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Research Article

CONNECTING THE DOTS: INVESTIGATING THE RELATIONSHIP BETWEEN HBA1C AND LIPID PROFILE

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ABSTRACT

Objectives: To determine the association between lipd profile and HbA1c. Hemoglobin A1c (HbA1c) is used to monitor blood sugar levels. HbA1c is one among the panel of tests that is done for patients who come for routine master health check-ups. This helps us to identify pre-diabetic and diabetic individuals. Diabetic individuals are at increased risk for dyslipidemia. The aim of this study is to look into the association between lipid profile and HbA1c.

Methodology: This study was done in a multispecialty hospital in the Western part of Tamil Nadu among the patients who came for master health check-ups between 2017 and 2024. Ethical Committee approval was obtained (EC/AP/1100/12/2023). From the laboratory database of 67,000 patients, patients who reported for the 1st time and had their HbA1c and lipid profile levels evaluated were selected. They were categorized into normal, pre-diabetic, and diabetic based on HbA1c values. Data were analyzed using the Statistical Package for Social Sciences 27. Categorical variables were expressed as frequency and percentages whereas continuous variables were expressed as mean and standard deviation. Analysis of variance (ANOVA) was used to find if there was a significant difference in lipid profile among the three groups.

Results: Our study had 23,238 participants. Out of them 7168 (30.84%) had normal HbA1c levels, 8347 (35.91%) were pre-diabetics, and 7955 (34.23%) were diabetic patients. The mean total cholesterol (TC) level (186.8±40.14) and low-density lipoprotein (LDL) cholesterol level (129.74±37.20). It was high for pre-diabetic patients. The median very LDL (VLDL) cholesterol (29.00(21–39) levels were higher for diabetic patients. The mean high-density lipoprotein (HDL) cholesterol levels (39.54±9.40) were less for diabetic patients. One-way ANOVA revealed a significant difference in TC, HDL cholesterol, LDL cholesterol, and VLDL cholesterol levels between the three groups. Pearson correlation coefficient showed a positive correlation between VLDL, LDL, TC, and HbA1c. HbA1c and HDL cholesterol were negatively correlated.

Conclusion: Our study revealed a significant correlation between HbA1c and these changes signify a higher risk of cardiovascular complications in individuals with diabetes mellitus. Understanding these associations underscores the need for vigilant monitoring and proactive management of lipid profiles among pre-diabetics and diabetics to reduce the risk of cardiovascular diseases and enhance their overall health.

Keywords: Diabetes mellitus, Lipid profile, Hemoglobin A1c, Tamil Nadu.

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INTRODUCTION

Diabetes mellitus (DM) is an endocrine disease characterized by elevated blood sugar levels. The global incidence of diabetes increased from 108 million in 1980 to an estimated 422 million in 2014. The age-standardized worldwide prevalence of diabetes has risen from 4.7% to 8.5% in the adult population since 1980. The World Health Organization estimated that 170 million people were diagnosed with diabetes globally in 2002, and by 2030, it is projected to increase to 366 million or more [1]. The INDIAB survey indicates that 10.1 crore people have diabetes [2].

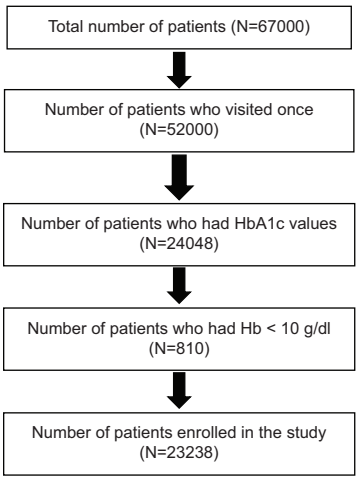
The glycemic status and lipid profile are frequently evaluated using laboratory test panels. Total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol, as well as triglyceride (TG) levels, are components of the common lipid profile; elevated levels suggest an increased risk of cardiovascular morbidity [3]. The measurement of the glycosylated hemoglobin A1c (HbA1c) level is the accepted method which helps to determine glucose homeostasis. The red blood cells glycated component of HbA1c represents the glycemic control over the preceding 3 months [4]. This offers a foundation for evaluating the effectiveness of blood glucose control.

Health-care practitioners can evaluate the efficacy of diabetic treatment regimens and do necessary adjustments to guarantee optimal glycemic control with the support of routine monitoring of HbA1c levels. In addition, HbA1c readings can be used to determine at risk individuals [5]. Increased HbA1c levels are a sign of pre-diabetes. This allows for early lifestyle modifications and intervention to stop the condition from developing into diabetes [6]. The American Diabetes Association (ADA) states that pre-diabetic people may be identified with HbA1c levels between 5.7% and 6.4%; however, a level of more than 6.5% is advised for the diagnosis of diabetes [7]. The limited intra-individual variability of the HbA1c level, which is a reflection of the average glycemic status during the preceding 2–3 months, as well as the assessment's practicality without the requirement for fasting, are factors that promote its use in diagnosing and monitoring of DM [6].

