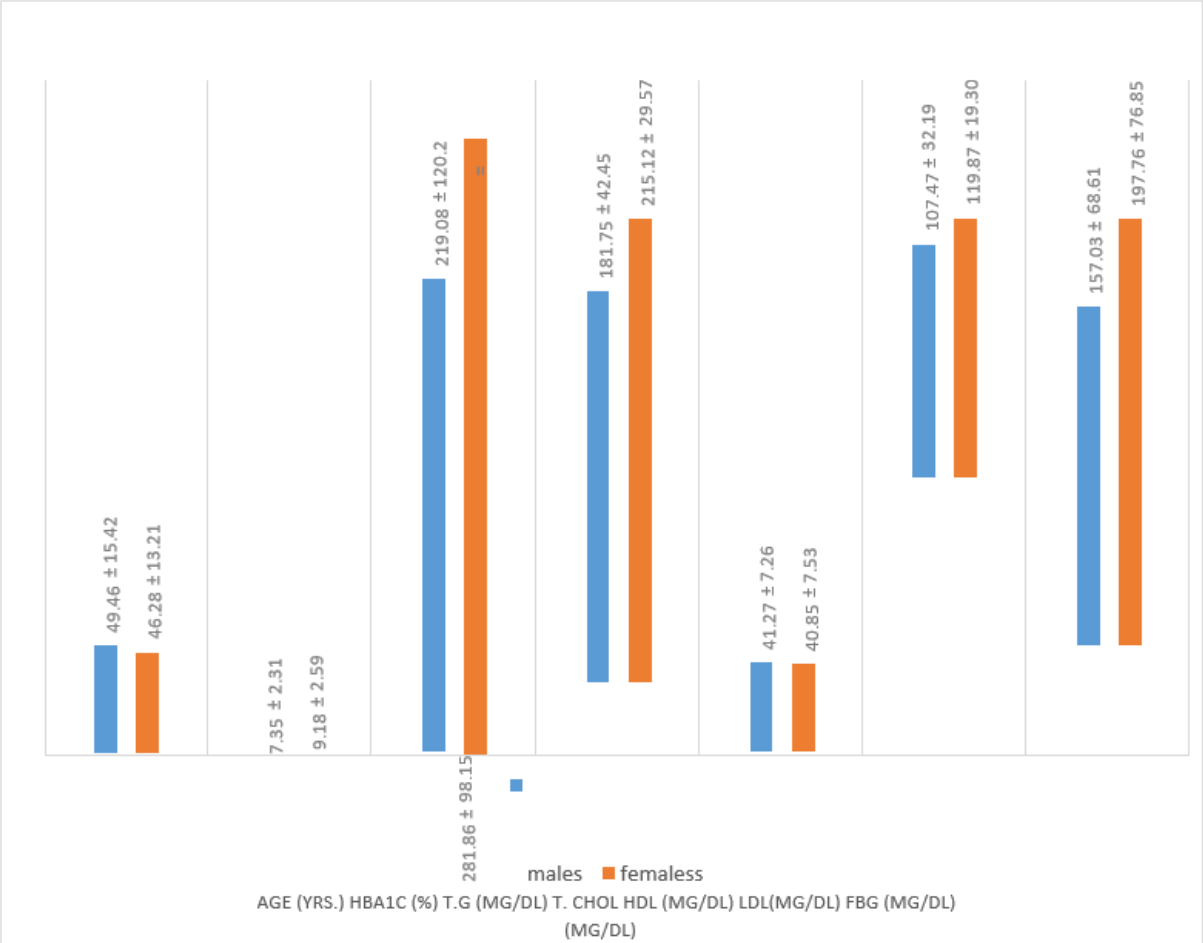

Figure 9: HbA1c results and lipid profile parameters of total 60 subjects

In the first part of the study, a total of 60 subjects were divided into four groups based on their HbA1c cutoff values. These groups were named as diabetic dyslipidemia, diabetic, pre-diabetic, and normal. The assignment of subjects to each group was based on their HbA1c levels.

Group 1, referred to as diabetic dyslipidemia, consisted of 42 patients with HbA1c levels ≥7.0. These patients were categorized as having dyslipidemia due to their poor glycemic control. The mean HbA1c in the diabetic dyslipidemia group was 9.47 ± 2.46.

In the diabetic group, the mean HbA1c was 6.52 ± 0.12. For the pre-diabetic group, the mean HbA1c was 6.03 ± 0.19, while the normal group had a mean HbA1c of 5.4 ± 0.20.

The mean values of total cholesterol (TC) in the diabetic dyslipidemia group were 215.4 ± 30.78.

In the diabetic group, the mean TC was 156.5 ± 49.88. The pre-diabetic group had a mean TC of 171.6 ± 36.14, and the normal group had a mean TC of 180.83 ± 27.0.

