Cardiovascular Mortality in Diabetes: The Role of Lipid ratios and Apolipoprotein (Apo) A-I /Apo B ratio as a Predictive Marker

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KEYWORDS

Type 2 diabetes mellitus, Cardiovascular Disease, Dyslipidaemia, Lipid ratios, Apolipoproteins, Apo A-I/Apo B ratio

ABSTRACT:

Dyslipidaemia is a common complication among individuals with type 2 diabetes mellitus (T2DM), significantly increasing the risk of cardiovascular disease (CVD). This cross-sectional study investigated the clinical relevance of lipid ratios and apolipoprotein (Apo) B/Apo A-I ratio as predictive markers of cardiovascular risk in 150 participants, categorized into three groups: controls (n=50), T2DM without CVD (n=50), and T2DM with CVD (n=50). Serum lipid profiles and apolipoproteins were measured using enzymatic and immunoturbidimetric methods, and statistical analyses, including ANOVA and receiver operating characteristic (ROC) curve evaluation, were performed.

The results revealed that participants with T2DM and CVD exhibited significantly higher fasting and postprandial glucose levels, total cholesterol, low-density lipoprotein (LDL-C), and triglycerides (TG), along with lower high-density lipoprotein (HDL-C) levels compared to controls and non-CVD diabetics ($p<0.001$). Lipid ratios, such as total cholesterol: HDL-C and TG: HDL-C, and Apo B/Apo A-I ratio were markedly elevated in the CVD group, indicating pronounced dyslipidaemia. ROC analysis demonstrated that the non-HDL ratio (AUC = 0.608) and Apo A-I/Apo B ratio (AUC = 0.525) provided moderate predictive validity for CVD risk.

The study concludes that combining traditional lipid profiles with apolipoprotein assessments enhances cardiovascular risk stratification in T2DM patients. Comprehensive evaluation of lipid ratios and Apo metrics may improve early identification of high-risk individuals, guiding personalized interventions to mitigate adverse cardiovascular outcomes.

1. Introduction

Individuals with diabetes who have poor glycemic control often exhibit dyslipidaemia, characterized by elevated triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C), along with reduced high-density lipoprotein cholesterol (HDL-C).(1) For those with both diabetes and metabolic syndrome—a condition involving hypertension, dyslipidaemia, abdominal obesity, and hyperglycaemia—the risk of cardiovascular complications is even more pronounced. Managing both glycemic and lipid profiles is essential to prevent the progression of diabetes-related microvascular and macrovascular complications. (2)

In addressing dyslipidaemia, the European Society of Cardiology (ESC) emphasizes strict LDL-C control, recommending levels below 70 mg/dL for high-risk patients, such as those

with coronary artery disease (CAD) or diabetes, underlining the significance of lipid profiles in managing cardiovascular risk in diabetic populations. [3]

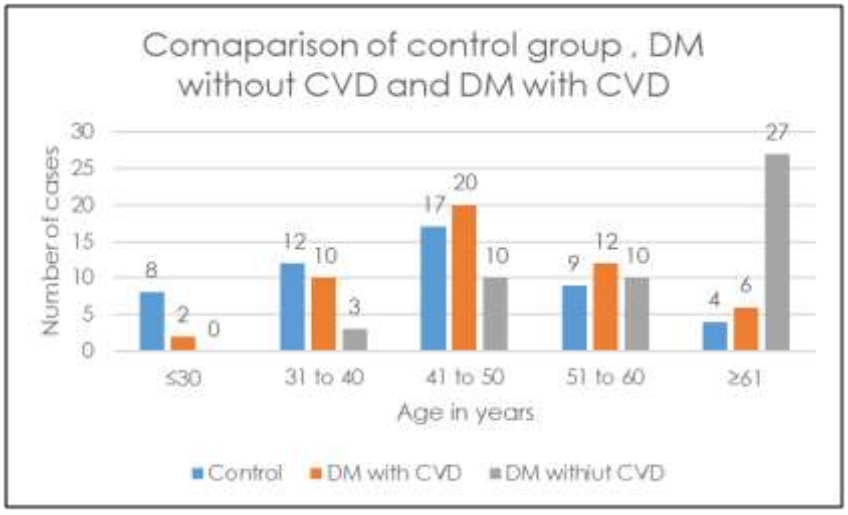
A study by Lin et al. [4] highlights that diabetic patients tend to have higher levels of LDL-C, total cholesterol, and TG, along with unfavourable lipid ratios like TG/HDL and LDL/HDL, in comparison to non-diabetics. Furthermore, there's a positive correlation between lipid profiles and HbA1c levels, suggesting that effective glycemic control could improve lipid balance, making lipid measures useful markers for assessing glycemic management in type 2 diabetes. [5]

