Correlation Between Hba1c Levels And Untraditional Lipid Panels In Prediabetics

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Abstract

Background: Prediabetes is a condition where glucose metabolism is disrupted; it is defined by high blood glucose levels that are below the diabetes diagnostic cutoff.

Aim: To investigate the correlation among HbA1c levels and lipid panel parameters in individuals with prediabetes.

Patients and Methods: This prospective cross-sectional research was performed on 500 individuals aged between 18 and 65 years with confirmed prediabetes.

Results: The analysis demonstrated significant positive associations among HbA1c as well as cholesterol ($\rho = 0.534$, $p < 0.001$), triglycerides ($\rho = 0.460$), LDL ($\rho = 0.375$), in addition to VLDL ($\rho = 0.310$). A negative association was identified between HbA1c and high-density lipoprotein (HDL), suggesting that elevated HbA1c levels corresponded with diminished HDL levels. Furthermore, Group 2 (HbA1c 6.0%–6.4%) had a markedly elevated LDL/HDL ratio, cholesterol/HDL ratio, and triglyceride/HDL ratio in comparison to Group 1 (HbA1c 5.4%–5.9%). The AUC values indicated that total cholesterol had the highest predictive value (AUC = 0.802), followed by low-density lipoprotein (LDL) (AUC = 0.701) and triglycerides (AUC = 0.731). HDL exhibited the lowest predictive value (AUC = 0.437).

Conclusion: We concluded that cases with higher HbA1c levels (6.0%–6.4%) had significantly worse lipid profiles, specifically in terms of cholesterol, triglycerides, LDL, LDL, VLDL, LDL/HDL ratio, cholesterol/HDL ratio, and triglyceride/HDL ratio compared to those with lower HbA1c (5.4%–5.9%) within the prediabetic range. Untraditional lipid panels may be considered promising biomarkers to predict progression from prediabetes to type 2 diabetes mellitus (T2DM).

Introduction

Elevated blood glucose levels that fall short of the criteria for a diabetes diagnosis characterize prediabetes, a disease in which the body's glucose metabolism is compromised. In those at high risk of developing diabetes, prediabetes is defined by glycemic characteristics that fall somewhere in the normal to diabetic range **(1).** Diagnostic criteria for impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) often include measurements of blood glucose or the outcomes of an oral glucose tolerance test (OGTT). Glycosylated hemoglobin (HbA1C) levels can also affect this process **(2).**

Prediabetes lasts for an estimated 8.5 to 10.3 years and is one of two asymptomatic stages of hyperglycemia. The second stage, known as preclinical latent diabetes, lasts for four to seven years and begins when the disease begins to manifest biologically and ends when it is clinically diagnosed. Individuals with pre-diabetes display a phenotype similar to that of T2DM, marked by an increased risk of progression to T2DM, hypertension, and dyslipidemia **(3).**

A worldwide increase in the incidence of impaired glucose metabolism is projected to lead to an estimated 600 million new cases of diabetes or prediabetes by the year 2045. Nearly 7.3 percent of adults have prediabetes at present, with a five to ten percent yearly progression rate to overt T2DM **(4)**. Recent studies demonstrate that diabetes prevention is most effective when initiated in the early phases of the disease, as treatment becomes increasingly difficult with progression. Early identification and screening of prediabetes are essential strategies in the prevention of diabetes and its related consequences **(5).**

Among the parameters commonly monitored in prediabetic individuals are glycated hemoglobin (HbA1c) levels and lipid profiles **(6).** While studies have extensively explored the relationship between HbA1c and various metabolic markers, the association among HbA1c and lipid profile components in prediabetes remains less elucidated. This study aimed to investigate the correlation between HbA1c levels and lipid panel parameters in individuals with prediabetes.

Patients and Methods

This prospective cross-sectional research was performed on 500 individuals with high blood glucose but not high enough to be diagnosed as diabetes, HbA1c in the prediabetic stage according to ADA.

Inclusion Criteria: Individuals aged 18 to 65 years with verified prediabetes.

Exclusion Criteria: Individuals with a history of T2DM, T1DM, hepatic disease, cardiovascular diseases, patients on thiazolidinediones, insulin, or metformin, any malignancies, other diseases or drugs involving octreotide, thiazide diuretics, corticosteroids, beta blockers, statins (lipid-lowering medication), in addition to antipsychotics that alter glucose metabolism, as well as pregnant women.

Methods

Throughout the clinical interview, the researchers gathered data on sociodemographic indicators, lifestyle factors, and relevant medical history. A fasting blood sample was obtained to evaluate the CBC with differential, lipid profiles (including total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, and VLDL cholesterol), liver and renal panels, glucose, and HbA1c levels.