The mean values of triglycerides (TG) in the diabetic dyslipidemia group were 309.27 ± 89.2. In the diabetic group, the mean TG was 130.4 ± 42.55. The pre-diabetic group had a mean TG of 130.3 ± 36.69, and the normal group had a mean TG of 128.88 ± 46.45.

The mean values of fasting blood glucose (FBG) in the diabetic dyslipidemia group were 209.26 ± 73.23. In the diabetic group, the mean FBG was 137.7 ± 14.75. The pre-diabetic group had a mean FBG of 116.1 ± 10.41, and the normal group had a mean FBG of 94.4 ± 9.66.

Regarding LDL cholesterol, the mean value in the diabetic dyslipidemia group was 118.12 ± 25.82. In the diabetic group, the mean LDL cholesterol was 85.4 ± 42.4. The pre-diabetic group had a mean LDL cholesterol of 98.4 ± 19.22, and the normal group had a mean LDL cholesterol of 114.86 ± 22.52.

It was observed that patients with high HbA1c levels (≥7.0%) had elevated levels of FBG, TC, TG, and LDL compared to the other groups.

However, they had significantly lower levels of HDL cholesterol with a mean of 39.5 ± 6.84. In comparison, the diabetic group had a higher mean value of HDL cholesterol at 45.25 ± 6.0, the pre-diabetic group had a mean HDL value of 44.6 ± 6.14, and the normal group had an even higher mean value of HDL cholesterol.

The study concluded that diabetic patients with elevated HbA1c levels and dyslipidemia are at a very high risk for cardiovascular diseases. It was also observed that as HbA1c values increase, the severity of dyslipidemia worsens in diabetic patient.

Table 5: An evaluation and comparison of lipid parameters were conducted among Dyslipidemia, Diabetic, Pre-Diabetic, and Normal subjects, based on various HbA1c cutoff values

Total no. of patients (n=60)	**n=42**	**n=4**	**n=6**	**n=8**
	HbA1c≥7.0 (%)	**HbA1c≥6.5— 6.9 (%)**	**HbA1c 5.4-6.4 (%)**	**HbA1c≤5.4 (%)**
	Mean ±SD	**Mean ±SD**	**Mean ±SD**	**Mean ±SD**
HbA1c (%)	9.47 ±2.46	6.52 ±0.12	6.03 ±0.19	5.4 ±0.21
TG (mg/dl)	309.27 ±89.2	130.4 ±42.55	130.33 ±36.69	128.88 ±46.45
T. Chol (mg/dl)	215.4 ±30.78	156.5 ±49.88	171.67 ±36.18	180.83 ±27.98
HDL mg/dl)	39.5 ±6.84	45.25 ±6.0	44.6 ±6.15	44.17 ±10.47
LDL (mg/dl)	118.12 ±25.82	85.4 ±42.4	98.41 ±19.22	114.87 ±32.52
BSF (mg/dl)	209.26 ±73.23	137.75 ±14.75	116.16 ±10.42	94.4 ±9.6

