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EVALUATION OF HBA1C AS A MARKER OF GLYCEMIC CONTROL AND DYSLIPIDEMIA IN TYPE 2 DIABETES

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Abstract

Background: *Type 2 Diabetes Mellitus (T2DM) is a major global health challenge, with cardiovascular disease (CVD) being its most significant complication. Dyslipidemia, a common co-morbidity in T2DM, is a primary driver of this CVD risk. While Glycated Hemoglobin (HbA1c) is the established marker for long-term glycemic control, its specific relationship with various lipid parameters, particularly atherogenic particles like Very Low-Density Lipoprotein (VLDL), needs further exploration to improve risk assessment.*

Objective: *The primary objective of this study was to investigate the correlation between HbA1c levels and lipid profile parameters in patients with T2DM and to compare these profiles between pre-diabetic and diabetic individuals.*

Methods: *This observational cross-sectional study analyzed data from 100 individuals, categorized as pre-diabetic (n=22) or diabetic (n=78) based on HbA1c levels. Spearman's correlation and Mann-Whitney U tests were used to evaluate the relationship between HbA1c and lipid parameters.*

Results: *The diabetic group showed significantly elevated VLDL levels compared to the pre- diabetic group (p=0.015). Correlation analysis across all participants confirmed a significant positive correlation between HbA1c and both VLDL (rs=.253, p=.011) and triglycerides (rs=.232, p=.020), and a significant negative correlation with HDL (rs=-.254, p=.011). No significant correlations were found with LDL or total cholesterol.*

Conclusion: *The progression from pre-diabetes to diabetes is specifically marked by a significant increase in VLDL, highlighting its role as a sensitive marker for diabetic dyslipidemia. This finding suggests that cardiovascular risk assessment in T2DM should prioritize triglyceride-rich lipoproteins like VLDL, in addition to standard cholesterol panels. HbA1c serves as a valuable indicator for both glycemic control and this atherogenic lipid pattern.*

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood sugar levels resulting from defects in insulin production, insulin action, or both. While all forms of diabetes share the common feature of hyperglycemia, they differ significantly in their causes, risk factors, and management approaches.[1] It has been considered a global problem due to its high prevalence in both advanced and low – medium income countries coupled with a high incidence of cardiovascular disease (CVD) in these subjects. Although there is high prevalence of type 1 diabetes mellitus, however, type 2 diabetes mellitus accounts for over 90% of all cases.[2]

The Types of Diabetes are as follows:

Type 1 Diabetes (T1DM) is an autoimmune condition where the body's immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas.[3]

Type 2 Diabetes (T2DM) is the most common form, accounting for 90-95% of all diabetes cases. It occurs when the body becomes resistant to insulin or when the pancreas cannot produce enough insulin to meet the body's needs.[4]

Gestational diabetes (GDM) occurs during pregnancy when hormonal changes make the body's cells less responsive to insulin. This condition usually develops around the 24th to 28th week of pregnancy and typically resolves after childbirth.[5]

MODY (Maturity-Onset Diabetes of the Young) it is the rare form of Diabetes. It is a genetic disorder that affects insulin production and is often mistaken for Type 1 or Type 2 diabetes. [6]

LADA (Latent Autoimmune Diabetes in Adults) which is a slow-progressing form of Type 1 diabetes that develops in adulthood. Initially, it may be managed with oral medications, but like T1DM, it eventually requires insulin therapy. [7]

The hallmark of type 2 diabetes mellitus (Type 2 DM) is characterized by the persistent hyperglycemia, which can be caused by a variety of factors, including abnormalities in insulin secretion, action, or combo of each. Type 2 DM is growing progressively and thought to be the consequences of food customs, sedentary lifestyles, physical inactivity and obesity.[8]

According to the WHO estimates, 422 million adults worldwide had diabetes in 2023. Type 2 DM is the most prevalent type making for around 90% of all cases of the diabetes.3 According to the International Diabetes Federation (IDF), there were approximately 90 million adults in south Asian countries (aged 20-79) who had diabetes.[9] A U.S.-based and international consensus supports the use of HbA1c as the gold standard for assessing long-term glycemic control in patients with Type 2 diabetes. Clinical guidelines typically recommend maintaining HbA1c at or below **7.0%** to effectively reduce cardiovascular risk. Observational studies have shown a consistent association between HbA1c levels and coronary artery disease severity: each 1% absolute increase in HbA1c is linked to approximately a 13–18% elevated risk of major adverse cardiovascular events (MACEs) and CAD in diabetic individuals. [10]

