Section: General Medicine

Original Research Article

SERUM GAMMA GLUTAMYL TRANSFERASE (GGT) LEVEL IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS PATIENTS AND ITS CORRELATION WITH HbA1C LEVEL

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ABSTRACT

Background: Gamma-glutamyl transferase (GGT), traditionally used as a marker of hepatobiliary disease, has recently been recognized as an indicator of oxidative stress and metabolic dysfunction. Elevated serum GGT has been associated with insulin resistance and type 2 diabetes mellitus (T2DM). This study evaluated serum GGT levels and their correlation with glycated haemoglobin (HbA1c) in newly diagnosed patients with T2DM. **Materials and Methods:** This hospital-based cross-sectional observational study with prospective patient recruitment included 100 consecutive adults with newly diagnosed T2DM attending a tertiary care hospital over six months. Serum GGT, fasting blood sugar (FBS), postprandial blood sugar (PPBS), and HbA1c were measured using standard laboratory methods. Patients were categorized into GGT <40 U/L and ≥40 U/L groups. Comparisons were performed using the independent samples t-test, and Pearson's correlation coefficient was used to assess associations between GGT and glycaemic parameters. **Result:** The mean age of participants was 52.27 ± 9.29 years, and 79% were males. Mean serum GGT and HbA1c levels were 40.17 ± 13.03 U/L and 7.98 ± 1.55%, respectively. Patients with GGT ≥40 U/L had significantly higher HbA1c (9.13 ± 1.44% vs. 6.96 ± 0.71%), FBS (278.77 ± 77.59 vs. 191.74 ± 42.75 mg/dL), and PPBS (395.38 ± 117.60 vs. 274.06 ± 47.41 mg/dL) than those with GGT <40 U/L (all p<0.001). Serum GGT showed strong positive correlations with HbA1c (r=0.830), FBS (r=0.721), and PPBS (r=0.719) (all p<0.001). **Conclusion:** Serum GGT was significantly associated with HbA1c, fasting blood glucose, and postprandial blood glucose in newly diagnosed T2DM. As an inexpensive and widely available test, serum GGT may serve as a useful adjunctive biomarker for identifying patients with poorer glycaemic control and greater metabolic dysfunction at diagnosis.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the fastest-growing public health problems worldwide. According to the 11th edition of the IDF Diabetes Atlas, an estimated 11.11% of adults worldwide were living with diabetes in 2024, and this is projected to increase to 12.96% by 2050.[1] India reflects this growing trend, with the recent ICMR-INDIAB-17 national survey reporting an overall weighted diabetes prevalence of 11.4% among Indian adults.[2] T2DM is diagnosed using the American Diabetes Association criteria and is often detected only after a prolonged period of asymptomatic hyperglycaemia, during which significant metabolic abnormalities may already be present.[3]

Glycated haemoglobin (HbA1c) is the established marker for assessing long-term glycaemic control. However, identifying additional inexpensive and readily available biochemical markers at the time of diagnosis that reflect broader metabolic risk remains clinically important.[4]

Serum gamma-glutamyl transferase (GGT), traditionally used as a marker of hepatobiliary disease and alcohol intake, has recently gained attention as a marker of oxidative stress and metabolic dysfunction, even in the absence of overt liver disease. Epidemiological studies have shown that serum GGT, including levels within the normal range, may serve as an early indicator of oxidative stress.4 A large prospective study involving 132,377 non-diabetic adults followed for an average of 5.8 years

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found that elevated GGT, along with alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase, was independently associated with the development of type 2 diabetes.[5] Similar findings have been reported by the Insulin Resistance Atherosclerosis Study, the British Women's Heart and Health Study, and other long-term cohort studies, all of which demonstrated that elevated serum GGT is associated with an increased risk of developing T2DM.[6-9]

GGT is a cell-surface enzyme involved in glutathione metabolism, an essential component of cellular antioxidant defence.[10] Chronic hyperglycaemia and hepatic insulin resistance increase oxidative stress and glutathione turnover, leading to elevated circulating GGT levels. Therefore, increased GGT is considered a marker of oxidative and metabolic stress rather than hepatocellular injury alone. However, whether GGT plays a direct causal role in the development of diabetes or simply reflects underlying metabolic dysfunction remains under investigation.[11-12]

Given its low cost, wide availability, and consistent association with metabolic dysfunction, serum GGT may serve as a useful adjunctive biomarker in patients with newly diagnosed T2DM. Therefore, this study was undertaken to evaluate serum GGT levels and their correlation with HbA1c in newly diagnosed T2DM patients.

Aim: The primary aim of my study is to evaluate the serum values of gamma-glutamyl transferase and the correlation with the HbA1C in newly diagnosed type 2 diabetes mellitus patients.

MATERIALS AND METHODS

This hospital-based cross-sectional observational study with prospective patient recruitment was conducted in the Department of General Medicine, Government Rajaji Hospital, Madurai Medical College, Madurai, Tamil Nadu, India, over a period of six months. The study was undertaken after obtaining approval from the Institutional Ethics Committee, and written informed consent was obtained from all participants before enrolment.

