Glycemic Control and Lipid Profiles: Exploring the Correlation Between HbA1c and Non-HDL Cholesterol in Type 2 Diabetic Patients

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Abstract

Diabetes mellitus is a group of common metabolic disorders characterized by chronic hyperglycemia, resulting from defects in insulin secretion, insulin action, or both. Among the various forms of diabetes, type 2 diabetes mellitus (T2DM) is the most prevalent, and is often associated with a range of metabolic abnormalities, including dyslipidemia. Patients with T2DM frequently exhibit dyslipidemia, characterized by elevated triglycerides, increased low-density lipoprotein cholesterol (LDL-C), and decreased high-density lipoprotein cholesterol (HDL-C) levels, contributing to an increased risk of cardiovascular diseases.

In recent years, Non-HDL cholesterol has emerged as an important lipid marker, offering a more comprehensive risk assessment for cardiovascular diseases than LDL-C alone. Non-HDL cholesterol includes all atherogenic lipoproteins, such as VLDL, IDL, and LDL, and serves as a more accurate predictor of cardiovascular risk, especially in patients with elevated triglycerides (≥200 mg/dl). Non-HDL cholesterol is also considered a more reliable marker for assessing the burden of Apo-B carrying lipoproteins, which are directly implicated in atherosclerosis.

This study aims to evaluate the correlation between glycated hemoglobin (HbA1c) levels, a marker of long-term glycemic control, and Non-HDL cholesterol, along with other lipid profile parameters in patients with type 2 diabetes mellitus compared to non-diabetic individuals. By exploring these relationships, this study seeks to better understand the association between glycemic control and lipid abnormalities in type 2 diabetes and to highlight the potential of Non-HDL cholesterol as an important marker for diabetic dyslipidemia and cardiovascular risk.

Objective: The aim of this study was to examine the correlation between HbA1c and various metabolic parameters, including fasting blood sugar (FBS), lipid profile components (Non-HDL cholesterol, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), and the LDL/HDL-C ratio in patients with type 2 diabetes mellitus (T2DM). Additionally, we evaluated the impact of HbA1c levels on lipid profile by categorizing patients based on their glycemic control.

Methods: This study utilized Karl Pearson's correlation coefficient method to assess the relationship between HbA1c and the aforementioned metabolic parameters in a cohort of T2DM patients. The patients were categorized into three groups based on their HbA1c levels: Group A (Normal, HbA1c ≤6.4%), Group B (Good glycemic control, HbA1c 6.5-8%), and Group C (Poor glycemic control, HbA1c ≥8%). The differences in metabolic parameters across these groups were evaluated using ANOVA.

Results: The correlation between HbA1c and FBS was moderate and statistically significant ($r = 0.530$, $p < 0.05$). Strong positive correlations were observed between HbA1c and Non-HDL cholesterol ($r = 0.657$), total cholesterol ($r = 0.661$), LDL cholesterol ($r = 0.587$), and LDL/HDL-C ratio ($r = 0.363$), all with statistically significant p-values ($p < 0.05$). However, there was a weak and non-significant correlation between HbA1c and HDL cholesterol ($r = 0.120$) and triglycerides ($r = 0.189$). The comparison of metabolic parameters across the three glycemic control groups revealed significant differences in FBS, HbA1c, total cholesterol, LDL cholesterol, triglycerides, and Non-HDL cholesterol, with the most pronounced differences between Group A and Group C ($p < 0.05$ for all). HDL cholesterol did not show significant differences between the groups.

Conclusion: HbA1c levels are positively correlated with FBS, lipid profile components, and LDL/HDL-C ratio in patients with T2DM, highlighting the detrimental impact of poor glycemic control on lipid metabolism. Patients with poor glycemic control exhibit significantly worse lipid profiles, particularly in terms of Non-HDL cholesterol and total cholesterol, suggesting the importance of effective glycemic management in reducing cardiovascular risk in T2DM.