Globally, cardiovascular disease (CVD) contributes to 30% of all deaths, with the highest impact in low- and middle-income countries. Dyslipidaemia accelerates atherosclerosis, increasing the risk of CVD, especially in individuals with diabetes. Apolipoproteins are crucial for lipid transport: Apo B is linked with LDL and VLDL and is associated with increased cardiovascular risk, whereas Apo A-I, found in HDL, aids in reducing plaque formation by promoting cholesterol removal. The Apo B/Apo A-I ratio is an established indicator of cardiovascular risk, providing a valuable metric for assessing atherogenic burden and guiding risk management. [6-7] The aim of the study is to investigate the clinical relevance of lipid ratios and Apo B/Apo A-I ratio as predictive biochemical models for assessing cardiovascular risk in patients with type 2 diabetes mellitus (T2DM)

2. Methodology

A Cross-sectional study included total 150 participants and were divided into three groups. Group II involves 50 type 2 diabetes mellitus without any complication and Group III involves 50 type 2 diabetic mellitus with CVD as cases and Group I involves 50 healthy subjects taken as controls. Blood glucose levels, lipid profile and apolipoproteins were measured. Serum is used for the measurement of Serum lipid profile by Enzymatic methods and serum apolipoprotein A-I & B by Immunoturbidimetric method. Lipid ratios and Apolipoprotein (Apo) A-I /Apo B ratio was calculated. The study was approved by Ethics Committee. MS Excel and SPSS-Software Version-26 were used to analyze the data in the study. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data. Receiver operating characteristic curve (ROC) will be plotted to estimate the cut-off values. Results were considered statistically significant at P value ≤0.05.

3. Results



Graph 1: Age distribution of the study samples.

Graph 1 shows the age differences across all three groups, with CVD diabetics having the highest mean age (61.28 years) compared to controls and non-CVD diabetics ($p<0.001$).

Table 11: Comparison of glucose levels between all three groups

Subjects (N=150)	Groups						p-value#
	Controls (N=50)		DM without CVD (N=50)		DM with CVD (N=50)		
	Mean	SD	Mean	SD	Mean	SD	
Duration of DM (in months)	-	-	34.20	21.32	112.56	45.67	<0.001*
FPG (mg/dL)	91.54	13.79	169.62	78.33	207.52	79.90	<0.001*
PPPG (mg/dL)	121.82	15.84	260.34	93.85	291.76	88.51	<0.001*

One Way ANOVA
* Statistically significant

Table 1 highlights marked differences in glucose levels among the three groups. Diabetics with CVD exhibit the highest fasting blood sugar (FBS) levels (207.52 mg/dL), followed by diabetics without CVD (169.62 mg/dL) and controls (91.54 mg/dL, p<0.001). Similarly, post-prandial blood sugar (PPBS) levels are significantly elevated in CVD diabetics (291.76 mg/dL) compared to non-CVD diabetics (260.34 mg/dL) and controls (121.82 mg/dL, p<0.001).