The prevalence of Type 2 Diabetes Mellitus (T2DM) in Pakistan has reached alarming levels. According to the International Diabetes Federation (IDF), Pakistan had the highest age-adjusted prevalence of diabetes in the world as of 2025, with an estimated 31.4% of adults aged 20–79 affected. This equates to approximately 34.5 million adults, and the number is projected to rise to over 70 million by 2050. Contributing factors include poor diet, physical inactivity, urbanization, and lack of awareness and screening, with nearly 1 in 4 diabetic individuals remaining undiagnosed. [11]

RISK FACTOR OF TYPE 2 DIABETES [11]

- Insulin Resistance: Body cells fail to respond properly to insulin, requiring more insulin to regulate blood sugar.
- Beta-Cell Dysfunction: Over time, the pancreas cannot produce enough insulin to compensate.
- Lifestyle Factors: Obesity, physical inactivity, and poor diet (high sugar, processed foods).
- Genetics: Family history increases

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risk.

- Age & Ethnicity: More common in adults over 45, but rising in younger populations; higher risk in African Americans, Hispanics, and Asians.

Figure 1 RISK FACTOR OF TYPE 2 DIABETES MELLITUS

Glycosylated hemoglobin (HbA1c) is formed when glucose chemically binds to hemoglobin and serves as a reliable biomarker of long-term glycemic control. In addition to reflecting average glucose levels over the preceding 2–3 months, HbA1c has been identified as a significant predictor of lipid profile abnormalities and cardiovascular risk. Monitoring HbA1c in patients with Type 2 diabetes can therefore help to detect those at greater risk of dyslipidemia and cardiovascular complications, even when traditional lipid values appear borderline or normal.[12,13]

One of the most widely used tools for assessing long-term blood sugar control is glycated hemoglobin (HbA1c).[14] The HbA1c is now recommended as a standard of care (SOC) for testing and monitoring diabetes, specifically the type 2 diabetes.[15]

Unlike daily finger-prick glucose tests that only provide a momentary snapshot, HbA1c reflects average blood sugar levels over the past two to three months. This makes it an invaluable marker for both diagnosing diabetes and evaluating how well treatment is working. The American Diabetes Association (ADA) [16] recommends maintaining HbA1c levels below 7% for most adults with diabetes to reduce complications. However, HbA1c is more than just a number—it may also offer clues about other metabolic disturbances, particularly dyslipidemia, a common companion of diabetes that significantly raises cardiovascular risk. [17]

Atypical lipid profile parameters are thought to be the most significant risk factors contributing to the development of CVD, aside from metabolic syndrome.[18] Dyslipidemia—an imbalance of blood fats like cholesterol and triglycerides—is a major concern in T2DM. People with diabetes often have a distinct lipid profile: high triglycerides, low HDL ("good" cholesterol), and small, dense LDL particles that are particularly harmful to blood vessels. [19] Research suggests that poor blood sugar control, indicated by elevated HbA1c, may worsen these lipid abnormalities. For example, when blood sugar remains high, the liver produces more very-low-density lipoprotein (VLDL), leading to increased triglycerides. At the same time, insulin

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resistance impairs the breakdown of fats, further contributing to dyslipidemia.[20]

Despite its advantages, HbA1c isn't flawless. Certain conditions, like anemia, kidney disease, or genetic blood disorders, can skew results, leading to misleadingly high or low readings Additionally, some ethnic groups may have naturally higher or lower HbA1c levels at the same blood glucose concentration, raising concerns about universal diagnostic cutoffs. Alternative markers, such as fructosamine and glycated albumin, have been explored, but none have matched HbA1c's convenience and widespread clinical validation. [21]

Given that diabetes and heart disease often go hand in hand, understanding how HbA1c relates to lipid metabolism could improve early intervention strategies. If consistently high HbA1c levels reliably signal worsening cholesterol and triglyceride levels, doctors could use this marker to identify patients at greater risk for heart attacks and strokes before symptoms appear. Some experts even argue that HbA1c should be part of cardiovascular risk assessment in diabetes, alongside traditional cholesterol tests. [22]

MATERIAL AND METHODS

4.1 STUDY DESIGN

A observational cross sectional study was carried out.

