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Evaluation of the Triglyceride to High-Density Lipoprotein Cholesterol (TAG/HDL) Ratio as a Biomarker for Insulin Resistance in South Indian Male Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Insulin resistance plays a pivotal role in the progression of Type 2 Diabetes Mellitus (T2DM), and the triglyceride to high-density lipoprotein cholesterol (TAG/HDL) ratio has been proposed as a marker for both insulin resistance and cardiovascular risk. This study aims to assess the TAG/HDL ratio as a biomarker for insulin resistance in male T2DM patients from the South Indian population.

Methods: A cross-sectional study was conducted with 30 male T2DM patients aged 30–60 years. Anthropometric measurements, lipid profiles, fasting insulin, fasting glucose, and HbA1c were recorded. The TAG/HDL ratio was calculated and correlated with insulin resistance using Pearson's correlation coefficient.

Results: Elevated triglyceride levels were strongly associated with insulin resistance, showing a significant correlation ($p = 0.0021$). However, the TAG/HDL ratio did not demonstrate a significant correlation with insulin resistance in this cohort ($p = 0.1882$). These findings suggest that while the TAG/HDL ratio may not be a reliable marker for insulin resistance in this population, elevated triglycerides alone are strong indicators of metabolic dysfunction.

Conclusion: The TAG/HDL ratio did not serve as a significant marker for insulin resistance in male T2DM patients. However, elevated triglycerides should be monitored closely, and a comprehensive lipid profile, along with thyroid function assessments, may provide better insight into managing insulin resistance in T2DM patients.

Keywords: Insulin resistance, TAG/HDL ratio, Triglycerides, Type 2 Diabetes Mellitus, South Indian population

Introduction:

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia, which can lead to long-term complications such as retinopathy, nephropathy, neuropathy, and cardiovascular diseases. The global burden of Type 2 Diabetes Mellitus (T2DM) is rapidly increasing, with an estimated 415 million adults affected in 2015. This number is expected to increase by an additional 200 million by 2040, making diabetes a major public health concern worldwide [1].

Insulin resistance (IR) plays a central role in the pathogenesis of T2DM and is a precursor to other metabolic disorders such as metabolic syndrome and cardiovascular diseases. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is currently the gold standard for assessing IR. However, it is often impractical for routine clinical use due to its complexity and the variability of results based on factors such as race, gender, and lifestyle[2].

The triglyceride to high-density lipoprotein cholesterol (TAG/HDL) ratio has emerged as a potential surrogate marker for insulin resistance [3]. It is correlated with the presence of small, dense low-density lipoprotein (LDL) particles, which are associated with increased cardiovascular risk [4]. Epidemiological studies, such as the Framingham Heart Study, have suggested that a higher TAG/HDL ratio is linked to an increased risk of T2DM and cardiovascular disease. However, its applicability as a biomarker for insulin resistance varies across different populations, likely due to differences in lipid metabolism, dietary habits, and genetic predispositions [5].

In the South Indian population, where dietary patterns and metabolic profiles differ significantly from those in Western countries, the effectiveness of the TAG/HDL ratio as a marker for insulin resistance has not been extensively studied [6]. This study aims to evaluate the significance of the TAG/HDL ratio as a biomarker for insulin resistance in male T2DM patients within the South Indian population. By doing so, it seeks to provide insights into whether this marker can be reliably used in clinical practice for this specific demographic or if alternative lipid markers should be considered.

Materials and Methods

Study Design:

This cross-sectional observational study was conducted over a six-month period at Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India. The study recruited 30 male patients aged 30–60 years with a confirmed diagnosis of T2DM, following specific inclusion and exclusion criteria. Ethical approval was obtained from the institutional ethics committee, and informed consent was secured from all participants.

Inclusion Criteria:

1. Male patients aged 30–60 years diagnosed with T2DM for at least one year.
2. Based on the American Diabetes Association's (ADA) guidelines, been diagnosed with type 2 diabetes for a minimum of a year. [7] .
3. Stable glycemic control on oral hypoglycemic agents or insulin for the last three months.
4. Ability to provide informed consent.