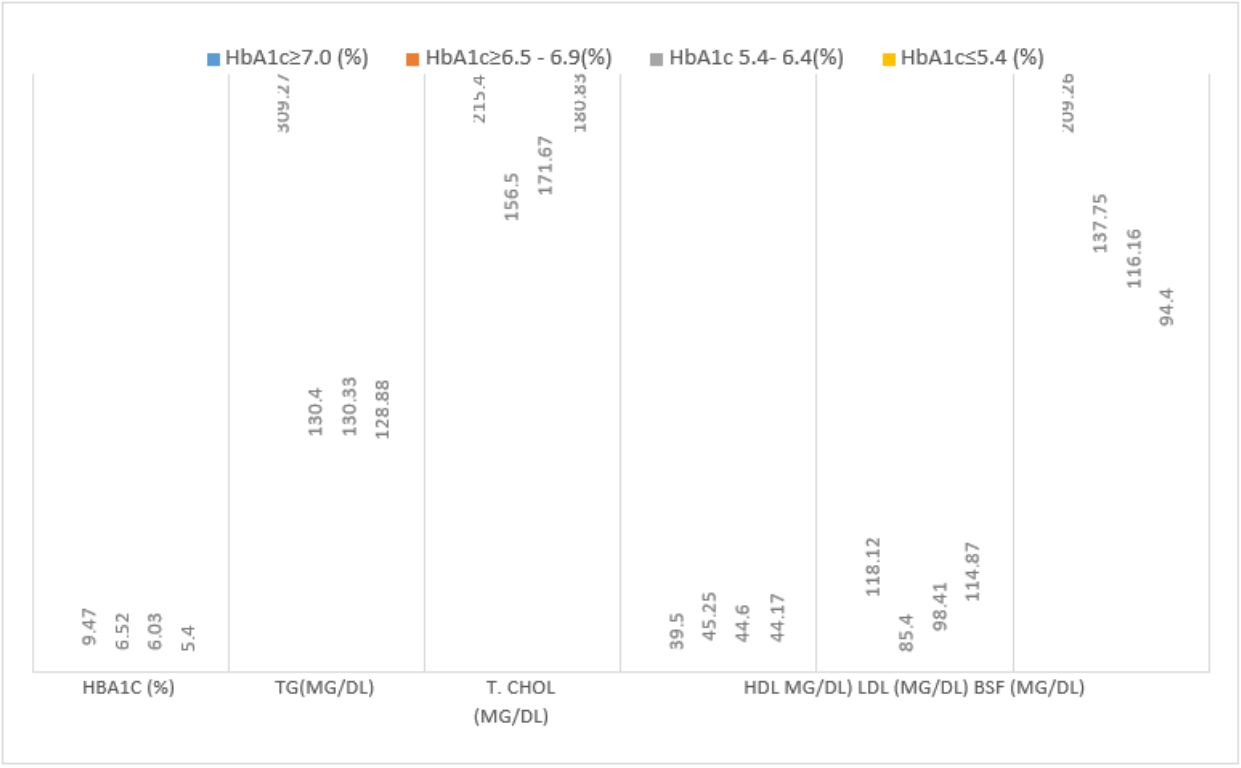

Figure 10: Graphical representation of HbA1c levels and lipid Parameters in Dyslipidemia, Diabetic, Pre- Diabetic and in Normal Subjects

In the second part of the study, diabetic patients were divided into two groups based on their HbA1c levels: Group 1 included patients with HbA1c ≥7.0%, and Group 2 consisted of patients with HbA1c ≤7.0%. Table--- provided information about dyslipidemia individuals, with 15 males and 27 females included in the study.

Among these individuals, the mean HbA1c value was found to be 9.47 ± 2.46, which was significantly higher than those with HbA1c ≤7.0%, who had a mean HbA1c of 5.8 ± 0.46.

Regarding lipid parameters, the mean LDL cholesterol in diabetic dyslipidemia patients was 118.12 ± 25.82, which was higher compared to Group 2, where the mean LDL cholesterol was 103.8 ± 27.51.

Similarly, the mean TC in dyslipidemia patients was 215.4 ± 30.78, whereas in those with good diabetes control (HbA1c ≤7.0%), the mean TC was 165.83 ± 37.3.

Furthermore, dyslipidemia patients had a higher mean TG value of 281.86 ± 98.15, whereas patients with well-controlled diabetes had a lower mean TG of 127.01 ± 37.65.

Additionally, the mean FBG in dyslipidemia individuals was 209.26 ± 73.23, while in normal subjects, it was 111.5 ± 20.1. In terms of HDL cholesterol, dyslipidemia patients had a mean value of 39.5 ± 6.84, which was lower compared to those with good diabetes control, who had a mean HDL cholesterol of 45.07 ± 7.19.

In summary, the findings from this part of the study highlighted the differences in lipid parameters among dyslipidemia individuals and those with well-controlled diabetes.

Dyslipidemia patients with higher HbA1c levels exhibited elevated levels of LDL cholesterol, TC, TG, and FBG, while having lower levels of HDL cholesterol compared to those with good diabetes control. These results emphasize the impact of glycemic control on lipid profiles in diabetic patients with dyslipidemia.

Table 6: Evaluations and Comparison of Lipid Profile results based on glycemic control (HbA1c ≥7.0 & ≤ 7.0%) in Type -2 diabetic Patients

Parameters	Group 1 (Poor glycemic control)	Group 2 (good glycemic control)
	Diabetic dyslipidemia ≥ 7.0 (%)	Diabetic ≤ 7.0 (%)
	mean ± SD	Mean ± SD
Total no. of patients = (60)	n=42	n=18
HbA1c (%)	9.47±2.479.47	5.8±0.46
T.G (mg/dl)	309.27±89.29	127.01±37.65
T.CHOL (mg/dl)	215.4±30.79	165.83±37.33
HDL (mg/dl)	39.53±6.84	45.07±7.19
LDL (mg/dl)	118.13±25.83	143.85±27.52
BSF (mg/dl)	209.26±73.23	111.5±20.11