4.2 STUDY SETTINGS

The subjects for the present study were selected from Galaxy lab, Lahore.

4.3 STUDY DURATION

The study duration was 4 month after the approval of synopsis.

4.4 SAMPLE SIZE

The data of 100 people was calculated by Cochran's formula .It will be collected from the Galaxy Lab Lahore.

4.5 INCLUSION CRITERIA:

1. The female patients age (18 and above) were included
2. The patients who were willing to participate and provide informed consent were included.
3. **Diagnosis:** Confirmed diagnosis of Type 2 Diabetes Mellitus (per ADA criteria) was included.
4. Duration of diabetes ≥1 year was considered
5. **Clinical Status:**

- Minimum of two documented HbA1c tests within past 6 months
- Fasting lipid profile available within 2 weeks of HbA1c measurement

6. **Treatment Stability:** Stable glucose-lowering regimen (no medication changes in past 3 months)

4.6 EXCLUSION CRITERIA:

1. The Patients who are unwilling were excluded from the study.
2. The patients who were currently using medication such as lipid-lowering therapy (statins, fibrates, PCSK9 inhibitors) and Systemic corticosteroids or immunosuppressant's were excluded

3. **Pregnancy:** Current or recent pregnancy (<6 months postpartum) female were excluded
4. **Data Limitations:** Incomplete medical records and Non-fasting lipid measurements were excluded.

DATA ANALYSIS PROCEDURE

Data was analyzed by using SPSS software. Depending on variables different statistical technique were performed including standard deviation (SD), mean median, mode, T-test, and correlation coefficient etc.

RESULTS

Frequency of Gender Distribution:

The study included a total of 100 participants, with a slightly higher proportion of males (n = 56, 56.0%) compared to females (n = 44, 44.0%). This indicates a fairly balanced gender distribution among the study population. The representation of both genders ensures that the findings regarding glycemic control and lipid profile

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parameters in type 2 diabetes are applicable to both male and female patients.