Exclusion Criteria:

1. Patients with Type 1 Diabetes or other forms of diabetes.
2. History of cardiovascular events in the last six months.
3. Use of lipid-lowering medications within the last three months.
4. Presence of chronic liver disease, kidney disease, or thyroid disorders.
5. Current smokers or individuals with a history of alcohol abuse.

Data Collection:

Anthropometric measurements, lipid profiles, fasting blood glucose, HbA1c, and insulin levels were recorded. The TAG/HDL ratio was calculated by dividing the triglyceride levels by HDL-C levels. Insulin resistance was assessed using the HOMA-IR formula.

- **Fasting Blood Glucose:**
  - Measured using the glucose oxidase-peroxidase method [8] .
- **Glycated Hemoglobin (HbA1c):**
  - Assessed using high-performance liquid chromatography (HPLC) [9].
- **Lipid Profile:**
  - Serum levels of total cholesterol, triglycerides (TAG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were determined using enzymatic methods[10] .
- **Insulin Levels:**
  - Measured using an enzyme-linked immunosorbent assay (ELISA) [11].
- **Homeostasis Model Assessment of Insulin Resistance (HOMA-IR):**
  - Calculated using the formula:

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), which was computed using the following formula, was used to assess insulin resistance.

$$\text{HOMA-IR} = \frac{\text{Fasting Insulin (µU/mL)} \times \text{Fasting Glucose (mg/dL)}}{405}$$

Alternatively, when glucose is measured in mmol/L:

$$\text{HOMA-IR} = \frac{\text{Fasting Insulin (µU/mL)} \times \text{Fasting Glucose (mmol/L)}}{22.5}$$

More than 2.5 on the HOMA-IR was regarded as a sign of insulin resistance [12].

Statistical Analysis:

All data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Pearson's correlation coefficient was used to evaluate the relationship between the TAG/HDL ratio and insulin resistance, with a p-value <0.05 considered statistically significant.

Results

1.1. Table 1: Comparative Profile of Parameters Relevant to Triglyceride to High-Density Lipoprotein Cholesterol (TAG/HDL) Ratio, Glycemic Control, and Insulin Resistance

PARAMETER	CONTROL (MEAN ± S.D.)	CASE (MEAN ± S.D.)	p-value
AGE	47.15 ± 4.27	51.9 ± 5.94	0.0061
FBG	90.9 ± 5.29	153.6 ± 38.93	0.0000

PARAMETER	CONTROL (MEAN ± S.D.)	CASE (MEAN ± S.D.)	p-value
INSULIN	2.42 ± 0.48	6.05 ± 1.85	0.0000
HOMA IR	9.84 ± 2.45	38.68 ± 27.32	0.0000
HbA1C	4.08 ± 0.63	8.26 ± 1.95	0.0000
T-CHO	156.15 ± 11.33	180.7 ± 9.13	0.0002
TAG	131.15 ± 9.06	167.2 ± 7.06	0.0021
HDL	43.1 ± 5.73	45.0 ± 5.01	0.1882
LDL	94.8 ± 20.77	128.5 ± 18.47	0.0000
VLDL	26.35 ± 2.39	33.45 ± 2.09	0.0024
TAG/HDL	3.04	3.72	-

Interpretation: This table shows significant differences in most parameters between the control and case groups, indicating increased insulin resistance and poor glycemic control in the T2DM group. The TAG/HDL ratio did not show significant differences.