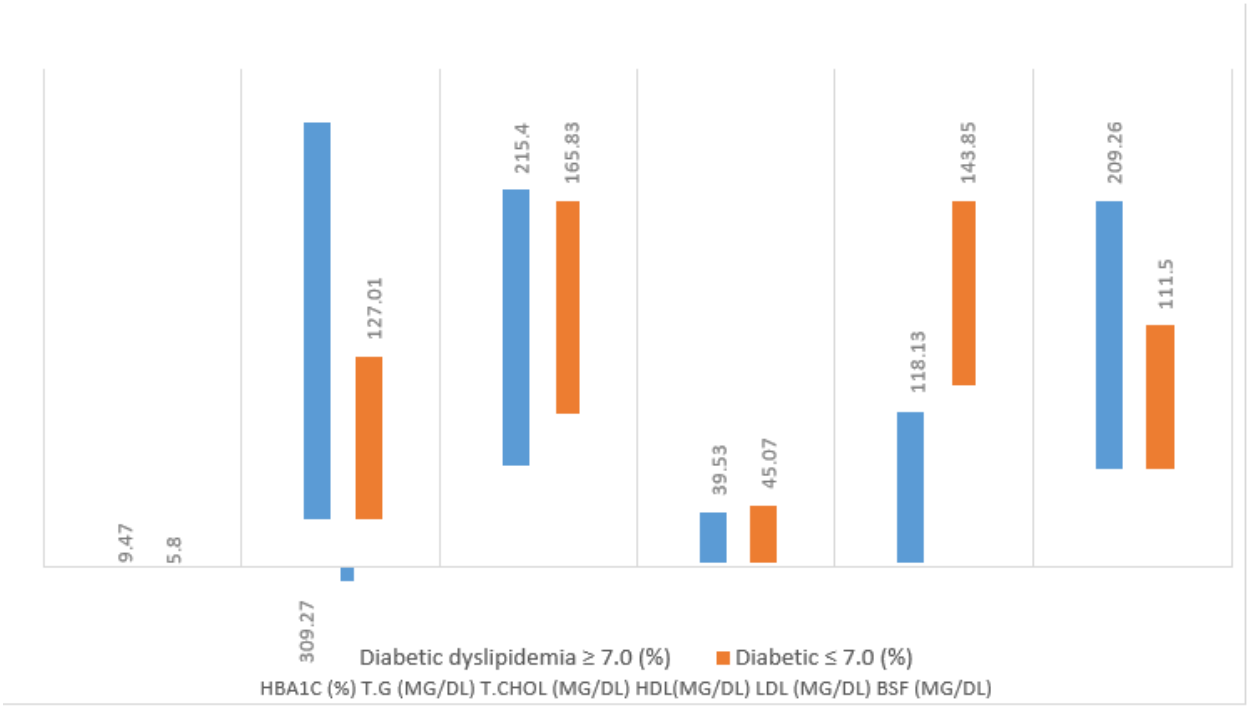

Figure11: Lipid Profile results based on glycemic control (HbA1c cut off ≥ 7.0% and ≤ 7.0%) inType -2 diabetic Patients

Triglycerides vs. HbA1c

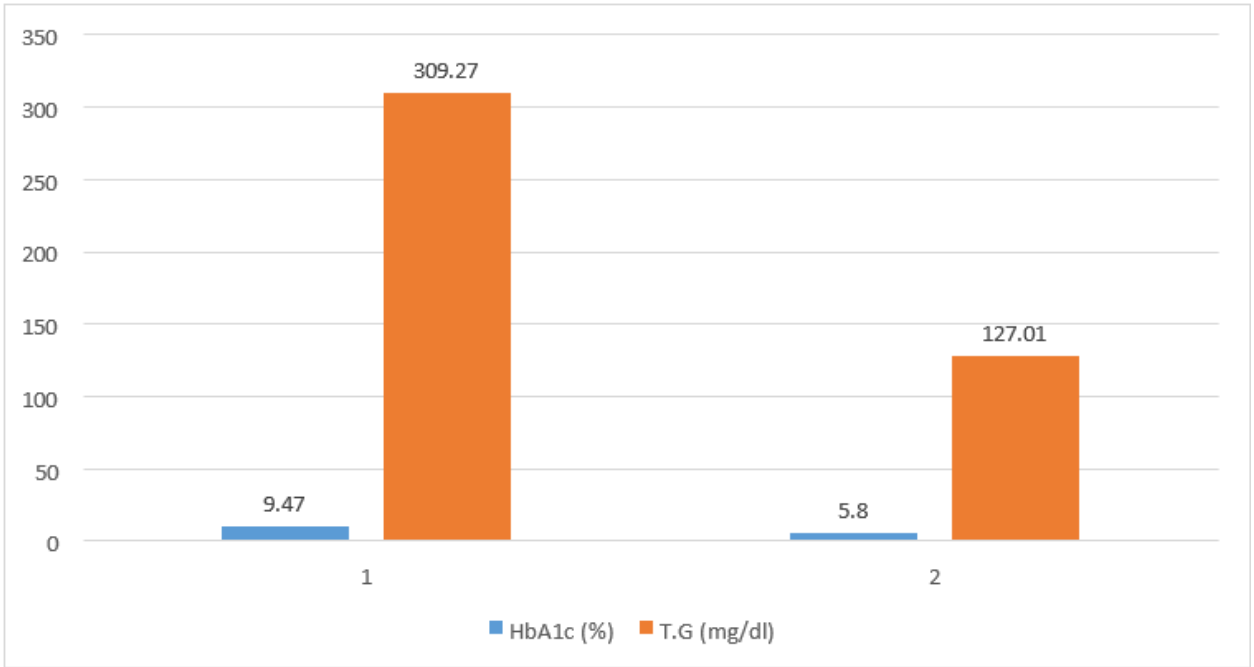

Figure 12: Graphical representation, showing correlation of Triglycerides with Poor glycemic control (HbA1c ≥7.0%) and Good glycemic control HbA1c ≤ 7.0%)

Group 1 - Hyper triglyceridemia.

