



A comparative study on fasting insulin and gamma-glutamyl transferase (GGT) levels as biomarkers in metabolic syndrome

Dr. Sen Sebin Kurian¹, Dr. Nazeer Ahamad², Dr. Himakara³

¹ Department of General Medicine, KVG Medical College & Hospital, Sullia, Karnataka, India

² Professor, Department of General Medicine, KVG Medical College & Hospital, Sullia, Karnataka, India

³ Assistant Professor, Department of General Medicine, KVG Medical College & Hospital, Sullia, Karnataka, India

Abstract

Background: Metabolic syndrome (MetS) is a constellation of metabolic abnormalities that significantly increases the risk of type 2 diabetes mellitus and cardiovascular disease. Insulin resistance plays a central role in its pathogenesis. While fasting insulin is traditionally used as a surrogate marker of insulin resistance, Gamma-Glutamyl Transferase (GGT), an enzyme associated with oxidative stress and hepatic steatosis, has recently emerged as a potential biomarker.

Objectives: To evaluate and compare fasting insulin and serum GGT levels as biomarkers in metabolic syndrome.

Methods: A cross-sectional study was conducted among 80 subjects diagnosed with metabolic syndrome at K.V.G. Medical College & Hospital, Sullia, over one year (August 2023–August 2024). Diagnosis was made according to the criteria proposed by the International Diabetes Federation. Fasting insulin and GGT levels were measured and correlated with metabolic syndrome components using Pearson's correlation coefficient.

Results: Fasting insulin showed strong positive correlations with waist circumference ($r=0.65$), triglycerides ($r=0.55$), and blood pressure ($r=0.48$), and a negative correlation with HDL cholesterol ($r=-0.60$). GGT demonstrated significant positive correlations with waist circumference ($r=0.55$), triglycerides ($r=0.57$), blood pressure ($r=0.57$), and a negative correlation with HDL cholesterol ($r=-0.45$). Both biomarkers correlated strongly with overall metabolic syndrome severity.

Conclusion: Both fasting insulin and GGT are significantly associated with metabolic syndrome components, suggesting their potential utility as diagnostic and risk-stratification biomarkers.

Keywords: Metabolic syndrome, insulin resistance, fasting insulin, gamma-glutamyl transferase (GGT), oxidative stress, hepatic steatosis

Introduction

Metabolic syndrome has emerged as one of the most significant public health challenges of the 21st century. It represents a cluster of interconnected metabolic abnormalities that collectively increase the risk of cardiovascular morbidity and mortality. These abnormalities include central obesity, hypertriglyceridemia, low HDL cholesterol levels, elevated blood pressure, and impaired fasting glucose. The International Diabetes Federation established a globally accepted definition of metabolic syndrome, emphasizing central obesity as a mandatory criterion along with at least two additional metabolic derangements. In the Indian population, lower waist circumference cut-offs (≥ 90 cm in men and ≥ 80 cm in women) reflect the increased cardiometabolic risk at lower body mass indices.

The pathophysiological basis of metabolic syndrome revolves around insulin resistance, a concept first articulated comprehensively by Gerald M. Reaven in 1988 [3]. Insulin resistance results in impaired glucose uptake in peripheral tissues, increased hepatic gluconeogenesis, compensatory hyperinsulinemia, and dysregulated lipid metabolism. Fasting insulin levels are commonly used as a surrogate marker of insulin resistance. Elevated fasting insulin indicates compensatory hyperinsulinemia in response to decreased insulin sensitivity. However, fasting insulin measurement is not routinely performed in all healthcare settings.

Gamma-Glutamyl Transferase (GGT) is an enzyme involved in glutathione metabolism and cellular antioxidant

defense. Traditionally regarded as a marker of hepatobiliary disease and alcohol consumption, GGT has gained recognition as an indicator of oxidative stress and metabolic dysfunction. Elevated GGT levels have been associated with non-alcoholic fatty liver disease, insulin resistance, type 2 diabetes mellitus, and cardiovascular disease.

Given the rising prevalence of metabolic syndrome in India, identifying simple, cost-effective, and reliable biomarkers is crucial for early detection and intervention. This study aims to compare fasting insulin and GGT levels in patients with metabolic syndrome and evaluate their correlation with individual metabolic components.

Objectives

1. To evaluate fasting insulin as a diagnostic marker in metabolic syndrome.
2. To assess the diagnostic potential of serum GGT levels.
3. To compare correlations of fasting insulin and GGT with individual components of metabolic syndrome.