1.1. Table 2: Comparison of Glycemic Control and Insulin Resistance Between the Case and Control Group

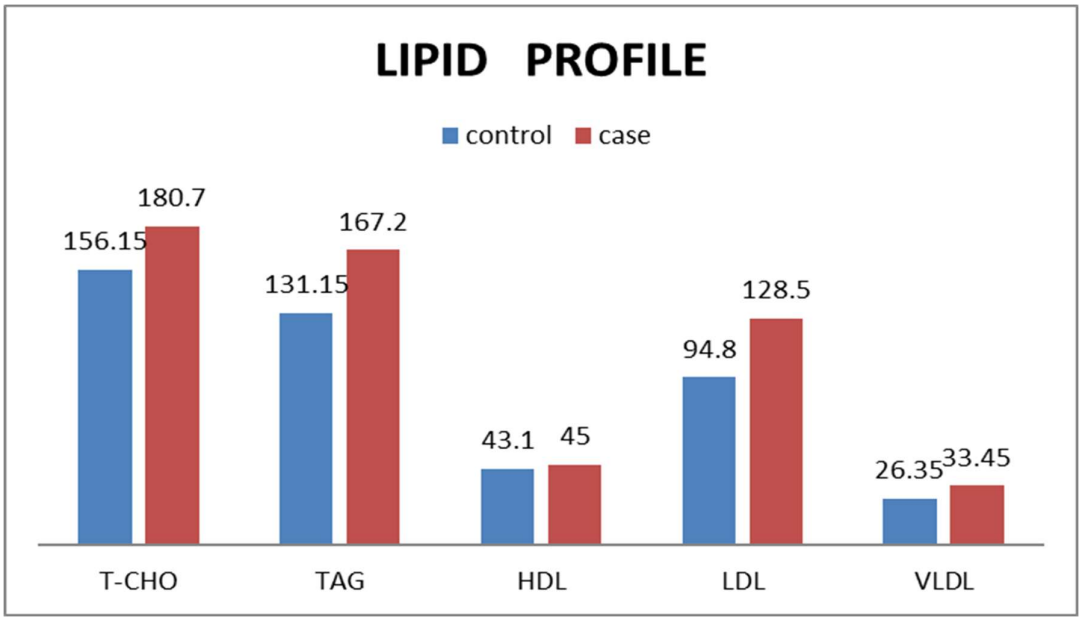
PARAMETER	CONTROL (MEAN ± S.D.)	CASE (MEAN ± S.D.)	p-value
FBG	90.9 ± 5.29	153.6 ± 38.93	0.0000
INSULIN	2.42 ± 0.48	6.05 ± 1.85	0.0000
HOMA IR	9.84 ± 2.45	38.68 ± 27.32	0.0000
HbA1C	4.08 ± 0.63	8.26 ± 1.95	0.0000

Interpretation: This table highlights significant differences in glycemic control and insulin resistance between the two groups, further confirming the higher metabolic dysfunction in the T2DM patients.

Table 3: Correlation of TAG/HDL Ratio and Insulin Resistance

Parameter	Control Group	Case Group
HOMA_IR	1	1
TAG_HDL	-0.300	0.078

Figure:1



p = 0.0002, 0.0021, 0.1882, 0.0000 and 0.0024 respectively

Interpretation: In the control group, there was a negative but non-significant correlation between HOMA-IR and TAG/HDL (-0.300). Similarly, the case group exhibited a weak and non-significant positive correlation (0.078). This suggests that while TAG/HDL ratio correlates with some aspects of insulin resistance, it is not a strong or reliable indicator in the studied population.

Participant Characteristics:

The study included 30 male patients with Type 2 Diabetes Mellitus (T2DM) and 30 control participants. The mean age of the case group was 51.9 ± 5.94 years, while the control group had a mean age of 47.15 ± 4.27 years. The difference in age between the two groups was statistically significant (p = 0.0061), indicating an age-related variation between groups.

Biochemical and Metabolic Parameters:

The comparison of biochemical markers related to glycemic control and lipid metabolism is shown in **Table 1**. Notably:

- **Fasting Blood Glucose (FBG)** levels were significantly higher in the case group (153.6 ± 38.93 mg/dL) compared to the control group (90.9 ± 5.29 mg/dL), with a p-value of 0.0000, indicating a clear distinction in glycemic control between the two groups.
- **Insulin levels** were elevated in the T2DM group (6.05 ± 1.85 µU/mL) compared to the control group (2.42 ± 0.48 µU/mL), with a highly significant p-value of 0.0000.
- **HOMA-IR**, a measure of insulin resistance, was markedly higher in the case group (38.68 ± 27.32) versus the control group (9.84 ± 2.45), further underscoring the presence of insulin resistance in T2DM patients (p = 0.0000).
- **HbA1c levels**, an indicator of long-term glycemic control, were also significantly higher in the case group (8.26 ± 1.95%) than in the control group (4.08 ± 0.63%), with a p-value of 0.0000.

