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*Article*

# Correlation of Serum Gamma-Glutamyl Transferase Levels and The Risk of Developing Dm in Pregnancy

***Article History:***

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*Abstract*: ***Introduction***: The global burden of diabetes mellitus is rising at an alarming rate, with the World Health Organization (WHO) reporting an increase in prevalence among adults over the age of 18 from 4.7% in 1980 to 8.5% in 2014. This surge reflects the growing impact of lifestyle- related metabolic diseases across the world. AIM: To study the correlation of serum gamma- glutamyl transferase levels and the risk of developing gestational diabetes mellitus in pregnancy in north western Rajasthan. ***Methodology***: This hospital-based cross-sectional study was conducted in the Department of Obstetrics and Gynaecology at PBM Hospital, Bikaner, over a duration of one year. The study population included pregnant females with gestation up to 14 weeks who attended the OPD during the study period of 1yr from march 2024 to feb 2025. RESULT: This study found a low GDM prevalence (1.5%) compared to global data, with all GDM cases occurring in overweight/obese women and diagnosed between 12–14 weeks gestation. No significant associations were found with age or gravida, but early elevated GGT levels (>23 U/L) showed strong correlation with later GDM diagnosis (p = 0.0001). Mean GGT levels were significantly higher in GDM cases (41.33 IU/L vs. 16.90 IU/L). These findings support GGT and BMI as early predictive markers for GDM. ***Conclusion***: Elevated early pregnancy GGT levels and higher BMI are strong predictors of GDM, highlighting their utility in first-trimester screening. Early identification can enable timely interventions to reduce maternal and fetal complications.

***Keywords:*** Gestational diabetes mellitus, GGT levels, screening.

## INTRODUCTION

The global burden of diabetes mellitus is rising at an alarming rate, with the World Health Organization (WHO) reporting an increase in prevalence among adults over the age of 18 from 4.7% in 1980 to 8.5% in 2014[1]. This surge reflects the growing impact of lifestyle-related metabolic diseases across the world. India, in particular, faces a disproportionate share of this burden and is frequently referred to as the "diabetes capital of the world." According to the International Diabetes Federation, the number of individuals living with diabetes in India was estimated at 40.9 million in 2006, and this figure is projected to reach 69.9 million by 2025. [2] Among the various forms of diabetes, Gestational Diabetes Mellitus (GDM) has emerged as a significant public health issue. GDM is defined as glucose intolerance of varying severity that is first recognized during pregnancy. It is distinguished from overt diabetes diagnosed during pregnancy and is recognized by both the International Association of Diabetes and Pregnancy Study Groups (IADPSG) and WHO as a separate clinical entity. The pathophysiology of GDM is intricately linked to the normal hormonal changes of pregnancy, which include insulin resistance and compensatory hyperinsulinemia. While these changes are physiologically necessary to ensure adequate glucose availability for the growing fetus, they may lead to the development of GDM in women who are genetically predisposed or metabolically vulnerable. The prevalence of GDM varies widely across different populations[3], with South Asian populations, particularly Indians, showing markedly higher susceptibility. Reported prevalence rates in India range from as low as 1% to over 50%, depending on the diagnostic criteria used, the gestational age at screening, and the population under study. The recent adoption of the IADPSG criteria has

led to a 2–3-fold increase in GDM detection, as these guidelines employ lower threshold values for plasma glucose levels, thereby enhancing sensitivity. Early detection of GDM is critical as it is associated with multiple adverse maternal and fetal outcomes, including preeclampsia, macrosomia, shoulder dystocia, cesarean delivery,[4] neonatal hypoglycemia, and increased risk of developing type 2 diabetes mellitus in both mother and child later in life. Given the substantial implications for both short-term and long-term health, there is a growing emphasis on identifying high-risk women early in pregnancy to allow for prompt intervention. Recent scientific investigations have highlighted the potential utility of biochemical markers in predicting the risk of GDM, particularly those involved in hepatic function and oxidative stress pathways. One such promising marker is gamma-glutamyl transferase (GGT), a membrane-bound enzyme involved in glutathione metabolism and antioxidant defense. GGT is widely expressed in tissues such as the liver, kidney, and pancreas, and plays a key role in maintaining intracellular glutathione levels by catalyzing the breakdown and resynthesis of glutathione[5], a major antioxidant. Elevated GGT levels are thought to reflect increased oxidative stress and subtle liver dysfunction, both of which are implicated in the pathogenesis of insulin resistance. As insulin resistance is the central mechanism underlying GDM, a rise in GGT levels, even within the normal range, may serve as an early biochemical signal of developing metabolic disturbances in pregnancy. Furthermore, compared to other oxidative stress biomarkers like F2-isoprostanes or 8- hydroxy deoxyguanosine, GGT offers a more accessible and cost-effective alternative for large-scale screening, especially in resource-constrained settings such as many parts of India. During a normal pregnancy, physiological changes in liver enzyme levels, including GGT, are expected[6]. Typically, GGT levels tend to remain at the lower end of the reference range throughout gestation. However, recent studies suggest that even mild elevations in GGT—particularly in the first and second trimesters—could be predictive of GDM development. These findings reinforce the idea that GGT may not only serve as a marker of liver function but also reflect systemic metabolic and oxidative stress states that precede overt glucose intolerance. As such, incorporating GGT measurement into early antenatal screening protocols may improve risk stratification and allow for more personalized care in pregnant women. In India, where the background prevalence of type 2 diabetes and prediabetes is already high, universal screening for GDM is recommended[7]. The Diabetes in Pregnancy Study Group India (DIPSI) advocates for a single-step, non-fasting 75-gram oral glucose challenge test, with a 2-hour post-load plasma glucose level of ≥140 mg/dL considered diagnostic of GDM. This method is patient-friendly, does not require fasting, and can be conveniently administered in primary care settings. For confirmatory diagnosis or in research contexts, the IADPSG-recommended 75-gram oral glucose tolerance test (OGTT) is used, with specific cut- off values for fasting (≥92 mg/dL), 1-hour (≥180 mg/dL), and 2-hour (≥153 mg/dL) plasma glucose levels. The combination of these approaches ensures both ease of screening and diagnostic accuracy, helping to address the growing burden of GDM in the Indian population[3]. Collectively, these strategies underscore the importance of early and universal screening, along with the exploration of novel biomarkers such as GGT, to mitigate the impact of GDM on maternal and child health.