Keywords – Non high density lipoprotein, glycated haemoglobin, type2 diabetes mellitus, dyslipidemia

Introduction

Diabetes mellitus (DM) is a group of common metabolic disorders characterized by chronic hyperglycemia.[1] It is a heterogeneous collection of multifactorial, polygenic syndromes that result from either a relative or absolute deficiency of insulin, leading to elevated blood glucose levels. This condition is typically marked by an increase in fasting blood glucose levels due to impaired insulin secretion, insulin action, or both, which causes a disruption in glucose homeostasis. Over time, uncontrolled hyperglycemia can lead to a variety of complications, including cardiovascular diseases, nephropathy, neuropathy, and retinopathy, making it a significant public health concern.[2]

According to the World Health Organization (WHO), the number of adults suffering from diabetes worldwide reached 422 million in 2014, up from 108 million in 1980.[3] In India, diabetes has evolved from an epidemic to a pandemic, with the country now being referred to as the "diabetic capital of the world." In 2017, approximately 72.9 million Indians were living with diabetes. The impact of diabetes on health is profound, as it is responsible for 1.5 million deaths annually. Additionally, diabetes contributes to an increased risk of coronary artery disease (CAD) and other related conditions, resulting in 2.2 million deaths due to these complications. This alarming rise in diabetes prevalence underscores the urgent need for effective prevention and management strategies to address the growing burden of the disease.[3]

It is well-documented that most patients with type 2 diabetes mellitus (T2DM) exhibit varying degrees of dyslipidemia, which is typically characterized by elevated levels of triglycerides and low-density lipoprotein cholesterol (LDL-C), along with decreased levels of high-density lipoprotein cholesterol (HDL-C). Additionally, studies have shown that T2DM patients with cardiovascular disease (CVD) tend to have significantly higher levels of hypercholesterolemia and hyperlipidemia compared to diabetic patients without CVD. These lipid abnormalities are associated with an increased risk of mortality in this population. Recent data has suggested that lipid ratios, such as the LDL/HDL-C ratio, may be more sensitive indicators of coronary heart disease (CHD) morbidity and severity than individual lipid markers. However, some studies have indicated a minimal relationship between glycated hemoglobin (HbA1c) levels and lipid profile components in patients with T2DM, raising questions about the extent to which long-term glycemic control influences lipid metabolism in these individuals.[4]

Non-HDL cholesterol (Non-HDL-C) was introduced as a refined method for assessing cardiovascular risk beyond LDL-C, particularly in individuals with elevated triglyceride levels (≥200 mg/dl). Non-HDL-C represents the total concentration of all ApoB-carrying lipoproteins, including VLDL, IDL, LDL, and remnants, making it a more comprehensive marker of atherogenic lipid particles.[5] Given its ability to reflect the burden of all atherogenic lipoproteins, Non-HDL-C is considered a practical and cost-effective surrogate for measuring ApoB, especially in patients with hypertriglyceridemia and those with diabetes.[6]

Non-HDL-C is calculated by subtracting HDL cholesterol from total cholesterol, and it has been shown to be a better marker for cardiovascular disease (CVD) risk than LDL-C alone. One of the advantages of Non-HDL-C is that it can be measured from a non-fasting blood sample, unlike LDL-C, which typically requires fasting. Additionally, Non-HDL-C is less expensive and provides a measure of LDL particle number and total ApoB concentration, both of which are important indicators of cardiovascular risk. This makes Non-HDL-C a valuable and accessible tool for risk stratification, particularly in diabetic and hypertriglyceridemic patients.[7]

The National Cholesterol Education Program (NCEP) and the Adult Treatment Panel (ATP) III have recommended the use of Non-HDL cholesterol (Non-HDL-C) as an important tool for assessing cardiovascular disease (CVD) risk, particularly in patients with diabetes. ATP III guidelines suggest that the therapeutic target for Non-HDL-C should be <130 mg/dl for individuals with diabetes who do not have acute coronary syndrome (ACS). However, for patients with ACS, a more stringent target of <100 mg/dl is recommended. These guidelines emphasize the importance of managing dyslipidemia in diabetic patients to reduce the risk of cardiovascular events, highlighting Non-HDL-C as a key marker for cardiovascular risk assessment and therapeutic decision-making in this population.[7]