Cholvs. HbA1c

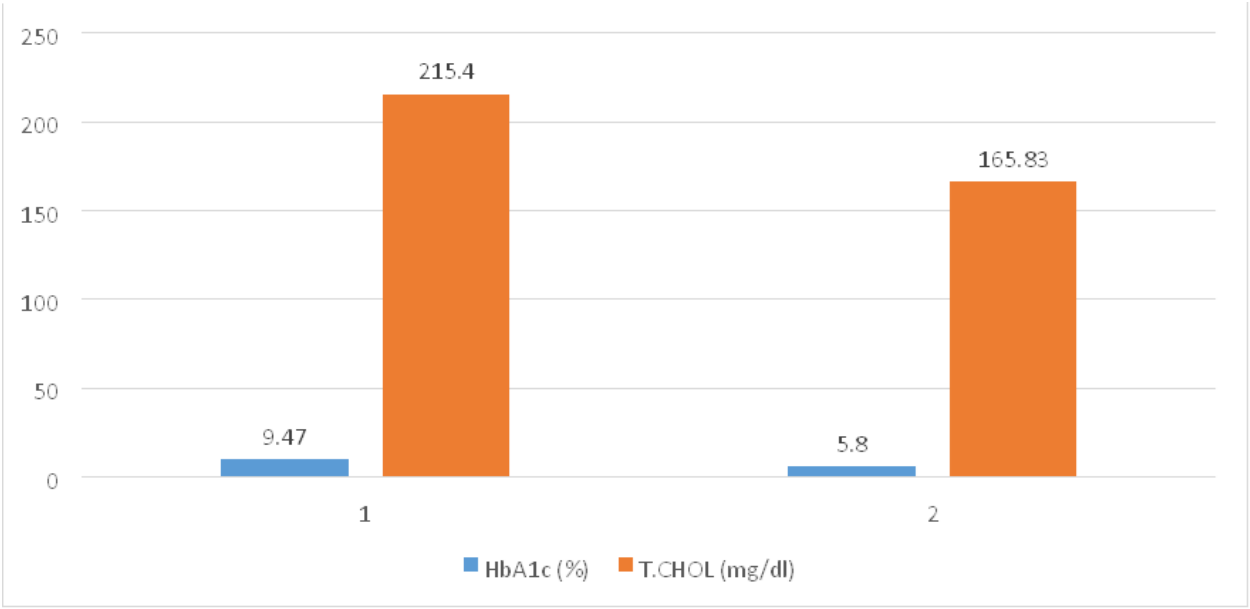

Figure 13: Graphical representation illustrating the correlation between HbA1c levels and Total cholesterol in individuals with both poor and good glycemic control