Diabetes affects the rates of morbidity, atherosclerosis, hypertension, and dyslipidemia more frequently. Diabetics have more risk of atherogenic dyslipidemia, which is linked to microvascular conditions such as nephropathy and neuropathy as well as macrovascular complications such as heart disease and stroke [8,9]. High serum TG, low HDL, and high LDL are indicative of atherogenic dyslipidemia [10]. Understanding the association between HbA1c and lipid profile holds clinical significance, as it may provide insights into the mechanisms underlying cardiovascular risk in diabetes and inform personalized therapeutic strategies.

METHODS

This study was conducted in a medical college in the Western part of Tamil Nadu. Our laboratory database contained records of 67,000 patients who reported for master health check-ups between 2017 and 2024. From this database, we included patients who reported to master health check-ups for the 1st time. Among them, those patients who had HbA1c values and complete lipid profiles were included in the study. Those who had HbA1c <10 g/dL were excluded from the study as HbA1c levels are affected by lower HbA1c values.



Study participants were categorized into three groups based on HbA1c values as normal patients, pre-diabetic patients, and diabetic patients. The cut-off values for HbA1c were based on ADA. As per ADA those who have HbA1c <5.7% were in the normal group, 5.7–6.4% pre-diabetic and those who had HbA1c more than or equal to 6.5% were considered diabetic. The categorization of TC values was: Normal <200 mg/dL, borderline 200–239 mg/dL, and high >240 mg/dL. The categorization of LDL values was as follows: Normal <100 mg/dL, near-optimal 100–129 mg/dL, borderline 130–159 mg/dL, high 160–189 mg/dL, and very high >190 mg/dL. For the categorization of patients based on HDL values 40 mg/dL was taken as cutoff. The data were analyzed using the Statistical Package for Social Sciences. Categorical variables were expressed as frequency and percentages and continuous variables were expressed as mean and standard deviation. Analysis of variance was used to find if there was a significant difference in lipid profile among the three groups. Institute Ethical Committee approval was obtained.

Table 1: Mean values of lipid profile among non-diabetic, pre-diabetic, and diabetic patients

Parameters	Non-diabetic (Mean±SD)	Pre-diabetic (Mean±SD)	Diabetic (Mean±SD)
VLDL	22 (6,523)*	25.00 (19–35)*	29.00 (21–39)*
Total cholesterol	184.9±36.72	186.8±40.14	184.06±45.81
HDL cholesterol	42.97±10.44	41.17±10.01	39.54±9.40
LDL cholesterol	127.76±34.46	129.74±37.20	124.55±40.05
FBS	91.14±8.99	116.5±49.94	166.65±65.30

*Median (inter-quartile range). The mean TC and LDL cholesterol were high for pre-diabetic patients. The median VLDL cholesterol was high for patients with diabetes. The mean HDL cholesterol levels were less for diabetic patients. The mean FBS was higher for diabetics. VLDL: Very low-density lipoprotein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

RESULTS AND DISCUSSION

There were 23,238 study participants. Out of them 7168 (30.84%) had normal HbA1c levels, 8347 (35.91%) were pre-diabetics, and 7955 (34.23%) were diabetic patients. Among the study participants, 65.9% had cholesterol levels within the normal limits, 25.3% had cholesterol levels within the borderline limit, and 8.8% of patients had high TC levels. Among the study participants, 22% of the patients had LDL levels within normal limits, 30.5% had near optimal LDL values, 28.8% had borderline LDL values, 13.4% had high LDL values, and 5.3% had very high LDL values. Among the study participants, 51.5% of the patients had HDL levels less than 40 mg/dL and 48.5% of the patients had HDL values more than 40 mg/dL.

The mean TC and LDL cholesterol were high for pre-diabetic patients. The median VLDL cholesterol was high for patients with diabetes. The mean HDL cholesterol levels were less for diabetic patients (Table 1).

There was significant difference in lipid levels among the three group of patients (Table 2).

Pearson correlation coefficient showed a positive correlation between very LDL (VLDL), LDL, TC, and HbA1c. HDL and HbA1c were negatively correlated (Table 3).

The present study had 23,238 participants. Our study was done to know the relation between HbA1c levels and lipid profile. The current study showed that the median VLDL cholesterol levels were high for diabetic patients. A study by Kumar *et al*. [11] also showed that VLDL cholesterol levels were higher for diabetics when compared to non-diabetics. A study by Artha *et al*. [12] also showed that the VLDL levels were raised in patients with type 2 DM. TG-rich lipoprotein digestion is greatly hampered when the activity of insulin is very low because lipoprotein lipase synthesis is considerably suppressed. TG-rich lipoproteins rise as a result, and chylomicron and VLDL clearance are delayed. One further result of insulinopenia that leads to free fatty acid release into the bloodstream, is a significant increase in lipolysis in adipose tissue. An increase in blood fatty acid levels leads to increased synthesis of TG in the liver along with enhanced production and secretion of VLDL [11].