This study was conducted to examine the correlation between HbA1c and various metabolic parameters, including fasting blood sugar (FBS), lipid profile components (Non-HDL cholesterol, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), as well as the LDL/HDL-C ratio in patients with type 2 diabetes mellitus (T2DM).[8] Additionally, the study evaluated the impact of HbA1c levels on the lipid profile by categorizing patients based on their glycemic control. The goal was to better understand how glycemic control, as measured by HbA1c, influences lipid metabolism and to assess the relationship between HbA1c and lipid abnormalities in this patient population.[9]

The use of Non-HDL-C and HbA1c together can serve as more comprehensive markers of diabetic dyslipidemia and cardiovascular risk compared to LDL cholesterol alone. Non-HDL-C provides a broader measure of atherogenic lipoproteins, while HbA1c reflects long-term glycemic control. By incorporating both markers, healthcare providers can better assess cardiovascular risk in patients with diabetes, leading to more effective management strategies to reduce complications associated with dyslipidemia and poor glycemic control.[10]

Materials and Methods

The present case-control study was conducted at KLE Society's Dr. Prabhakar Kore Charitable Hospital, Belagavi, India, from January 2018 to January 2019. A total of 102 type 2 diabetes mellitus (T2DM) patients of both genders and 102 age- and gender-matched healthy controls, aged between 30 to 70 years, who attended the medicine outpatient department (OPD), were included in the study.

Inclusion criteria for the study were newly diagnosed T2DM patients or known cases of T2DM, with or without treatment, including oral hypoglycemic drugs, insulin, or hypolipidemic medications. The control group consisted of healthy individuals who were matched for age and gender with the diabetic patients.

Exclusion criteria included type 1 diabetes mellitus, females on oral contraceptive pills, anemia, nephrotic syndrome, chronic renal failure, cirrhosis or other liver diseases, pregnancy, thyroid disorders, and hemoglobinopathy. Diagnosis of T2DM was confirmed based on the American Diabetes Association (ADA) guidelines, with HbA1c levels ≥6.5% and fasting blood sugar (FBS) levels ≥126 mg/dl.[11]

The study was conducted in accordance with ethical guidelines, and informed consent was obtained from all participants prior to their inclusion in the study.

Estimation of fasting blood sugar (FBS) and serum fasting lipid profile was performed using standard laboratory techniques. Fasting blood sugar was measured by the Hexokinase method.[12,13,14] Similarly, the serum fasting lipid profile, including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, was estimated using enzymatic methods.[15,16,17,18] All assays were conducted using a Roche/Hitachi COBAS fully automated analyzer to ensure accuracy and reliability.

HbA1c levels were estimated using the Bio-Rad D-10 HbA1c program, which employs high-performance liquid chromatography (HPLC) to provide precise measurement of HbA1c levels, in accordance with established guidelines.

Statistical analysis was performed using Karl Pearson’s correlation coefficient to assess the strength and direction of the relationship between HbA1c and various metabolic parameters, including fasting blood sugar and lipid profile components. Pearson’s correlation was used to determine the degree of association between HbA1c and these variables, with significance set at $p < 0.05$. Additionally, ANOVA (Analysis of Variance) was used to compare the means of different groups (normal, good, and poor glycemic control) for various metabolic parameters.

The ANOVA test helped identify significant differences between groups in terms of fasting blood sugar, lipid profile components, and HbA1c levels.

Results

In this study a total 204 patients were evaluated. The overall distribution of patients is as shown in table 1.

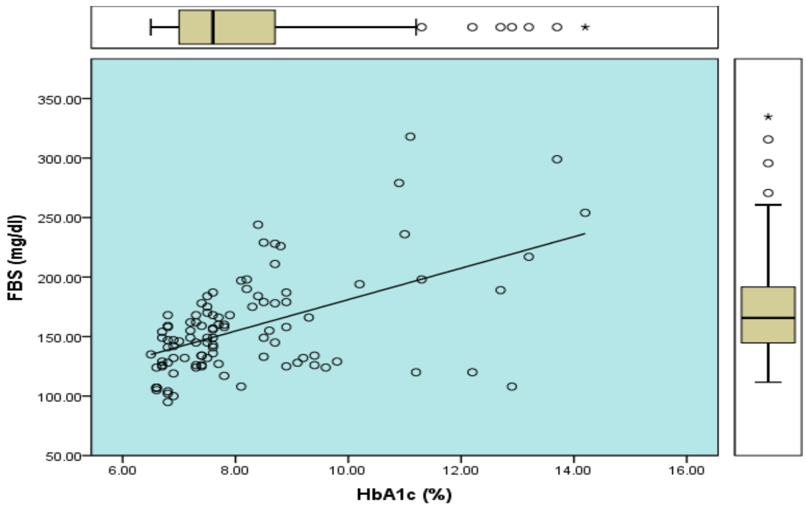
Table 1: Distribution of patients by gender