The HbA1c readings that were obtained were, in accordance with the diagnostic criteria of the ADA, interpreted as follows: HbA1c readings that were less than 5.7 percent were utilized to define normoglycemia, while HbA1c values that were from 5.7 percent to 6.4 percent were utilized to define prediabetes.

Statistical analysis: A statistical program developed for the social sciences by SPSS Inc. in Chicago, Illinois, USA, known as SPSS version 22.0, was used to analyze the recorded outcomes. The mean ± SD showed the quantitative data that followed a normal distribution. The median and interquartile range (IQR) were used to identify variables that did not follow a normal distribution. In addition, numerical numbers and percentages were used to quantify qualitative qualities. The student t-test was applied for two parametric variables and the Mann-Whitney U test for non-parametric variables. The chi-square tests contrasted category groups. Our correlation analysis utilized Spearman's rank correlation coefficient. This study will evaluate the predictive usefulness of lipid profile characteristics for the transition from prediabetes to T2DM utilizing receiver operating characteristic (ROC) analysis.

Results

Table (1): Descriptive Statistics

Variable		Mean ± SD	Minimum	Maximum
Gender	Male N (%)	244 (48.8%)		
	Female N (%)	256 (51.2%)		
Age (years)		41.09 ± 11.72	20	87
Cholesterol (mmol/l)		4.67 ± 0.60	3.00	6.42
Triglycerides (mmol/l)		1.92 ± 0.44	0.56	3.38
HDL (mmol/l)		1.15 ± 0.20	0.62	1.78
LDL (mmol/l)		2.85 ± 0.54	1.21	4.95
VLDL (mmol/l)		0.93 ± 0.33	0.20	1.75
HbA1c (%)		5.93 ± 0.27	5.40	6.40

The current research examined 500 individuals who were at risk of developing prediabetes. With ages that varied from 20 to 65 years, the average age was 42.22 ± 12.94 years. With 244 men (48.8 percent) and 256 females (51.2 percent), the gender distribution was roughly equal. The key descriptive statistics for lipid parameters and HbA1c levels are summarized in Table 1.

Table (2): Spearman's Correlation Among Lipid Profile Parameters and HbA1c

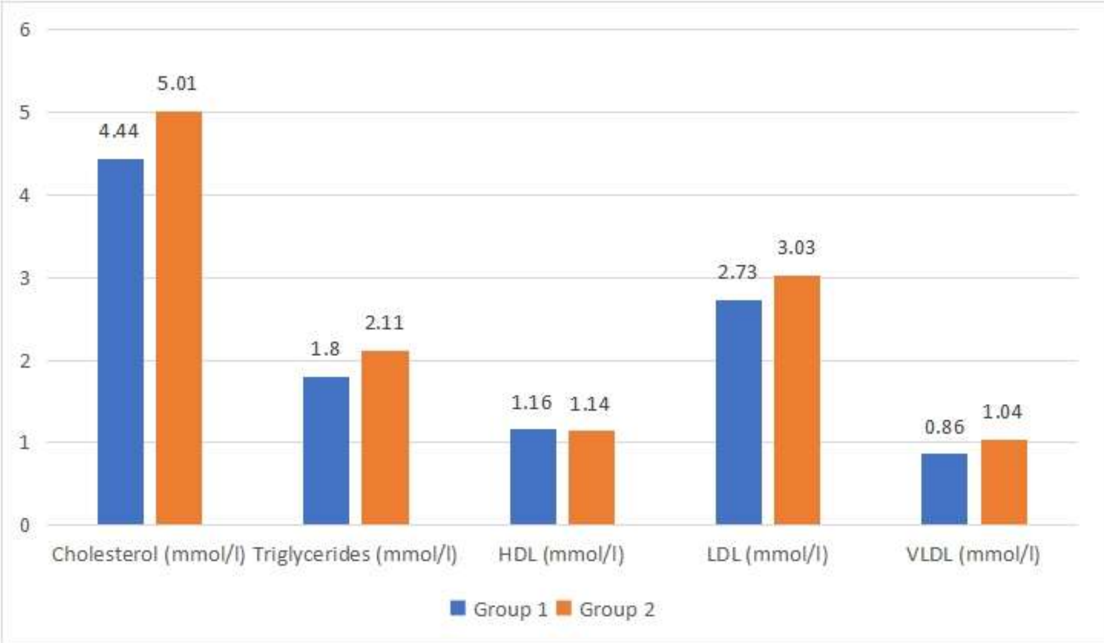
Lipid Profile Parameter	Correlation Coefficient (ρ)	p-value	Significance
Total Cholesterol (mmol/l)	0.534**	0.000	Significant
Triglycerides (mmol/l)	0.460**	0.000	Significant
HDL (mmol/l)	-0.121**	0.007	Significant
LDL (mmol/l)	0.375**	0.000	Significant