Table 1 Frequency of Gender Distribution

Gender	Frequency	Percent %
Male	56	56.0
Female	44	44.0
Total	100	100.0

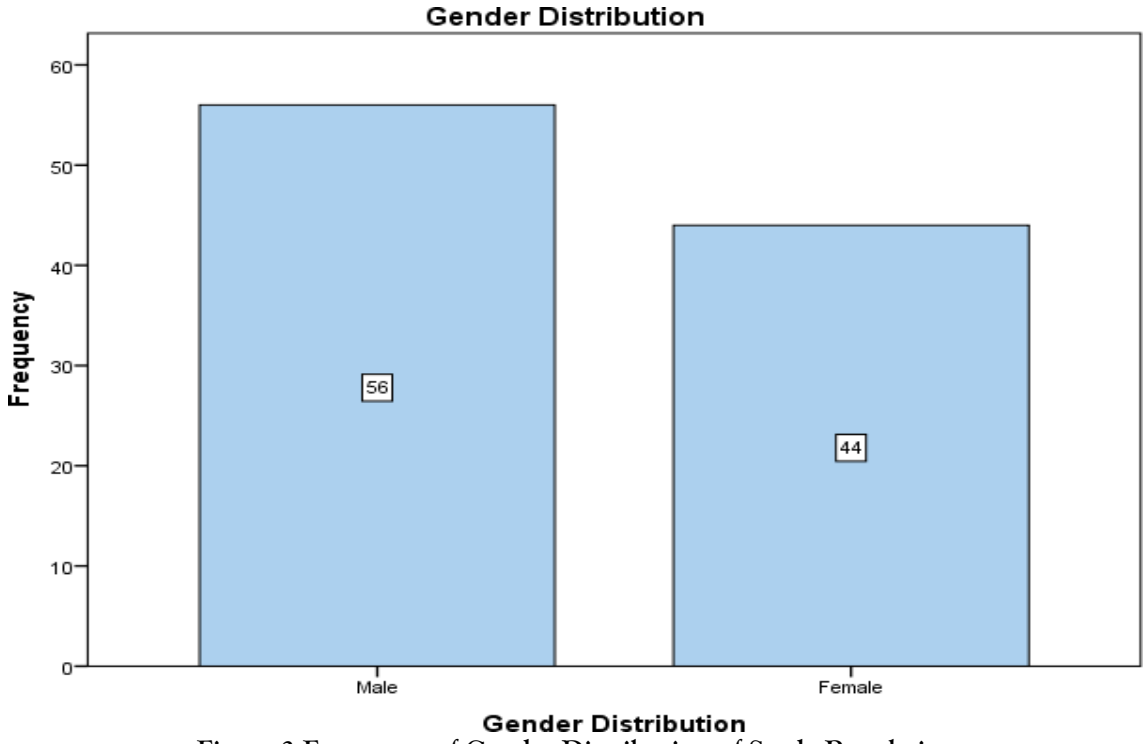

Figure 3 Frequency of Gender Distribution of Study Population

Frequency of Age categories:

The ages of the 100 participants ranged from 27 to 78 years, with a mean age of 53.37 ± 11.84 years. This indicates that the study population primarily consisted of middle-aged adults, with a moderate spread of ages including both younger and older patients with type 2 diabetes.

Table 2 Statistics of Age distribution

	N	Minimum	Maximum	Mean	Std. deviation
Age of patients	100	27	78	53.37	11.83613

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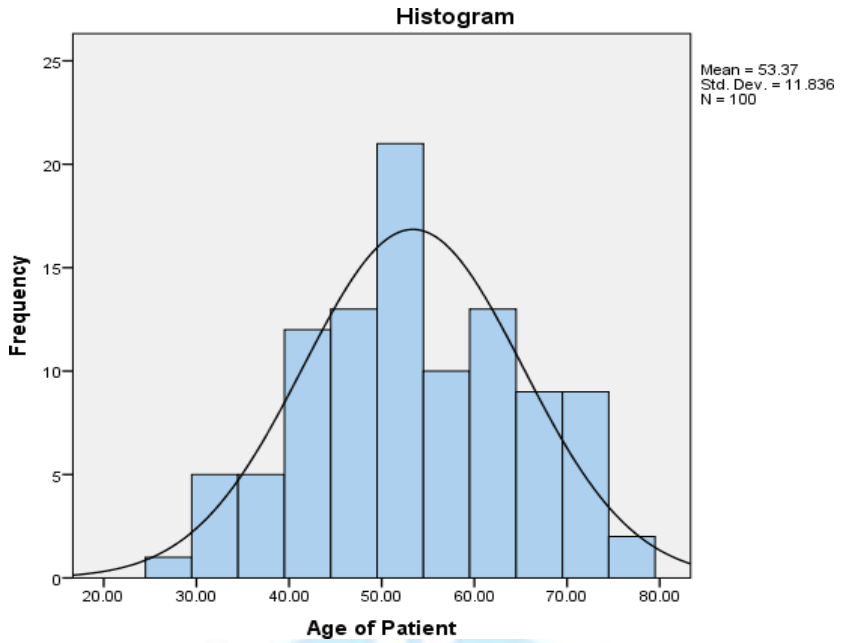

Figure 4 Age Distribution of Study population

Age Categories And Its Frequency Distribution:
The age distribution of the participants showed that the majority were older than 41 years (n = 83, 83.0%), while 17 participants (17.0%) were between 21 and 40 years of age. No participants were younger than 20 years, which aligns with the low prevalence of type 2 diabetes in adolescents. Overall, the study population predominantly consisted of middle-aged and older adults, which is representative of the typical demographic affected by type 2 diabetes

Table 3 Frequency of Age Categories of Study Population

Age Categories	Frequency	Percent %
Less than 20	0	0.0
21-40	17	17.0
More than 41	83	83.0
Total	100	100.0

Frequency of HbA1c Distribution:
Among the 100 participants, 78 (78.0%) were diagnosed with type 2 diabetes, while 22 participants (22.0%) were classified as pre-diabetic. This distribution indicates that the majority of the study population had established diabetes, providing a suitable cohort to assess the relationship between HbA1c levels and lipid profile parameters.