Study Population and Sampling: A total of 100 consecutive patients with newly diagnosed T2DM who attended the Department of General Medicine during the study period and fulfilled the eligibility criteria were included in the study. Patients were enrolled consecutively as they presented during the study period using a convenience sampling method.

Inclusion Criteria

Patients with newly diagnosed T2DM were included in the study.

Exclusion Criteria

Patients with a history of chronic smoking or alcohol consumption were excluded. Patients with comorbid conditions including chronic liver disease, renal disease, cardiac disease, or chronic lung disease were excluded. Patients with thyroid disorders, pregnant women, individuals receiving warfarin therapy, patients with anaemia, and those with a history of splenectomy were also excluded from the study.

Methods: After obtaining informed consent, all eligible participants underwent detailed clinical evaluation, including history taking and physical examination. Demographic details and relevant clinical information were recorded using a structured proforma.

Venous blood samples were collected after an overnight fast for fasting blood glucose and other biochemical investigations. A second venous blood sample was collected 2 hours after a regular meal for estimation of postprandial blood glucose (PPBS). Laboratory investigations included complete blood count, including serum GGT, fasting blood glucose (FBS), PPBS, and HbA1c. All biochemical analyses were performed in the Central Biochemistry Laboratory of the institution using standard laboratory protocols and quality control procedures.

The diagnosis of T2DM was established according to the American Diabetes Association (ADA) diagnostic criteria. Serum GGT levels were measured as part of the liver function test panel, and HbA1c was estimated to assess long-term glycaemic control. The relationship between serum GGT levels and HbA1c was subsequently analysed. For comparison analyses, participants were categorized into two groups using a serum GGT cutoff of 40 U/L, corresponding to the upper limit of the laboratory reference range used in our institution.

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± SD and categorical variables as frequencies and percentages. Comparisons between GGT groups (<40 U/L and ≥40 U/L) were performed using the independent samples t-test. Pearson's correlation coefficient (r) was used to assess the relationship between serum GGT and FBS, PPBS, and HbA1c. A two-tailed p value <0.05 was considered statistically significant.

RESULTS

The mean age of the participants was 52.27 ± 9.29 years, and 79 (79%) were male. The mean serum GGT level was 40.17 ± 13.03 U/L, while the mean HbA1c level was 7.98 ± 1.55% [Table 1].

Table 1: Baseline demographic and biochemical characteristics of the study population (N = 100)

Variable	Value
Age (years), mean ± SD	52.27 ± 9.29
Male, n (%)	79 (79%)
Female, n (%)	21 (21%)

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Serum GGT (U/L), mean ± SD	40.17 ± 13.03
HbA1c (%), mean ± SD	7.98 ± 1.55

Among the study participants, 53 had serum GGT levels <40 U/L, whereas 47 had serum GGT levels ≥40 U/L. The mean HbA1c was 6.96 ± 0.71% in patients with GGT <40 U/L and 9.13 ± 1.44% in those with GGT ≥40 U/L ($p < 0.001$). The mean FBS was 191.74 ± 42.75 mg/dL and 278.77 ± 77.59 mg/dL in the two groups, ($p < 0.001$). The mean PPBS was 274.06 ± 47.41 mg/dL in patients with GGT <40 U/L and 395.38 ± 117.60 mg/dL in patients with GGT ≥40 U/L ($p < 0.001$). There was no significant difference in age between the two groups ($p = 0.573$) [Table 2].

Table 2: Comparison of glycaemic parameters according to serum GGT levels

Variable	GGT <40 U/L (n = 53)	GGT ≥40 U/L (n = 47)	p value
Age (years)	52.47 ± 9.07	52.04 ± 9.63	0.573
FBS (mg/dL)	191.74 ± 42.75	278.77 ± 77.59	<0.001
PPBS (mg/dL)	274.06 ± 47.41	395.38 ± 117.60	<0.001
HbA1c (%)	6.96 ± 0.71	9.13 ± 1.44	<0.001

Correlation analysis demonstrated a significant positive correlation between serum GGT and HbA1c levels ($r = 0.830$, $p < 0.001$). Serum GGT also showed significant positive correlations with FBS ($r = 0.721$, $p < 0.001$) and postprandial blood sugar ($r = 0.719$, $p < 0.001$) [Table 3]. The correlation between serum GGT and HbA1c is shown in [Figure 1].

Table 3: Correlation of serum GGT with glycaemic parameters

Variable	Correlation coefficient (r)	p value
FBS	0.721	<0.001
PPBS	0.719	<0.001
HbA1c	0.83	<0.001

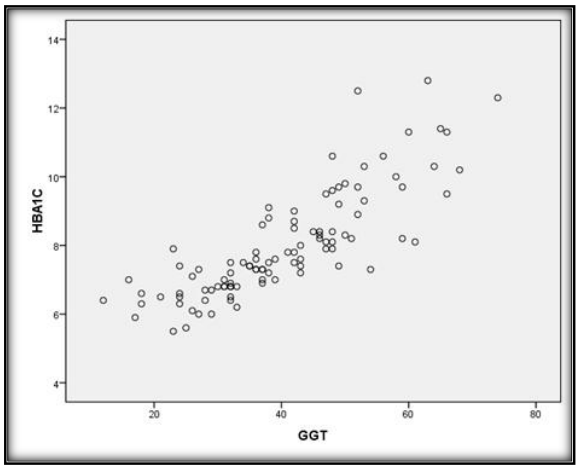

Figure 1: Scatter plot showing the correlation between serum GGT and HbA1c levels in newly diagnosed patients with T2DM.