The relationship among HbA1c levels and several lipid profile indicators was examined utilizing Spearman's correlation coefficient (ρ). The research demonstrated significant positive associations among HbA1c as well as LDL ($\rho = 0.375$), cholesterol ($\rho = 0.534$), and VLDL ($\rho = 0.310$) triglycerides ($\rho = 0.460$). A negative connection was identified between HbA1c and HDL ($\rho = -0.121$, $p = 0.007$), suggesting that elevated HbA1c levels corresponded with reduced HDL values. Table 2.

Table (3): Comparison of Lipid Profile Parameters Between HbA1c Groups (Pre-diabetic Range)

Lipid Profile Parameters	Group 1 (HbA1c 5.4%-5.9%) N=299	Group 2 (HbA1c 6.0%-6.4%) N=201	P-value
Cholesterol (mmol/l)	4.44 ± 0.54	5.01 ± 0.52	<0.001
Triglycerides (mmol/l)	1.80 ± 0.42	2.11 ± 0.41	<0.001
HDL (mmol/l)	1.16 ± 0.20	1.14 ± 0.18	0.165
LDL (mmol/l)	2.73 ± 0.51	3.03 ± 0.53	<0.001
VLDL (mmol/l)	0.86 ± 0.30	1.04 ± 0.34	<0.001
LDL/HDL Ratio	2.43 ± 0.68	2.75 ± 0.71	<0.001

Cholesterol/HDL Ratio	3.96 ± 0.92	4.53 ± 0.90	<0.001
Triglyceride/HDL Ratio	1.61 ± 0.52	1.91 ± 0.51	<0.001



Participants were separated into two subgroups based on HbA1c levels: Group 1, consisting of individuals with HbA1c levels among 5.4%–5.9% (n = 299), and Group 2, with HbA1c levels among 6.0%–6.4% (n = 201). The comparison between these groups revealed significant differences in several lipid profile parameters (Table 3), except for HDL levels.

Group 2 had a significantly greater cholesterol level (5.01 ± 0.52 mmol/l) than Group 1 (4.44 ± 0.54 mmol/l). In Group 2, triglyceride levels were 2.11 ± 0.41 mmol/l, which was significantly greater than Group 1's 1.80 ± 0.42 mmol/l.

LDL levels were also significantly elevated in Group 2 (3.03 ± 0.53 mmol/l) compared to Group 1 (2.73 ± 0.51 mmol/l).

VLDL levels showed a similar trend, with Group 2 having significantly higher values (1.04 ± 0.34 mmol/l) compared to Group 1 (0.86 ± 0.30 mmol/l).

A p-value of 0.165 indicates no significant variance in HDL levels across prediabetic individuals across the HbA1c range (1.14 ± 0.18 mmol/l in Group 2 vs. 1.16 ± 0.20 in Group 1).

These results indicate that individuals with higher HbA1c levels have significantly worse lipid profiles, specifically in terms of cholesterol, triglycerides, LDL, and VLDL, in contrast to those with lower HbA1c levels within the prediabetic range. The only exception to this pattern was HDL, which did not show a significant variation among the 2 groups.

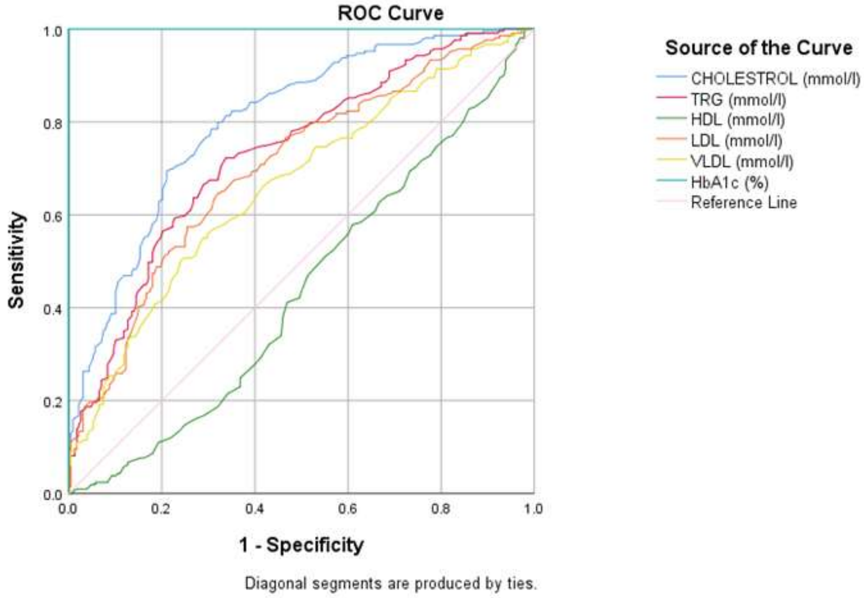
Additionally, significant variations were observed in the lipid ratios:

- LDL/HDL ratio: Group 2 had a significantly higher LDL/HDL ratio (2.75 ± 0.71) compared to Group 1 (2.43 ± 0.68), with a p-value < 0.001.
- Cholesterol/HDL ratio: The cholesterol/HDL ratio was also significantly higher in Group 2 (4.53 ± 0.90) than in Group 1 (3.96 ± 0.92), with a p-value < 0.001.
- Triglyceride/HDL ratio: Similarly, the triglyceride/HDL ratio was significantly elevated in Group 2 (1.91 ± 0.51) compared to Group 1 (1.61 ± 0.52).

Table (4): Area Under the Curve (AUC) for Predictive Value of Lipid Profile Parameters in Identifying Risk of Progression to T2DM

Test Result Variable(s)	Area
CHOLESTROL (mmol/l)	0.802
TRG (mmol/l)	0.731
HDL (mmol/l)	0.437
LDL (mmol/l)	0.701
VLDL (mmol/l)	0.662

A logistic regression analysis was conducted to assess the predictive value of lipid profile parameters for the progression from prediabetes to T2DM. Total cholesterol showed the highest predictive value (AUC = 0.802), followed by LDL (AUC = 0.701) and triglycerides (AUC = 0.731) in accordance with the AUC values. The limited function of HDL as a predictor of T2DM progression in this cohort is indicated by its lowest predictive value (AUC = 0.437).



Cholesterol, TRG, HDL, LDL, and VLDL have at least one tie between the positive and negative real state groups. Statistics may bias.

Discussion

The present research examined the correlation between HbA1c levels as well as lipid panel parameters in individuals with prediabetes.

The present research indicated that the average age was 42.22 ± 12.94 years, with a virtually equal gender distribution of 244 males (48.8 percent) as well as 256 females (51.2 percent).

Similarly, this study agreed with **Kumar et al., (7)** who aimed to determine any link among HbA1c levels and lipid profiles among individuals with diabetes, prediabetes, and those without diabetes. A thousand people, aged from eighteen to sixty years old, were involved in the research.

When insulin activity is significantly diminished, the production of lipoprotein lipase is substantially eliminated, which greatly hinders the metabolism of triglyceride-rich lipoproteins. This results in an elevation of triglyceride-rich lipoproteins and a postponement in the clearance of VLDL as well as chylomicrons **(8).** Adipose tissue lipolysis, which releases free fatty acids into the bloodstream, is dramatically increased in insulinopenia. Increased triglyceride synthesis, VLDL generation, and release, and an increase in the supply of fatty acids to the liver are all outcomes of raised blood fatty acid levels **(9).**

Our findings indicated a significant positive association among HbA1c and cholesterol, triglycerides, LDL, and VLDL. However, a significant inverse association was found between HbA1c and HDL, indicating that as HbA1c levels increased, HDL levels tended to decrease.

Also, our results were consistent with **Kumar et al., (7)** who reported that the concentrations of triglycerides, VLDL, and total cholesterol, in addition to LDL, were elevated in individuals with diabetes in contrast to those in the prediabetic stage. Statistical analysis revealed a statistically significant relationship among glycemic control and average levels of triglycerides and VLDL in the research population. Mean HDL levels were negatively correlated with glycemic control, however this correlation was not statistically significant.

Consistent with these findings, prior research indicated that triglyceride levels were raised in prediabetic and T2DM participants, and their favorable correlation with the risk of developing CVD was significantly acknowledged **(10).** In addition, it has been noted that individuals who appear to be healthy actually have oversecretions of insulin due to excessive serum triglyceride levels **(11).** Patients with hypertriglyceridemia had lower blood insulin levels and a lower occurrence of T2DM when their triglyceride serum levels were reduced, indicating a possible responsible link between hypertriglyceridemia and insulin resistance **(12).** Consequently, variations in triglyceride levels corresponded with alterations in the incidence of T2DM, with a 4 percent increased risk potentially related to each 10 mg/dL rise in triglyceride levels **(13).**

Our findings suggested that individuals with higher HbA1c levels had significantly worse lipid profiles, specifically in terms of cholesterol, TG, LDL, and VLDL, compared to those with lower HbA1c levels within the prediabetic range. HDL was the only exception to this pattern, as it did not exhibit a significant difference between the two groups. Furthermore, Group 2 exhibited a substantially higher LDL/HDL ratio, triglyceride/HDL ratio, as well as cholesterol/HDL ratio than Group 1.