Table 4 Frequency of HbA1c Distribution

Glycemic Status	Frequency	Percent %
Pre-Diabetic	22	22.0
Diabetic	78	78.0

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Total	100	100.0

Frequency of Lipid Parameters:

The distribution of lipid profile parameters among the 100 study participants is summarized in the table. For **Total Cholesterol (TC)**, 58% of participants had normal levels, 26% were borderline, and 16% were classified as high risk. **Triglycerides (TG)** showed a concerning pattern, with only 23% in the normal range, 24% borderline, and a majority of 53% at high risk. In terms of **HDL**, which represents "good" cholesterol, 34% were normal, none were borderline, and 66% were at high risk, indicating a widespread deficiency of protective HDL levels. **LDL** levels were relatively better, with 54% normal, 25% borderline, and 21% high risk. Similarly, **VLDL** showed a high-risk tendency, with 53% of participants in the high-risk category, 24% normal, and 23% borderline. Overall, these results indicate that dyslipidemia is prevalent among the participants, particularly for triglycerides, HDL, and VLDL, highlighting a substantial risk of cardiovascular complications in this population.

Table 5 Frequency of Lipid Parameter Distribution

Lipid Parameter	Normal	Borderline	High Risk	Total
Total Cholesterol	58	26	16	100
Triglyceride	23	24	53	100
HDL	34	0	66	100
LDL	54	25	21	100
VLDL	24	23	53	100

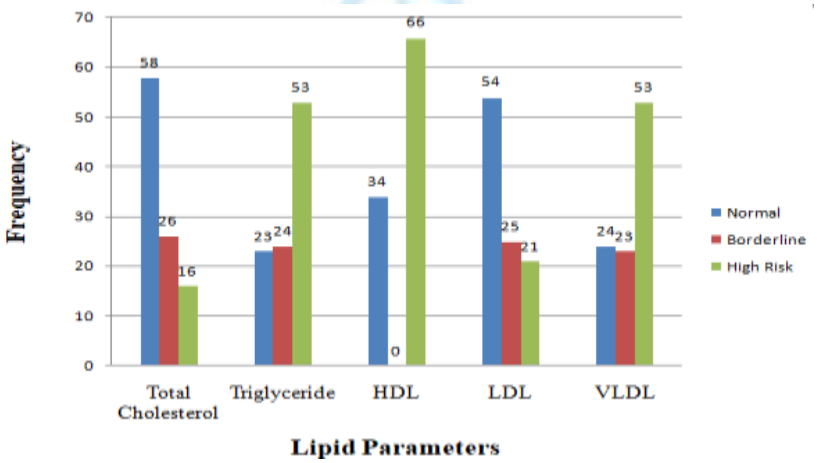

Figure 7 Frequency of Lipid Parameter of Study population

Test for Normal Distribution:

Normality of HbA1c was assessed for each lipid profile parameter using the **Kolmogorov- Smirnov** and **Shapiro-Wilk tests**. The results indicated that HbA1c was **not normally distributed** across all categories of Total Cholesterol, Triglycerides, HDL, LDL, and VLDL, with all p-values < 0.05. Therefore, non-parametric statistical tests were used for further analysis of the association between HbA1c and lipid parameter.

Table 6 Test for Normal Distribution

Lipid		Kolmogorov-Smirnov	Shapiro-Wilk

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Parameter	HBA1C	Statistic	Df	Sig.	Statistic	Df	Sig.
Total Cholesterol	Normal	.479	58	.000	.515	58	.000
	Borderline	.474	26	.000	.524	26	.000
	High	.492	16	.000	.484	16	.000
Triglyceride	Normal	.415	23	.000	.605	23	.000
	Borderline	.464	24	.000	.542	24	.000
	High	.511	53	.000	.428	53	.000
HDL	Normal	.498	66	.000	.469	66	.000
	High	.443	34	.000	.573	34	.000
LDL	Normal	.488	54	.000	.494	54	.000
	Borderline	.449	25	.000	.565	25	.000
	High	.492	21	.000	.484	21	.000
VLDL	Normal	.401	24	.000	.616	24	.000
	Borderline	.459	23	.000	.551	23	.000
	High	.518	53	.000	.400	53	.000

Comparison of Lipid Parameter between Pre-Diabetic and Diabetic Groups:

Mann-Whitney U tests were conducted to determine if there were differences in lipid parameters between pre-diabetic (n=22) and diabetic (n=78) participants. The results revealed a statistically significant difference in VLDL levels between groups (U = 1,122.50, p = .015), with diabetic participants showing elevated VLDL levels (Mean Rank = 59.69) compared to pre-diabetic participants (Mean Rank = 38.48).