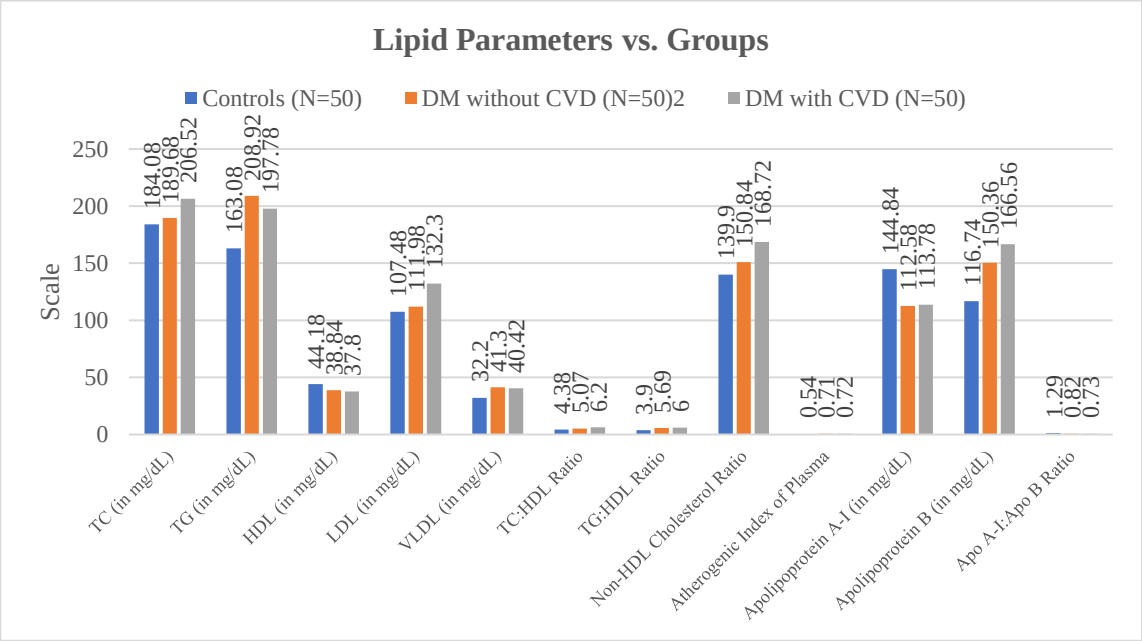


Figure 2: Comparison of lipid parameters between all three groups

Figure 2 represents the comparison of lipid parameters between all three groups. Diabetics with CVD have the highest mean total cholesterol (206.52 mg/dL) and low-density lipoprotein (LDL) levels (132.30 mg/dL), contrasting with lower levels in controls (p=0.017 and p=0.002, respectively). High-density lipoprotein (HDL) is lowest in CVD diabetics (37.80 mg/dL), and ratios such as TC: HDL and TG: HDL are significantly elevated in this group, indicating more pronounced dyslipidemia (p<0.001).

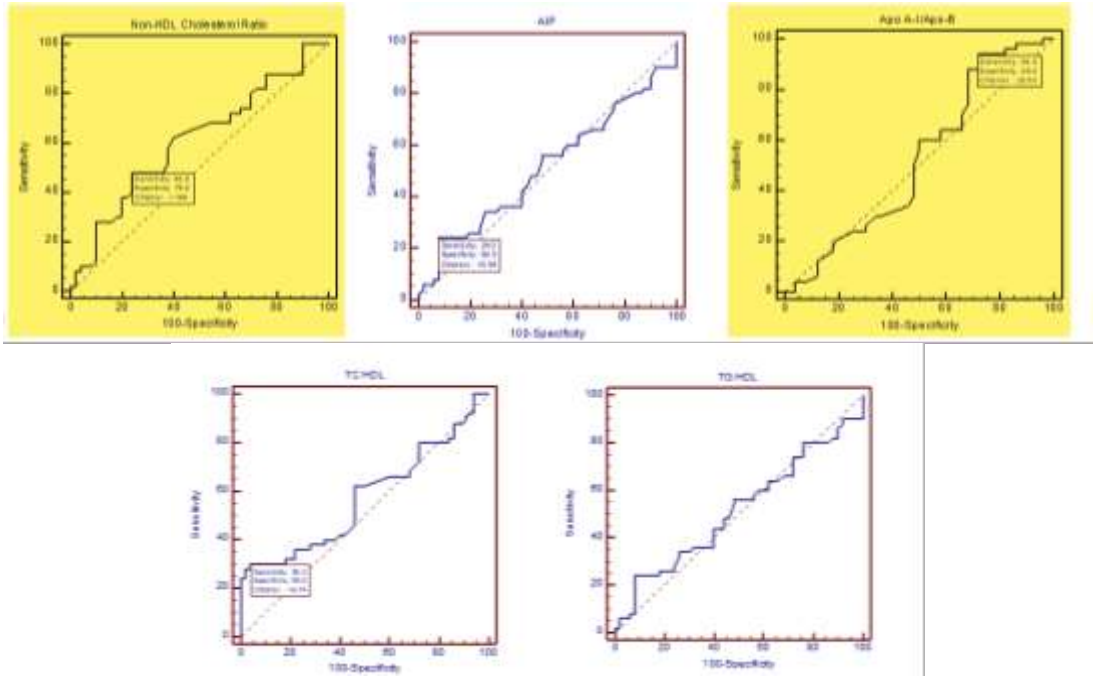


Figure 3: AUC of various ratios in predicting the risk of CVD among Diabetics

Figure 3 represents the AUC of various ratios in predicting the risk of CVD among Diabetics. Among all the ratios, the non-HDL cholesterol ratio as a predictor of CVD, yielding an AUof 0.608 and Apo A-I /Apo B ratio's predictive validity, with an AUC of 0.525