Group 1- hypercholesterolemia

HDL vs. HbA1c

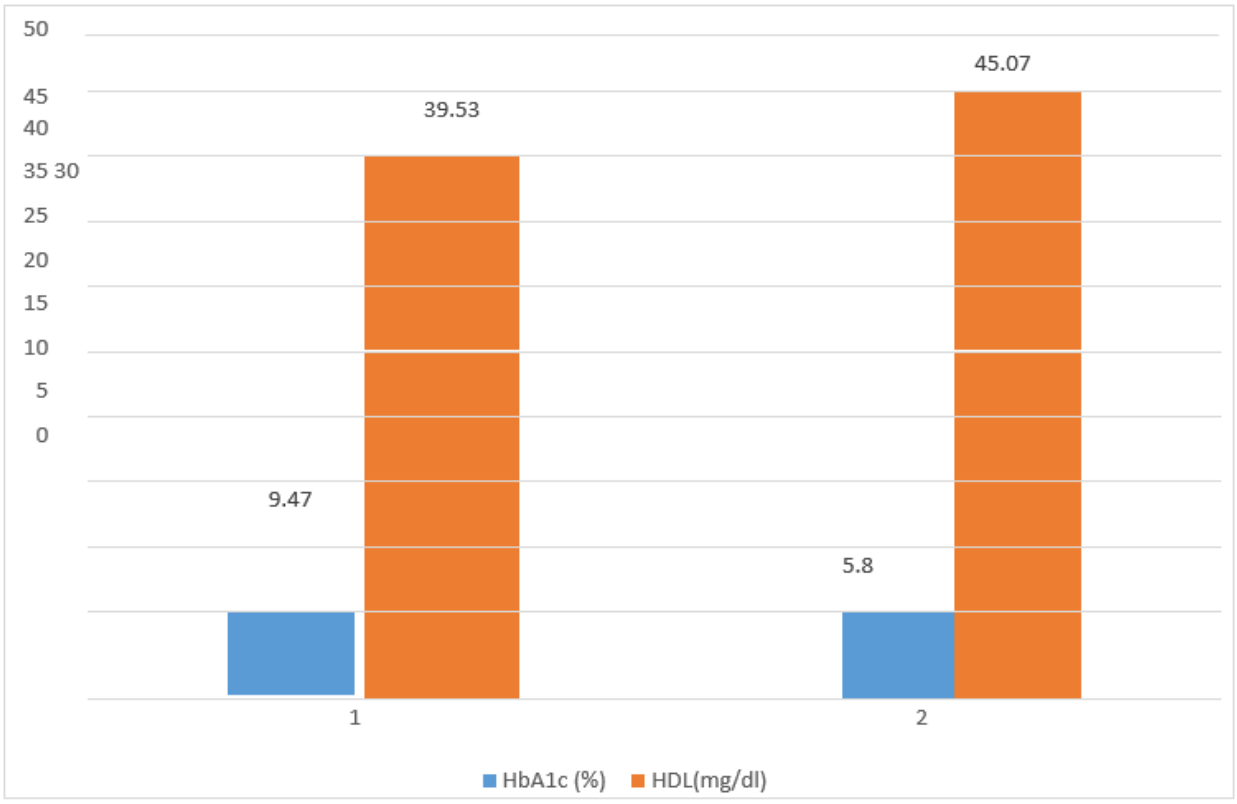

Figure 14: Graphical representation illustrating the negative relationship between HbA1c levels and HDL cholesterol in individuals with both poor and good glycemic control

LDL vs. HbA1c

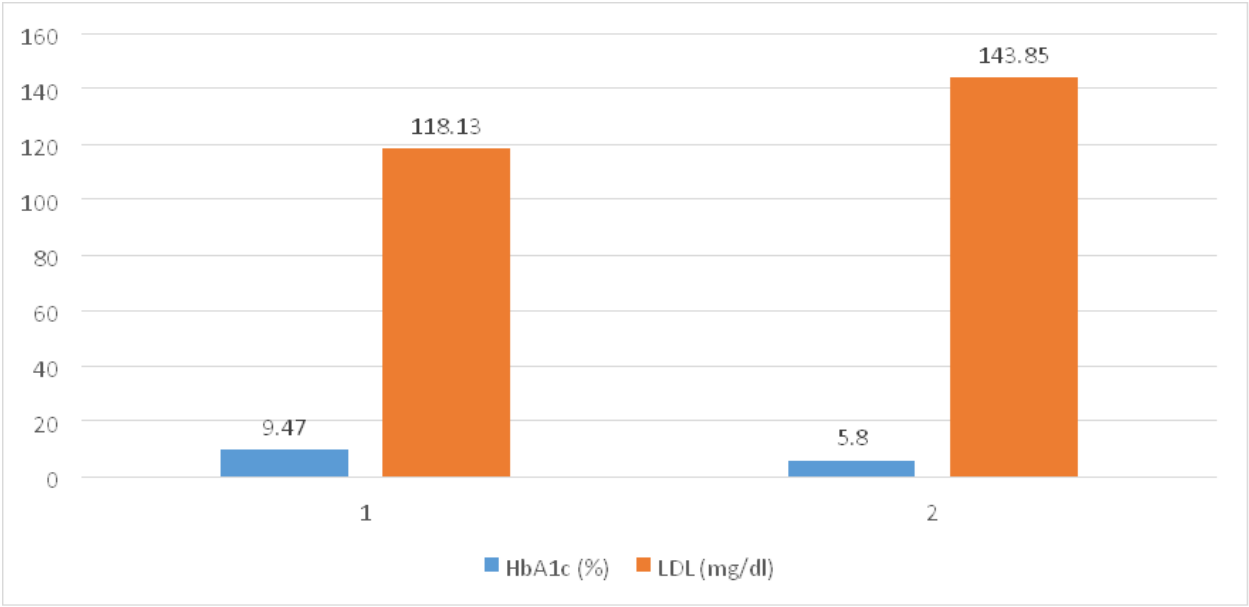

Figure 15: Correlation between LDL-cholesterol and HbA1c in poor and good glycemic control