Gender	Number of cases	Number of controls	Percentage (%)
Male	58	58	56.86
Female	44	44	43.14
Total	102	102	100

The correlation between HbA1c with FBS, Non-HDL cholesterol, lipid profile, and LDL/HDL-C ratio in all cases were done by Karl Pearson's correlation coefficient method.

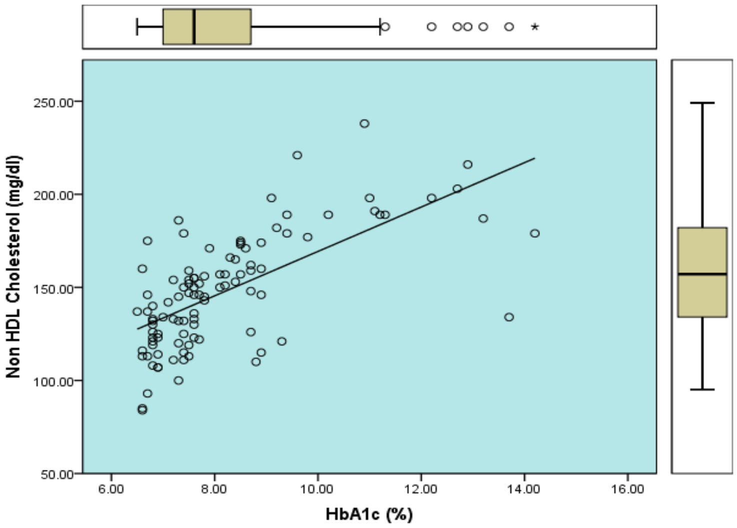
Correlation (r-value) between HbA1c and FBS was found to be 0.530 and it was statistically significant with $p< 0.05$ (Graph 1).

Graph-1: Scatter graph of correlation between HbA1c (%) and FBS (mg/dl) in all type 2 diabetes mellitus patients



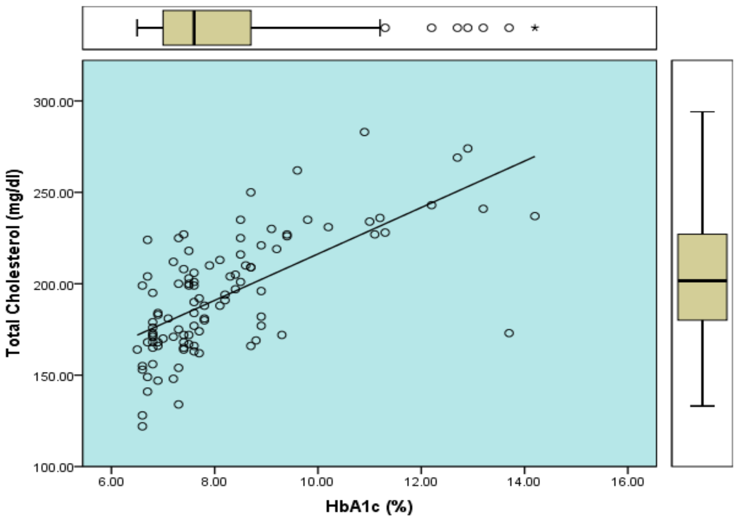
Correlation (r-value) between HbA1c and Non- HDL cholesterol was found to be 0.657 and it was statistically significant with $p < 0.05$ (Graph 2)

Graph-2: Scatter graph of correlation between HbA1c (%) and non-HDL-C (mg/dl) in all type 2 diabetes mellitus patients.