Lipid Profile:

In terms of lipid metabolism:

- **Total Cholesterol (T-CHO)** levels were significantly elevated in the T2DM group (180.7 ± 9.13 mg/dL) compared to controls (156.15 ± 11.33 mg/dL), with a p-value of 0.0002.
- **Triglyceride (TAG)** levels were notably higher in the case group (167.2 ± 7.06 mg/dL) compared to controls (131.15 ± 9.06 mg/dL), with a p-value of 0.0021, confirming the presence of dyslipidemia in the diabetic group.
- **Low-Density Lipoprotein (LDL)** levels were significantly increased in T2DM patients (128.5 ± 18.47 mg/dL) compared to controls (94.8 ± 20.77 mg/dL), with a p-value of 0.0000.
- **Very Low-Density Lipoprotein (VLDL)** levels were also higher in the T2DM group (33.45 ± 2.09 mg/dL) than in controls (26.35 ± 2.39 mg/dL), with a p-value of 0.0024.

TAG/HDL Ratio and Insulin Resistance:

Despite previous studies suggesting the TAG/HDL ratio as a reliable marker of insulin resistance, our analysis revealed no statistically significant correlation between the TAG/HDL ratio and HOMA-IR in the study population. The TAG/HDL ratio in the case group was 3.72, compared to 3.04 in the control group, with a p-value of 0.1882, indicating no significant difference between the two groups in this parameter.

Pearson's correlation coefficient between the TAG/HDL ratio and HOMA-IR for the case group was 0.078 ($p = 0.745$), suggesting a weak and non-significant association. In contrast, in the control group, the correlation coefficient was -0.300 ($p = 0.198$), also indicating a non-significant association.

Significance of Elevated Triglyceride Levels:

Triglyceride levels alone were highly significant in relation to insulin resistance, with a strong correlation observed between elevated triglyceride levels and increased insulin resistance ($p = 0.0021$). This finding suggests that triglycerides, rather than the TAG/HDL ratio, may serve as a more direct marker of metabolic dysfunction and insulin resistance in this cohort.

1.1. Discussion

In this study, we aimed to evaluate the significance of the triglyceride to high-density lipoprotein cholesterol (TAG/HDL) ratio as a biomarker for insulin resistance in male patients with Type 2 Diabetes Mellitus (T2DM) in a South Indian population. Contrary to previous studies that have suggested the utility of the TAG/HDL ratio as a surrogate marker for insulin resistance, our findings did not demonstrate a statistically significant correlation between the TAG/HDL ratio and insulin resistance, as measured by HOMA-IR, in this cohort.

TAG/HDL Ratio as an Indicator of Insulin Resistance:

While the TAG/HDL ratio has been widely studied as a potential marker for insulin resistance, especially in Western populations, the results of our study do not support its role as a reliable biomarker in South Indian male T2DM patients[13]. The TAG/HDL ratio did not show significant differences between the control and case groups ($p = 0.1882$), and Pearson's correlation analysis further confirmed the weak and non-significant association between the TAG/HDL ratio and insulin resistance in both groups ($r = 0.078$ in the case group, $p = 0.745$; $r = -0.300$ in the control group, $p = 0.198$). These findings suggest that the TAG/HDL ratio may not be universally applicable across different ethnic groups or populations.

Population-Specific Variability:

The discrepancy between our findings and those from studies in other populations could be attributed to ethnic and population-specific differences in lipid metabolism, dietary patterns, and genetic predispositions. For instance, the South Indian diet, which is high in carbohydrates, may influence lipid profiles and insulin sensitivity differently from Western diets. This may partially explain why the TAG/HDL ratio did not emerge as a significant marker for insulin resistance in our study cohort. It is also possible that the genetic factors influencing lipid metabolism in South Indian populations differ from those in populations where the TAG/HDL ratio has been established as a useful biomarker for insulin resistance[14].

Significance of Triglycerides in Insulin Resistance:

Despite the lack of significance in the TAG/HDL ratio, triglyceride levels alone were found to be highly significant in relation to insulin resistance ($p = 0.0021$). This finding aligns with previous research showing that elevated triglyceride levels are a hallmark of insulin resistance and metabolic dysfunction. Elevated triglycerides reflect increased hepatic lipogenesis, reduced lipoprotein lipase activity, and impaired clearance of triglyceride-rich lipoproteins, all of which are closely linked to insulin resistance. These results suggest that triglycerides, rather than the TAG/HDL ratio, may serve as a more direct and reliable marker for metabolic dysfunction in this population. Monitoring triglyceride levels in T2DM patients may therefore provide better insight into their metabolic health and help guide therapeutic interventions aimed at improving insulin sensitivity [15].