BSF vs. HbA1c

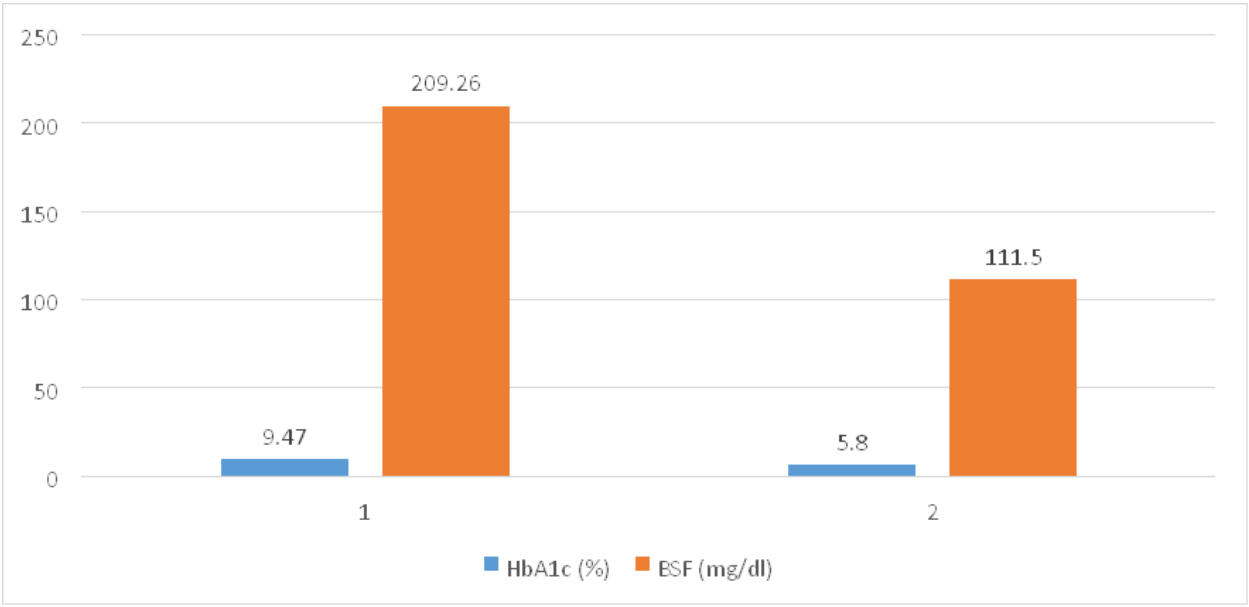

Figure 16. A graphical comparison depicting BSF (Blood Sugar Fasting) levels and HbA1c levels in individuals with both poor and good glycemic control

Group 1- Hyperglycemia.

7.Discussion

The study conducted found a positive correlation between HbA1c levels and dyslipidemia in individuals with type 2 diabetes mellitus. HbA1c is a reliable marker for assessing long-term glycemic control and is also indicative of the likelihood of developing diabetic dyslipidemia in type 2 diabetes patients. Dyslipidemia, characterized by abnormal lipid levels, is commonly observed in individuals with type 2 diabetes and significantly increases the risk of cardiovascular diseases and complications related to atherosclerosis. The persistent elevation of blood glucose levels, or hyperglycemia, leads to the glycosylation of various proteins, including collagen and matrix proteins within the arterial wall. Over time, this process gradually impairs the function of endothelial cells, contributing to the development of atherosclerosis. [64]

While the exact mechanisms underlying diabetic dyslipidemia are not yet fully understood, evidence from numerous research studies suggests that insulin resistance plays a central role in its development. Fat cells that are resistant to the effects of insulin release higher amounts of free fatty acids, which subsequently enter the liver. In the presence of sufficient glycogen stores within the liver, the increased influx of free fatty acids promotes the production of triglycerides, leading to the secretion of very low-density lipoprotein (VLDL), Apo lipoprotein B, and cholesterol. The impaired ability of insulin to inhibit the release of free fatty

acids exacerbates hepatic VLDL cholesterol production and contributes to the accumulation of fat within the liver.[65]

The specific features of diabetic dyslipidemia can vary, but the most common characteristics include elevated triglyceride levels, low levels of high-density lipoprotein (HDL) cholesterol, high total cholesterol levels, and high levels of low-density lipoprotein (LDL) cholesterol. Type 2 diabetes itself, particularly in the presence of hyperglycemia, poses a significant risk factor for cardiovascular diseases. Therefore, achieving tight glycemic control is crucial as it can improve the lipid profile of diabetic patients and reduce the associated risk of cardiovascular disease.[66]

The analysis of gender and HbA1c cutoff values in the study reveals that a significant proportion of individuals with type 2 diabetes have poor glycemic control, as depicted in Table 4. The findings indicate a positive association between HbA1c levels and several lipid markers, including triglycerides, total cholesterol, LDL cholesterol, fasting blood glucose (FBG), and HDL cholesterol, in both males and females. Although there are no substantial differences in the mean values of HbA1c and total cholesterol between genders, females tend to exhibit higher levels of both variables, as evidenced in Table 4. Furthermore, the average HbA1c and fasting blood glucose values were found to be higher in females compared to males. Among the circulating lipids, LDL cholesterol and triglyceride levels were notably elevated in females in comparison to males, while there was a slight elevation in mean HDL cholesterol levels in females, as illustrated in Figure 9.