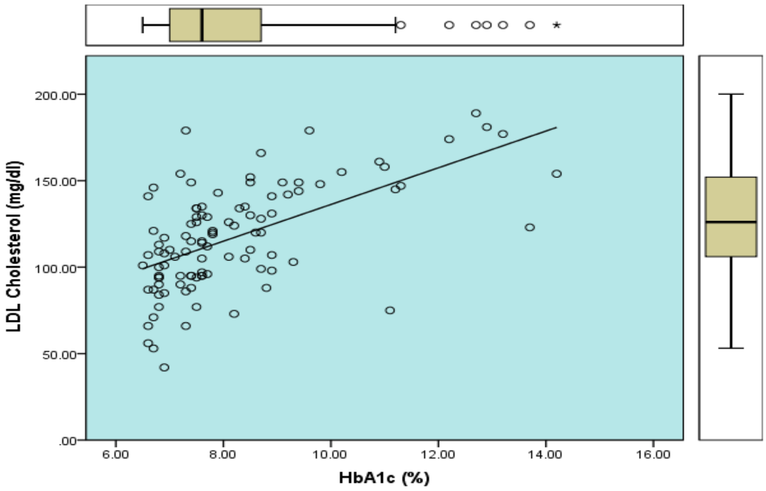
Correlation (r-value) between HbA1c and Total cholesterol was found to 0.661 and it was statistically significant with $p < 0.05$ (Graph 3)

Graph-3: Scatter graph of correlation between HbA1c (%) and total cholesterol (mg/dl) in all type 2 diabetes mellitus patients.



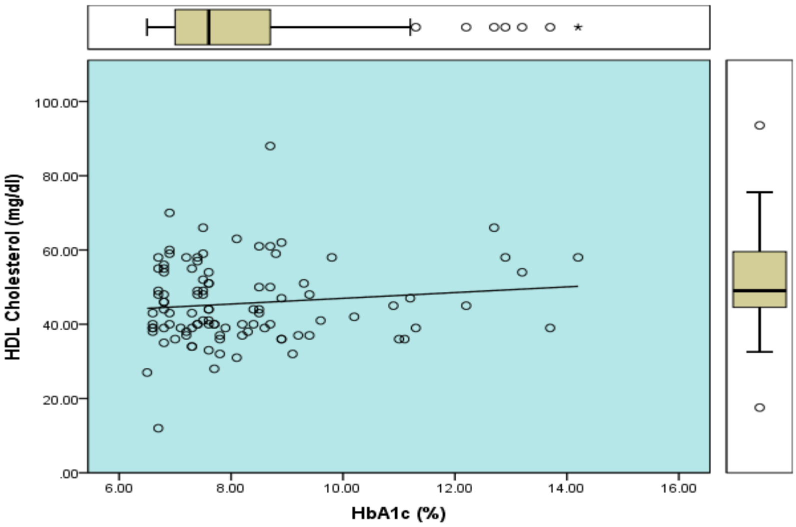
Correlation (r-value) between HbA1c and LDL-C was found to be 0.587 and it was statistically significant with $p < 0.05$ (Graph 4)

Graph-4: Scatter graph of correlation between HbA1c (%) and LDL-C (mg/dl) in all type 2 diabetes mellitus patients.



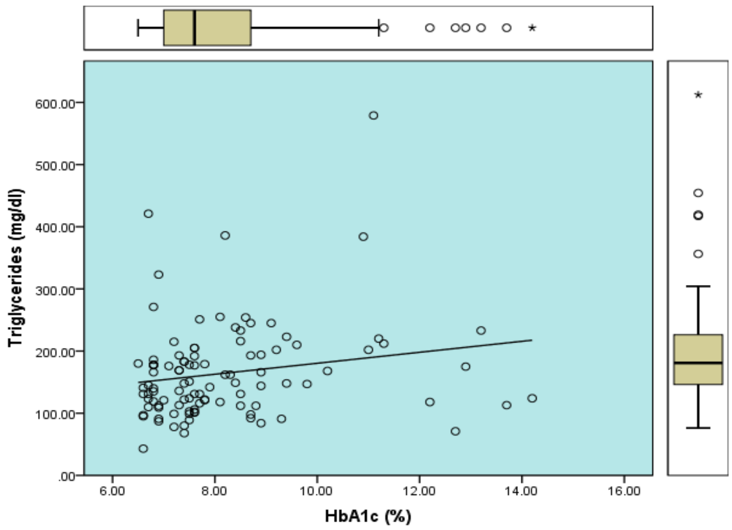
Correlation (r-value) between HbA1c and HDL-C was found to be 0.120 and it was not statistically significant with $p< 0.05$ (Graph 5)

Graph-5: Scatter graph of correlation between HbA1c (%) and HDL-C (mg/dl) in all type 2 diabetes mellitus patients.