Materials and Methods

Study Design: Cross-sectional observational study.

Study Setting: Department of General Medicine, K.V.G. Medical College & Hospital, Sullia, Karnataka.

Study Duration: August 2023 to August 2024.

Sample Size: 80 patients diagnosed with metabolic syndrome.

Inclusion Criteria

- Adults ≥ 18 years

- Diagnosed with metabolic syndrome according to IDF criteria

Exclusion Criteria

- Chronic liver disease
- Alcohol dependence
- Acute infection
- Endocrine disorders affecting insulin metabolism
- Patients receiving hepatotoxic medications

Data Collection Procedure

After obtaining informed consent, participants underwent detailed history taking and clinical examination. Anthropometric measurements including waist circumference and blood pressure were recorded using standardized techniques.

Fasting venous blood samples were collected after an overnight fast of 8–10 hours. Laboratory investigations included:

- Fasting plasma glucose
- Serum triglycerides
- HDL cholesterol
- Fasting insulin
- Serum GGT

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean \pm standard deviation. Pearson's correlation coefficient (r) was used to determine the relationship between biomarkers and metabolic syndrome components. A p -value <0.05 was considered statistically significant.

Results

Among the 80 participants, central obesity was highly prevalent, reflecting the diagnostic emphasis placed by IDF criteria. A substantial proportion of subjects also exhibited hypertriglyceridemia, reduced HDL cholesterol, elevated blood pressure, and impaired fasting glucose.

Correlation of Fasting Insulin

Fasting insulin demonstrated strong positive correlations with:

- Waist circumference ($r = 0.65$)
- Triglycerides ($r = 0.55$)
- Blood pressure ($r = 0.48$)

It showed a strong negative correlation with HDL cholesterol ($r = -0.60$).

These findings indicate that increasing insulin resistance parallels worsening dyslipidemia and central adiposity.

Correlation of GGT

Serum GGT levels demonstrated:

- Positive correlation with waist circumference ($r = 0.55$)
- Positive correlation with triglycerides ($r = 0.57$)
- Positive correlation with blood pressure ($r = 0.57$)
- Negative correlation with HDL cholesterol ($r = -0.45$)
- GGT also showed significant correlation with metabolic syndrome severity score ($r = 0.59$).

Comparative Findings

Fasting insulin exhibited slightly stronger correlations overall compared to GGT. However, both biomarkers

demonstrated statistically significant associations with metabolic syndrome components.

Discussion

This study highlights the strong association between fasting insulin levels and metabolic syndrome components, reaffirming the central role of insulin resistance in disease pathogenesis. Hyperinsulinemia promotes hepatic very-low-density lipoprotein (VLDL) production, contributing to hypertriglyceridemia, while also reducing HDL cholesterol levels.

The findings are consistent with the original insulin resistance hypothesis proposed by Gerald M. Reaven. Elevated fasting insulin serves as a direct indicator of compensatory response to reduced insulin sensitivity.

Serum GGT, though traditionally linked to liver pathology, has emerged as a marker of oxidative stress. Increased oxidative stress contributes to endothelial dysfunction, inflammation, and lipid peroxidation—key mechanisms underlying metabolic syndrome and cardiovascular disease.

The positive correlation between GGT and metabolic components may reflect underlying hepatic steatosis and systemic oxidative stress. Non-alcoholic fatty liver disease, often considered the hepatic manifestation of metabolic syndrome, may mediate this relationship. Although fasting insulin showed slightly stronger correlations, GGT offers several practical advantages:

- Widely available
- Cost-effective
- Routinely measured in biochemical panels
- No requirement for specialized assays

Thus, GGT may serve as a pragmatic screening tool, especially in resource-limited settings.

Limitations

- Small sample size
- Single-center study
- Cross-sectional design (no causal inference)
- Absence of longitudinal follow-up

Future multicentric prospective studies are warranted to validate these findings and explore predictive value for cardiovascular outcomes.

Conclusion

The present study demonstrates that both fasting insulin and serum GGT levels are significantly associated with metabolic syndrome components. Fasting insulin remains a robust marker of insulin resistance, while GGT represents a promising, cost-effective biomarker reflecting oxidative stress and hepatic involvement.

Early identification of metabolic syndrome using accessible biomarkers can facilitate timely lifestyle modification and pharmacological intervention, thereby reducing the burden of diabetes and cardiovascular disease in the Indian population.

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