No statistically significant differences were found in other lipid parameters:

- Total Cholesterol: U = 837.50, p = .850
- Triglycerides: U = 1,068.00, p = .054
- LDL: U = 837.50, p = .860
- HDL: U = 732.00, p = .201

Although triglyceride levels approached statistical significance (p = .054), suggesting a trend toward higher levels in the diabetic group (Mean Rank = 53.19) compared to pre-diabetic group (Mean Rank = 40.95), the effect did not reach the conventional threshold for statistical significance.

Table 7 Mann-Whitney U Test (Non-parametric Test)

Lipid Parameter	Mann-Whitney U	p-value	Diabetic Mean Rank (n=78)	Pre-Diabetic Mean Rank (n=22)
Total Cholesterol	837.50	.850	50.24	51.43
Triglycerides	1,068.00	.054	53.19	40.95
LDL	837.50	.860	50.24	51.43
VLDL	**1,122.50**	**.015**	**59.69**	**38.48**
HDL	732.00	.201	48.88	56.23

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Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Total_Cholesterol is the same across categories of HBA1C.	Independent-Samples Mann-Whitney U Test	.843	Retain the null hypothesis.
2	The distribution of Tryglyceride is the same across categories of HBA1C.	Independent-Samples Mann-Whitney U Test	.054	Retain the null hypothesis.
3	The distribution of LDL is the same across categories of HBA1C.	Independent-Samples Mann-Whitney U Test	.850	Retain the null hypothesis.
4	The distribution of VLDL is the same across categories of HBA1C.	Independent-Samples Mann-Whitney U Test	.015	Reject the null hypothesis.
5	The distribution of HDL is the same across categories of HBA1C.	Independent-Samples Mann-Whitney U Test	.201	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Figure 9 Hypothesis Test Summary

Spearman Co-relation:

Spearman's rank correlation analysis revealed a significant **negative correlation between HbA1c and HDL** (r = –0.254, p = 0.011) and a **positive correlation with Triglycerides (r = 0.232, p = 0.020)** and **VLDL (r = 0.253, p = 0.011)**. No significant relationship was found between HbA1c and Total Cholesterol or LDL. These results suggest that poor glycemic control is associated with low HDL and high Triglyceride and VLDL levels in type 2 diabetic patients.

Table 8 Spearman Co-relation analysis

			HBA1C	HDL	Total Cholesterol	Triglyceride	LDL	VLDL
	HBA1C	Correlation Coefficient	1.000	-.254*	.024	.232*	-.046	.253*
		Sig. (2-tailed)	.	.011	.815	.020	.649	.011
		N	100	100	100	100	100	100
	HDL	Correlation Coefficient	-.254*	1.000	.109	-.408**	.181	-.511**
		Sig. (2-tailed)	.011	.	.279	.000	.071	.000
		N	100	100	100	100	100	100
		Correlation Coefficient	.024	.109	1.000	.348**	.791**	.273**

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Spearman's rho	Total Cholesterol	Sig. (2-tailed)	.815	.279	.	.000	.000	.006
		N	100	100	100	100	100	100
	Triglyceride	Correlation Coefficient	.232*	-.408**	.348**	1.000	.018	.921**
		Sig. (2-tailed)	.020	.000	.000	.	.860	.000
		N	100	100	100	100	100	100
	LDL	Correlation Coefficient	-.046	.181	.791**	.018	1.000	-.034
		Sig. (2-tailed)	.649	.071	.000	.860	.	.736
		N	100	100	100	100	100	100
	VLDL	Correlation Coefficient	.253*	-.511**	.273**	.921**	-.034	1.000
		Sig. (2-tailed)	.011	.000	.006	.000	.736	.
		N	100	100	100	100	100	100

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

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

CHPATER 6
DISCUSSION

This study sought to investigate the relationship between glycemic control and lipid metabolism in type 2 diabetes. By employing both group comparisons and correlation analysis, our findings provide a multi-faceted understanding of how dyslipidemia manifests as glycemic control deteriorates. The results consistently highlight that the most pronounced lipid abnormality associated with rising HbA1c is an increase in triglyceride-rich lipoproteins, specifically VLDL, rather than a uniform worsening of all cholesterol parameters.