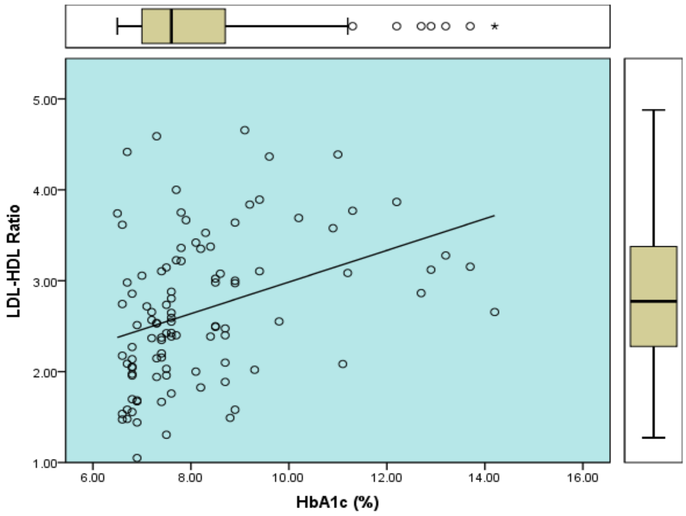
Correlation (r-value) between HbA1c and triglycerides was found to be 0.189 and it was not statistically significant with p< 0.05 (Graph 6)

Graph-6: Scatter graph of correlation between HbA1c (%) and triglycerides (mg/dl) in all type 2 diabetes mellitus patients.



Correlation (r-value) between HbA1c and LDL/HDL ratio was found to be 0.363 and it was statistically significant with p< 0.05 (Graph 7)

Graph-7: Scatter graph of correlation between HbA1c (%) and LDL/HDL-C ratio (mg/dl) in all type 2 diabetes mellitus patients.



The correlation of HbA1c on lipid profile and Non-HDL-C was evaluated by categorizing all the study population in three groups on the basis of HbA1c levels. Group A (Normal) consist of subjects with HbA1c value ≤6.4%, Group B (Good glycemic control) consist of subjects with HbA1c value 6.5-8% and Group C (Poor glycemic control) consist of subjects with HbA1c value ≥8%. The age (ANOVA) F=0.54 p=0.58 and HDL cholesterol (ANOVA) F=0.62 p=0.54 were not significantly correlated in group C and group B than in group A. The concentration of FBG (ANOVA) F=113.5 p<0.05, HbA1c (ANOVA) F=325.4 p<0.05, TC (ANOVA) F=52.81 p<0.05, LDL-C (ANOVA) F=40.74 p<0.05 and Triglyceride (ANOVA) F=9.38 p<0.05 were significantly different in group C and group B than in group A. The levels of Non-HDL-C (ANOVA) F=58.47 p<0.05 were significantly different in group C and group B than in group A.

Table-6: Comparison of mean, S.D, f-value and p-value of measured parameters of normal, good and poor glycemic control.

PARAMETER	Group A (Normal) HbA1c ≤6.4%		Group B (Good glycemic control) HbA1c 6.5-8%		Group C (Poor glycemic control) HbA1c ≥ 8%			
	Mean	SD	Mean	SD	Mean	SD	f-value	p-value
Age(year)	52.17	9.291	53.69	8.073	53.13	10.76	0.54	0.58
FBS(mg/dl)	99.96	12.94	141.7	22.21	181.2	52.69	113.5	< 0.0001*
HbA1c (%)	5.56	0.40	7.185	0.4028	9.747	1.712	325.4	< 0.0001*
TC (mg/dl)	158.6	33.12	177.7	23.38	217.6	28.89	52.81	< 0.0001*
LDL-C (mg/dl)	85.81	28.30	105.6	25.52	134.9	28.65	40.74	< 0.0001*
HDL-C (mg/dl)	46.05	9.69	44.73	10.16	46.95	11.65	0.62	0.54
Triglyceride (mg/dl)	136.96	54.72	147.9	60.98	190.2	94.93	9.38	< 0.0001*
Non-HDL-C (mg/dl)	111.26	31.19	133	21.55	170.7	27.99	58.47	< 0.0001*