The present study showed a significant difference in TC levels between the three groups. The mean TC levels were higher among the pre-diabetics. A study by Khil *et al*. [13] showed that the TC levels were higher in type 2 diabetics. Decreased plasma levels of campesterol, which is a marker of cholesterol absorption, and elevated levels of

Table 2: Association between diabetic status and lipid profile

Parameters	Non-diabetic (Mean±SD)	Pre-diabetic (Mean±SD)	Diabetic (Mean±SD)	F-value	p-value*
VLDL	22 (6,523)*	25.00 (19–35)	29.00 (21–39)*	235.3	<0.05
Total cholesterol	184.9±36.72	186.8±40.14	184.06±45.81	52.4	<0.05
HDL cholesterol	42.97±10.44	41.17±10.01	39.54±9.40	242.7	<0.05
LDL cholesterol	127.76±34.46	129.74±37.20	124.55±40.05	99.01	<0.05
Uric acid	5.28±1.52	5.39±1.40	4.81±1.37	379.74	<0.05
FBS	91.14±8.99	116.5±49.94	166.65±65.30	9.05	<0.05

*Analysis of variance showed that there was a significant difference in TC, HDL, LDL, and VLDL between the three groups. The mean uric acid level was higher for pre-diabetic patients and there was a significant difference in the levels of uric acid among the three groups VLDL: Very low-density lipoprotein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Table 3: Correlation between HbA1c and cholesterol levels

Lipid profile	Correlation Co-efficient	p-value
VLDL	0.15	<0.05
LDL	0.18	<0.05
HDL	−0.11	<0.05
Total cholesterol	0.02	<0.05

HbA1c: Hemoglobin A1c, VLDL: Very low-density lipoprotein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

lathosterol in plasma, which is a marker of synthesis of cholesterol, are observed among diabetics [14]. Diabetics have shown decreased absorption of cholesterol and higher production of cholesterol with the oral administration of isotopes [15]. A study among diabetics showed that liver fat content was found to be independently correlated with plasma lathosterol [16].

The present study showed a significant difference in HDL cholesterol levels among the three groups. Patients with diabetes were found to have lower HDL levels when compared to the other two groups of patients. A study by Mahran *et al.* [17] showed that HDL cholesterol levels were lower in diabetics when compared to non-diabetics. The possible reasons include insulin resistance, enhanced production of VLDL, and elevated endothelial lipase and cholesteryl ester transfer protein (CETP) activities. The capacity of HDLs to increase skeletal muscle glucose uptake and enhance insulin secretion from pancreatic beta cells has been demonstrated in recent studies [18,19]. These findings increase the possibility that low HDL may also worsen diabetic control or even accelerate the progression of pre-diabetes to diabetes. Consequently, a low HDL may decrease glycemic control in individuals with diabetes in addition to being a factor in increasing cardiovascular risk in diabetics [20].

Our study showed a significant association between uric acid levels and HbA1c among the three groups. A study by Jalal also showed a similar finding. Excessive uric acid levels have been linked to insulin resistance and glucose metabolism, which leads to poor glycemic management because they may directly damage pancreatic beta-cell function.

They may also interfere with insulin signaling pathways, which exacerbates insulin resistance [21]. First, uric acid alone has the ability to phosphorylate Akt (ser307) and insulin receptor substrate 1 (ser473), which inhibits insulin signaling in target cells [22,23]. Elevated uric acid can raise the xanthine oxidase and nicotinamide adenine dinucleotide phosphate oxidase activity, leading to increased production of reactive oxygen species (ROS). Pro-inflammatory factors can be activated by ROS and uric acid on the one hand, but ROS can also decrease NO bioavailability, which inhibits the NO-cGMP-dependent processes of GLUT4 translocation and glucose uptake [24,25]. However, literary evidence suggests that inflammation or changes in uric acid or lipid metabolism may have an effect on glucose homeostasis [26]. Uric acid induces apoptosis of beta cells and inhibits glucose-stimulated insulin secretion culminating in reduced beta-cell mass and dysfunction.

CONCLUSION

Our study provides valuable inputs into the association between HbA1c and lipid profile. Through comprehensive analysis, we have observed significant correlations between HbA1c and alterations in lipid parameters, including elevated levels of TC, VLDL, LDL, and decreased HDL. These findings underscore the intricate interplay between diabetes and lipid metabolism, highlighting the importance of lipid management in diabetic patients to mitigate cardiovascular risk.

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