The most compelling evidence from this study is the convergence of findings from different statistical methods. The **Mann-Whitney U test** revealed that VLDL levels were significantly higher in the diabetic group compared to the pre-diabetic group ($p = 0.015$). This group-level finding is powerfully reinforced by the **Spearman correlation analysis**, which demonstrated a significant positive correlation between continuous HbA1c values and VLDL levels across the entire cohort ($rs = .253$, $p = .011$).

This dual-confirmation underscores that the relationship is not merely a difference between two categories, but a **gradual, dose-responsive association**—as HbA1c increases, VLDL levels also tend to rise. The same pattern was observed for triglycerides, which showed a strong trend in the group comparison ($p = 0.054$) and a definitive significant correlation ($rs = .232$, $p = .020$). This consistency across methodologies strengthens the validity of our central finding and firmly establishes VLDL as a key lipid fraction disturbed in diabetic dyslipidemia.

Our results paint a clear and specific picture of dyslipidemia in our population. The significant correlations of HbA1c with VLDL and triglycerides, coupled with a significant **negative correlation with HDL** ($rs = -.254$, $p = .011$), classicially defines the "atherogenic lipid triad" of diabetes: high triglycerides, low HDL, and elevated remnant lipoproteins.

Conversely, the **absence of significant correlation with both LDL and Total Cholesterol** ($rs = -.046$, $p = .649$ and $rs = .024$, $p = .815$, respectively) is a crucial finding. It indicates that conventional cholesterol-centric lipid panels may provide a false sense of security if used in isolation. A diabetic patient with a "normal" LDL level may still harbor a significant residual cardiovascular risk

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driven by high VLDL and low HDL, a risk that is directly related to their degree of hyperglycemia.

Pathophysiologically, these findings align perfectly with the established mechanisms of insulin resistance. Poor glycemic control promotes increased free fatty acid flux to the liver, stimulating VLDL production. Simultaneously, insulin resistance suppresses lipoprotein lipase activity, impairing VLDL and triglyceride clearance from the bloodstream. Our results, which show a tight correlation between HbA1c and VLDL/triglycerides, provide clinical evidence for this underlying metabolic chaos.

The clinical implication is straightforward: **HbA1c is a dual-purpose marker**. It is not only a reflection of average blood glucose but also a reliable indicator of this specific, high-risk lipid pattern. This supports the notion that achieving HbA1c targets is likely beneficial not only for microvascular risk reduction but also for improving atherogenic dyslipidemia and reducing macrovascular risk.

Conclusion

This study demonstrates a strong link between glycated hemoglobin (HbA1c) and key lipid abnormalities in individuals with Type 2 Diabetes Mellitus (T2DM), highlighting that dyslipidemiaespecially elevations in triglycerides and VLDL alongside reduced HDL is closely associated with poor glycemic control. VLDL consistently emerged as the most sensitive marker distinguishing diabetic from pre-diabetic individuals, indicating its potential role as an early indicator of metabolic deterioration. The absence of significant relationships between HbA1c and LDL or total cholesterol suggests that traditional cholesterol measures may underestimate cardiovascular risk in this population. Overall, the findings emphasize that HbA1c reflects not only long-term glucose regulation but also the underlying atherogenic lipid pattern characteristic of T2DM. Integrating HbA1c with triglyceride-rich lipoprotein assessment may therefore offer a more comprehensive evaluation of cardiometabolic risk. Strengthening glycemic control could yield dual benefits improving both glucose homeostasis and lipid metabolism ultimately reducing long-term cardiovascular complications. Future studies with larger cohorts and longitudinal follow-up are needed to clarify causal mechanisms and guide targeted interventions.

7.1 Limitations:

While this study offers meaningful insights, certain limitations must be considered. Its cross-sectional design prevents causal interpretation, and the relatively small pre-diabetic subgroup may have reduced the ability to detect subtle differences. Additionally, unmeasured factors such as diet, physical activity, and medication use may have influenced lipid and glycemic outcomes. Despite these constraints, a notable strength is the combined use of group comparisons and correlation analyses, which together provide a more comprehensive and reliable understanding of the relationship between HbA1c and lipid parameters.

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