DISCUSSION

The study population was predominantly middle-aged with a male preponderance, a demographic profile commonly reported among patients with newly diagnosed T2DM. Similarly, Sathvika et al. studied 93 patients with T2DM and reported a mean age of 59.34 ± 10.7 years, with 67.7% being males.[13] The similarity in demographic characteristics indicates that our study population is comparable with other hospital-based cohorts.

In the present study, serum GGT was elevated in patients with newly diagnosed T2DM and showed a close relationship with glycaemic status. Sathvika et al. reported a mean GGT of 41.51 ± 24.8 and a mean HbA1c of 7.83 ± 1.59, findings comparable to those reported in diabetic populations.13 Similarly, Payal et al., in a study of 122 participants, reported progressively increasing mean GGT levels across non-diabetic, prediabetic and diabetic groups (16.6 ± 8.59, 24.64 ± 11.6 and 29.5 ± 11.6, $p < 0.001$), suggesting that GGT elevation may occur before overt hyperglycaemia and represent an early metabolic alteration.[14]

Patients with higher serum GGT levels had poorer glycaemic status than those with lower GGT levels. Pangajam et al. reported that mean serum GGT increased from 20.16 ± 8.37 in healthy individuals to 24.97 ± 14.62 in patients with T2DM without metabolic syndrome and 52.58 ± 48.10 in patients with both T2DM and metabolic syndrome ($p < 0.001$).[15] These observations show that serum GGT increases progressively across the spectrum of metabolic dysfunction rather than hyperglycaemia alone.

In our study, a strong positive relationship was observed between serum GGT and HbA1c. Sathvika et al. reported a correlation coefficient of r = 0.900.13 Hassan et al. reported a similar correlation (r = 0.838) in a study involving 300 participants and also demonstrated that mean serum GGT increased from 34.27 ± 15.07 in patients with HbA1c between 6.5% and 7% to 47.08 ± 20.56 in those with HbA1c above 7%.[16] Kunutsor et al., reported individuals in the highest third of baseline GGT had a 34% higher risk of developing T2DM than those in the lowest third (RR 1.34; 95% CI: 1.27–1.42).[17] These findings consistently indicate that serum GGT increases with worsening long-term glycaemic control.

Although published studies demonstrates a positive association between GGT and glycaemic status,

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whether this relationship is causal remains uncertain. Bi et al. observed that GGT was significantly associated with fasting plasma glucose and HbA1c. However, their Mendelian randomization analysis found no evidence of a linear causal relationship between genetically determined GGT and T2DM.[18] These findings suggest that elevated GGT reflect underlying metabolic dysfunction and oxidative stress than act as a direct causal factor, while still supporting its value as a marker of glycaemic status.

In our study, serum GGT also showed a positive relationship with fasting and PPBS. Teng et al. reported participants with higher baseline GGT experienced a greater annual increase in fasting blood glucose throughout follow-up, and repeated-measures analysis demonstrated a significant association between baseline GGT and increasing fasting blood glucose ($F = 8.78$, $p < 0.001$).[19] These longitudinal findings indicate that elevated GGT is associated not only with existing hyperglycaemia but also with progressive deterioration in glucose regulation.

GGT is a key enzyme in glutathione metabolism and antioxidant defence. Persistent hyperglycaemia increases oxidative stress and hepatic insulin resistance, leading to increased glutathione turnover and elevated circulating GGT levels. Thus, elevated GGT reflects oxidative and metabolic stress and may explain its positive association with glycaemic indices.[4,10]

The present findings support previous evidence that serum GGT is closely associated with glycaemic status in newly diagnosed T2DM. Given its routine availability in clinical practice, GGT may complement established glycaemic markers and warrants further evaluation in larger prospective studies to determine its role in risk stratification and metabolic assessment.

Limitations: This single-center cross-sectional study with a relatively small sample size may limit the generalizability of the findings. Because all variables were measured at a single point in time, temporal relationships and causality could not be established. Potential confounders such as body mass index, hepatic steatosis, alcohol intake, and non-alcoholic fatty liver disease were not systematically evaluated. Multivariable analysis was not performed; therefore, residual confounding by factors such as age and sex cannot be excluded. Larger prospective multicenter studies are needed to validate these findings.

CONCLUSION

Serum GGT levels were significantly associated with HbA1c, fasting blood glucose, and PPBS in newly diagnosed patients with T2DM. These findings suggest that serum GGT reflects underlying metabolic dysfunction and may serve as a simple, inexpensive adjunctive biomarker for assessing glycaemic status and identifying patients with poorer metabolic control at diagnosis.

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