This study was consistent with **Mulla et al., (14)** who revealed that Individuals with prediabetes exhibited substantially elevated levels of total cholesterol, LDL cholesterol, and VLDL cholesterol, as well as triglycerides, in comparison to the control group. Additionally, their HDL cholesterol levels were significantly decreased.

Similarly, this study agreed with **Calanna et al., (15),** who investigated lipid abnormalities and hepatic steatosis in cases with HbA1c-defined prediabetes and T2DM in contrast to those with HbA1c-defined normoglycemia. Individuals with prediabetes demonstrated reduced HDL cholesterol levels and increased triglyceride levels relative to controls. The researchers found that those with HbA1c-defined prediabetes and T2DM displayed variations in lipid profiles and liver steatosis, indicating an increased risk for cardiovascular and liver diseases.

Also, **Kumar et al., (7)** who revealed that In comparison to individuals in the prediabetic stage (HbA1c 5.7-6.4), the study found a higher prevalence of dyslipidemia between those with diabetes (HbA1c $\geq$6.5). There was a significant correlation between diabetes and dyslipidemia (TG > 150, VLDL > 30, CHOL > 200, in addition to LDL > 130). accordance with the findings, there was no significant correlation among the participants' HDL levels and their diabetes.

This study assessed the predictive value of lipid profile parameters for progression from prediabetes to T2DM using logistic regression analysis. The AUC values revealed that total cholesterol had the highest predictive value (AUC = 0.802), followed by LDL (AUC = 0.701) and triglycerides (AUC = 0.731). HDL had the lowest predictive value (AUC = 0.437), suggesting its limited role as a predictor for T2DM progression in this cohort.

In accordance with our findings, **Ad'hiah et al., (16)** aimed to determine whether lipid markers play a role in predicting the development of diabetes from pre-diabetes. The results showed that triglycerides, VLDL, the triglyceride/HDL ratio, and the triglyceride-FBG index were significant indicators of prediabetes and normoglycemia, according to the ROC curve analysis. According to their findings, triglycerides and VLDL are two important lipid indicators that, when combined with ROC curve analysis, can detect pre-diabetes and, when combined with logistic regression analysis, are associated with a higher risk of developing diabetes. The blood levels of both markers were significantly greater in people who were pre-diabetic or diabetic. In addition, the triglyceride-FBG index, which includes triglycerides, has a predictive value of 0.924 for differentiating between normoglycemia and pre-diabetes, and it is related to a 32.44-

fold increased chance of developing pre-diabetes, with the highest risk being among diabetic individuals (OR = 188.50). The triglyceride-FBG index and triglycerides alone are strong indicators of prediabetes and diabetes, respectively.

Individuals with prediabetes demonstrate compromised fasting glucose levels and/or glucose tolerance, and lifestyle alterations can diminish the advancement of prediabetes to diabetes by around 58 percent throughout a three-year period **(17).** Furthermore, insulin resistance may precipitate specific clinical occurrences associated with fat accumulation in insulin-sensitive tissues (e.g., the liver, visceral organs, and skeletal muscles) of prediabetic individuals, leading to low-grade inflammation as well as T2DM **(18).**Moreover, insulin resistance correlates with increased levels of VLDL (19).

Subsequent research confirmed that VLDL was more highly expressed in the blood of people with diabetes than in those at risk of developing the disease; nevertheless, levels were still significantly greater in both groups in comparison to healthy controls **(20).** The lipid profile is frequently highlighted as a substantial risk factor in all follow-up regimens for T2DM.

Conclusion

We concluded that individuals with higher HbA1c (6.0%–6.4%) levels had significantly worse lipid profiles, specifically in terms of triglycerides, cholesterol, VLDL, LDL, LDL/HDL ratio, cholesterol/HDL ratio and triglyceride/HDL ratio compared to those with lower HbA1c (5.4%–5.9%) levels within the prediabetic range. The four parameters' effects on pre-diabetes risk were validated by logistic regression analysis. Untraditional lipid panels may be considered promising biomarkers to predict progression from prediabetes to T2DM.

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