4. Discussion

Age differences across all three groups, with CVD diabetics having the highest mean age (61.28 years) compared to controls and non-CVD diabetics ($p<0.001$). This progression reflects the increased cardiovascular susceptibility in older and long-term diabetic individuals, emphasizing age and chronic diabetes duration as pivotal cardiovascular risk enhancers.

Table 1 highlights marked differences in glucose levels among the three groups. In the present study the levels of FPG and PPPG were significantly higher in T2DM patients with CVD as compared to Group I and II. Elevated glucose levels reflect poor diabetic control, signifying increased circulating glucose. However insufficient insulin availability reduces lipoprotein lipase activity, impairing the clearance of chylomicrons and VLDL cholesterol. Poor glycemic control worsens lipid and lipoprotein abnormalities, primarily due to insulin resistance and associated factors like excess adiposity. This process is driven by increased free fatty acid flux and elevated proinflammatory adipokines and cytokines released from expanded adipose tissue. Together, hyperglycemia and dyslipidemia lead to a highly atherogenic environment, promoting the progression of atherosclerosis and cardiovascular risk. [8,9]

Diabetics with CVD have the highest mean total cholesterol (206.52 mg/dL) and low-density lipoprotein (LDL) levels (132.30 mg/dL), contrasting with lower levels in controls ($p=0.017$ and $p=0.002$, respectively). High-density lipoprotein (HDL) is lowest in CVD diabetics (37.80 mg/dL), and ratios such as TC: HDL and TG: HDL are significantly elevated in this group, indicating more pronounced dyslipidaemia ($p<0.001$). These lipid abnormalities in CVD diabetics underscore the critical role of lipid management in mitigating cardiovascular risks.

The non-HDL ratio provides a balanced yet moderate prediction of cardiovascular risk. Its moderate specificity and sensitivity imply that while the non-HDL ratio is relevant, while the Apo A-I : Apo B ratio is sensitive in detecting risk, it lacks specificity. Thus their predictive accuracy might be enhanced when combined with other lipid parameters in diabetic individuals.

Our findings are in association with the study by Tajik B, et al. which highlights the clinical relevance of lipid ratios and apolipoprotein metrics as superior markers for identifying individuals at higher risk of developing CVD compared to traditional lipid profiles. Elevated levels of total cholesterol, LDL-C, and triglycerides were associated with an increased risk of

CVD, while higher HDL-C levels had a protective effect. Lipid ratios, such as total cholesterol/HDL-C and triglyceride/HDL-C, proved to be more predictive of CMM risk than individual lipid measures. Additionally, higher ApoB levels and an elevated ApoB/ApoA1 ratio were strongly linked to increased CMM risk, whereas ApoA1 alone was inversely associated [10]

In T2DM, where lipid metabolism is commonly altered, combining traditional lipid ratios with apolipoprotein assessments enhances cardiovascular risk stratification. This comprehensive approach aids in identifying high-risk patients, potentially guiding personalized interventions for better outcomes. Few limitations of the study includes small sample size from a single center reduces generalizability.

5. Conclusion

Lipid ratios and apolipoproteins each play critical roles in assessing cardiovascular risk in individuals with T2DM. Lipid ratios offer insight into lipid metabolism and the balance between atherogenic and anti-atherogenic lipoproteins. Elevated levels of Apolipoprotein B (Apo B), in particular, have been strongly associated with an increased risk of cardiovascular mortality, underscoring the importance of maintaining optimal Apo B levels to reduce adverse outcomes in patients with diabetes. In conclusion, a comprehensive assessment that includes lipid-related markers may be the most effective approach for identifying T2DM patients at higher risk of cardiovascular complications.

6. Financial support - Nil

7. Conflicts of interest -Nil

8. References

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