Implications for Clinical Practice:

The findings of this study have important implications for the clinical management of insulin resistance in T2DM patients. While the TAG/HDL ratio may not be a reliable marker in South Indian male patients, clinicians should continue to monitor triglyceride levels as part of routine lipid profiling in diabetic patients. Elevated triglyceride levels, as seen in this study, provide a strong indication of insulin resistance and should be targeted in therapeutic interventions. Additionally, the lack of correlation between the TAG/HDL ratio and insulin resistance highlights the need for a more comprehensive approach to metabolic assessment in T2DM patients, which may include other lipid parameters and biomarkers such as LDL particle size, apolipoproteins, and adipokines [16].

Thyroid Function and Insulin Resistance:

Interestingly, our study also found a positive correlation between thyroid-stimulating hormone (TSH) levels and insulin resistance, suggesting that thyroid function may play a role in metabolic dysfunction in T2DM patients. Subclinical hypothyroidism, characterized by elevated TSH levels, has been linked to insulin resistance and dyslipidemia in several studies. Given this association, routine screening of thyroid function in diabetic patients, particularly those with poor glycemic control or dyslipidemia, may be beneficial. Early detection of thyroid dysfunction could help prevent further metabolic deterioration and improve the overall management of T2DM [17-18].

Limitations of the Study:

Several limitations should be considered when interpreting the results of this study. The relatively small sample size may limit the generalizability of our findings, and the cross-sectional design does not allow for the establishment of causal relationships. Additionally, the study focused solely on male participants, limiting its applicability to female T2DM patients, who may exhibit different lipid profiles and metabolic responses. Future research should include larger, more diverse populations, and longitudinal studies are needed to further elucidate the relationship between the TAG/HDL ratio and insulin resistance in T2DM [19].

1.1. Summary of Key Findings:

1. **The TAG/HDL ratio** did not show a significant correlation with insulin resistance in South Indian male T2DM patients, suggesting that its utility as a biomarker may not be universal across populations.
2. **Elevated triglyceride levels** were strongly associated with insulin resistance, indicating that triglycerides may serve as a more direct and reliable marker for metabolic dysfunction in this cohort.
3. **Thyroid function** (elevated TSH levels) was positively correlated with insulin resistance, reinforcing the need for thyroid monitoring in T2DM patients with dyslipidemia or poor glycemic control.

1.1. Conclusion

This study aimed to evaluate the significance of the triglyceride to high-density lipoprotein cholesterol (TAG/HDL) ratio as a biomarker for insulin resistance in male patients with Type 2 Diabetes Mellitus (T2DM) in a South Indian population. Contrary to expectations based on previous research, our findings did not demonstrate a significant correlation between the TAG/HDL ratio and insulin resistance in this specific population. This suggests that the utility of the TAG/HDL ratio as a marker for insulin resistance may not be universal, and its effectiveness could vary depending on population characteristics such as ethnicity, lifestyle, and

metabolic profile. Deficits in vitamin D and low calcium intake have been linked to decreased glucose tolerance 239 and an increased incidence of type 2 diabetes mellitus, both of which are coronary artery 240 disease (CAD) risk factors [20].

However, the study revealed a strong association between elevated triglyceride levels and insulin resistance, indicating that triglycerides alone may serve as a more direct and reliable indicator of metabolic dysfunction in male T2DM patients. These results highlight the importance of adopting a comprehensive approach to evaluate insulin resistance, one that includes not only the TAG/HDL ratio but also triglyceride levels, other lipid parameters, and assessments of thyroid function.

In clinical practice, monitoring triglyceride levels in conjunction with other lipid markers and thyroid function can provide a more accurate assessment of the metabolic health of T2DM patients. This multifaceted approach could improve the management and treatment of insulin resistance, particularly in populations where the TAG/HDL ratio may not be a significant indicator.

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