Individuals with diabetes, regardless of gender, exhibit significant alterations in their lipid profiles.

However, females with diabetes have been found to be more prone to developing cardiovascular diseases. Studies have shown that diabetic women have an increased risk of cardiovascular mortality [67]. Moreover, diabetic women experience more unfavorable changes in vascular function and other cardiovascular risk factors compared to their male counterparts [68]. The results of the study demonstrate that female diabetic patients had significantly higher levels of cholesterol, LDL cholesterol, triglycerides, fasting blood glucose, and HbA1c when compared to males. These findings align with the conclusions drawn from various studies conducted by different researchers in diverse geographical regions.

In this particular study, diabetic patients were categorized into two groups based on their glycemic index. Group 1 consisted of 42 patients with an HbA1c value of ≥7.0%, while Group 2 included 18 patients with an HbA1c value of ≤7.0%. The findings demonstrated that individuals with an HbA1c value ≥7.0% exhibited a significant elevation in total cholesterol (TC), triglycerides (TG), fasting blood glucose (FBG), and notably lower levels of high-density lipoprotein (HDL) cholesterol compared to those with an HbA1c value ≤7.0% (as indicated in Table 6 and Figure 11). Patients with an HbA1c value ≥7.0% were classified as having diabetic dyslipidemia, whereas those with an HbA1c value ≤7.0% were considered diabetic but maintaining satisfactory glycemic control.

The current study also highlights a high prevalence of hypercholesterolemia, hypertriglyceridemia, hyperglycemia, elevated LDL cholesterol, and low HDL cholesterol in diabetic dyslipidemic patients. These patients were found to possess multiple risk factors for cardiovascular diseases. The study findings demonstrate a positive correlation between HbA1c levels and triglycerides (Fig. 12), HbA1c and total cholesterol (Fig. 13), HbA1c and LDL cholesterol (Fig. 15), and HbA1c and fasting blood glucose (Fig. 16). Additionally, a negative correlation was observed between HbA1c and HDL cholesterol in both groups (Fig. 14). The study reveals that diabetes significantly increases the risk of cardiovascular events in both groups, with Group 1 (HbA1c ≥7.0%) showing an exceptionally high risk of cardiovascular diseases. These results align with a previous study conducted by Ishfaq Ahmed et al. [69], which also reported a high prevalence of dyslipidemia in individuals with type 2 diabetes. The present study's findings on the positive correlations between HbA1c and fasting blood glucose are consistent with various other studies [70].

8.Conclusion

In summary, our study conducted at Metropolis Laboratory found a higher prevalence of dyslipidemia among female diabetic patients compared to males. Diabetic patients with elevated HbA1c levels and dyslipidemia were identified as being at a significantly higher risk for cardiovascular diseases. We observed that the severity of dyslipidemia worsened as HbA1c values increased in diabetic patients. The study emphasized the differences in lipid parameters between individuals with dyslipidemia and those with well-controlled diabetes. Dyslipidemia patients with higher HbA1c levels exhibited hypercholesterolemia, hypertriglyceridemia, elevated LDL cholesterol, and low HDL cholesterol. These lipid abnormalities contribute to the increased risk of cardiovascular diseases in diabetic patients. We also discovered positive correlations between HbA1c levels and triglycerides, total cholesterol, LDL cholesterol, and fasting blood glucose, while a negative correlation was found between HbA1c and HDL cholesterol in both groups. These correlations suggest that higher HbA1c levels are associated with worsened lipid and glucose control. Lastly, our study confirmed that diabetes significantly elevates the risk of cardiovascular events in both groups, with Group 1 (HbA1c ≥7.0%) displaying a particularly high risk.

Acknowledgement

All thanks and praise to the Almighty, the most beneficent and the most merciful. I am thankful to all my patients and their families, who despite the agony of their disease responded with an apparent magnanimity and overwhelming cooperation and helped me to understand my work.

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Finally, I owe everything to the Almighty to shower his blessings so that my efforts reach to the destination.

Abbreviations

DM	Diabetes Mellitus
T1DM	Type-1 Diabetes Mellitus
T2DM	Type-2 Diabetes Mellitus
CVD	Cardiovascular Disease
DCT	Diabetes Control and Complication Trials
NGPS	National Glycohemoglobin Standardization
ADA	American Diabetes Association
WHO	World health organization
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
USA	United States of America
UKPDS	United Kingdom Prospective Diabetes Study
IEC	International Expert Committee
IDFACE	International Diabetes federation and American College of endocrinology
IFCC	International federation of clinical chemistry
IFCCLM	International federation of clinical chemistry and laboratory medicine
A1C	Hemoglobin A1C

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