*p<0.05

Discussion

The present study was conducted on 102 clinically diagnosed type 2 diabetic patients, aged between 30 to 70 years, in accordance with the ADA guidelines. Of these, 58 were males and 44 were females. The findings were compared with 102 apparently healthy, age- and sex-matched controls. In this study, fasting blood sugar, HbA1c, lipid profile, and Non-HDL cholesterol levels were investigated. Diabetic patients are at a significantly higher risk of developing dyslipidemia, which, in turn, greatly increases their risk of cardiovascular disease (CVD) compared to non-diabetic individuals. Therefore, it is crucial to identify factors that may contribute to CVD risk in these patients. This study reveals a high prevalence of hypercholesterolemia, hypertriglyceridemia, elevated LDL cholesterol, increased Non-HDL cholesterol, and low HDL cholesterol levels, which are well-established risk factors for cardiovascular diseases.

In this study, we observed a significant positive correlation between HbA1c and fasting blood sugar (FBS), total cholesterol, LDL cholesterol, Non-HDL cholesterol, and the LDL-C/HDL-C ratio. This suggests that as HbA1c levels increase, there is a corresponding increase in these lipid parameters, which are known to contribute to the risk of cardiovascular diseases. Specifically, higher HbA1c levels, indicative of poor glycemic control, were associated with elevated total cholesterol, LDL-C, and Non-HDL-C, as well as a higher LDL-C/HDL-C ratio, all of which are considered atherogenic markers.

The findings of this study are consistent with those reported by Vinod Mahato R et al.[8], who also observed significant correlations between HbA1c and various lipid profile components in type 2 diabetes mellitus patients. Their study highlighted the relationship between poor glycemic control, dyslipidemia, and an increased risk of cardiovascular complications in diabetic patients, which aligns with the results of the present study. These consistent findings emphasize the importance of managing both blood glucose levels and lipid abnormalities to reduce cardiovascular risk in individuals with type 2 diabetes mellitus.

In the present study, we divided all the subjects into three groups based on their HbA1c values: Group A (≤6.4%), Group B (6.5-8%), and Group C (≥8%). We observed a significant increase in total cholesterol (TC), LDL cholesterol (LDL-C), triglycerides (TAG), and Non-HDL cholesterol as HbA1c values increased, while no significant alteration was seen in HDL cholesterol levels. These findings are consistent with the study conducted by Reddy A S et al.[9], who also reported a similar pattern of lipid abnormalities associated with increasing HbA1c levels. This suggests that elevated HbA1c contributes to the dyslipidemia commonly observed in type 2 diabetes, reinforcing the need for effective glycemic control to prevent cardiovascular complications.

Conclusion

This study demonstrates a strong positive correlation between HbA1c and Non-HDL cholesterol, with an r-value of 0.657, which was statistically significant ($p < 0.05$). This finding suggests that elevated HbA1c levels are closely associated with increased Non-HDL cholesterol, a key marker for cardiovascular risk in patients with type 2 diabetes mellitus. Additionally, HbA1c was positively correlated with other lipid parameters, such as total cholesterol, LDL cholesterol, and the LDL/HDL-C ratio, further emphasizing the negative impact of poor glycemic control on lipid metabolism. In contrast, there was no significant correlation between HbA1c and HDL cholesterol or triglycerides. The comparison of metabolic parameters across different HbA1c categories revealed that patients with poor glycemic control (Group C) had significantly higher levels of Non-HDL cholesterol, total cholesterol, LDL cholesterol, and triglycerides compared to those with normal glycemic control (Group A), reinforcing the importance of glycemic management in mitigating lipid abnormalities. Overall, these results highlight the critical role of Non-HDL cholesterol as a key marker in the relationship between glycemic control and lipid profile in type 2 diabetes, underscoring the need for comprehensive management strategies targeting both glycemic and lipid control to reduce cardiovascular risk in these patients.

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