## AIM

To study the correlation of serum gamma-glutamyl transferase levels and the risk of developing gestational diabetes mellitus in pregnancy in north western Rajasthan.

## METHODOLOGY

This hospital-based cross-sectional study was conducted in the Department of Obstetrics and Gynecology at PBM Hospital, Bikaner, over a duration of one year. The study population included pregnant females with gestation up to 14 weeks who attended the OPD during the study period of 1yr from march 2024 to feb 2025. Women aged 18 years or older and willing to participate were included. Patients were excluded if they refused consent or had a history of chronic conditions such as diabetes mellitus, hypertension, renal, cardiac, liver diseases, connective tissue disorders, or alcohol abuse. Those on long-term medications like anticonvulsants or painkillers, and those lost to follow-up, were also excluded. A convenience sampling technique was used to select the study participants.

## RESULT

**Table 1: Distribution of cases according to age group**

| Age | GDM | No GDM | P value |
|---|---|---|---|

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| Group (Year) | No. | % | No. | % | 1.000 |
|---|---|---|---|---|---|
| <25 | 2 | 1.00 | 100 | 50.76 | |
| 25-29 | 1 | 0.50 | 71 | 36.04 | |
| 30-34 | 0 | 0.00 | 22 | 11.17 | |
| >34 | 0 | 0.00 | 4 | 2.03 | |
| Gravida | | | | | |
| Primi Gravida | 2 | 1.00 | 101 | 51.27 | 0.958 |
| Multigravida | 1 | 0.50 | 96 | 48.73 | |

In this study of 200 participants, GDM was diagnosed in only 3 cases (1.5%), with no significant association found between age and GDM (p = 1.000). Most cases occurred in women below 30 years, with 2 cases under 25 years and 1 case in the 25–29 age group. No GDM cases were reported in women aged 30 years and above. In this study of 200 participants, GDM was observed in 3 cases (1.5%), with 2 cases in primigravida and 1 in multigravida women. Among the non-GDM group, 101 were primigravida and 96 were multigravida. The minimal difference and a p-value of 0.958 indicate no significant association between gravida and GDM occurrence.

In this study, all 3 GDM cases (1.5%) were found in women at 12–14 weeks of gestation, with no cases in earlier gestational age groups. The majority of non-GDM participants were between 8–10 weeks. A p-value of 0.0001 shows a highly significant association between gestational age and GDM occurrence.

**Table 2: BMI and percentage of GDM cases**

| BMI ($Kg/m^2$) | No. of GDM Cases | %. of GDM Cases | No. of non GDM Cases | % of non GDM Cases | Total |
|---|---|---|---|---|---|
| <18.5 | 0 | 0.00 | 1 | 0.50 | 1 |
| 18.5-24.9 | 0 | 0.00 | 151 | 75.50 | 151 |
| 25-29.9 | 1 | 0.50 | 33 | 16.50 | 34 |
| 30-34.9 | 2 | 1.00 | 12 | 6.00 | 14 |
| >35 | 0 | 0.00 | 0 | 0.00 | 0 |
| Total | 3 | 1.50 | 197 | 98.50 | 200 |
| p value | 0.0001*** | | | | |

In this study, all 3 GDM cases (1.5%) occurred in women with higher BMI—1 case in the overweight group and 2 in the obese group. No GDM was observed in participants with normal or very high BMI. A statistically significant p-value of 0.0001 indicates a strong association between higher BMI and GDM risk.

**Table 3: Association between GGT at 6-14 weeks and 75gm Oral Glucose Challenge test by DIPSI method at 24-28 weeks**

| Oral Glucose Challenge Test at 24-28 weeks (DIPSI Criteria) | GGT at 6-14 weeks ≤ 23 | | GGT at 6-14 weeks >23 | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| ≤ 140 | 161 | 80.50 | 28 | 14.00 | 189 | 94.50 |
| > 140 | 4 | 2.00 | 7 | 3.50 | 11 | 5.50 |

 

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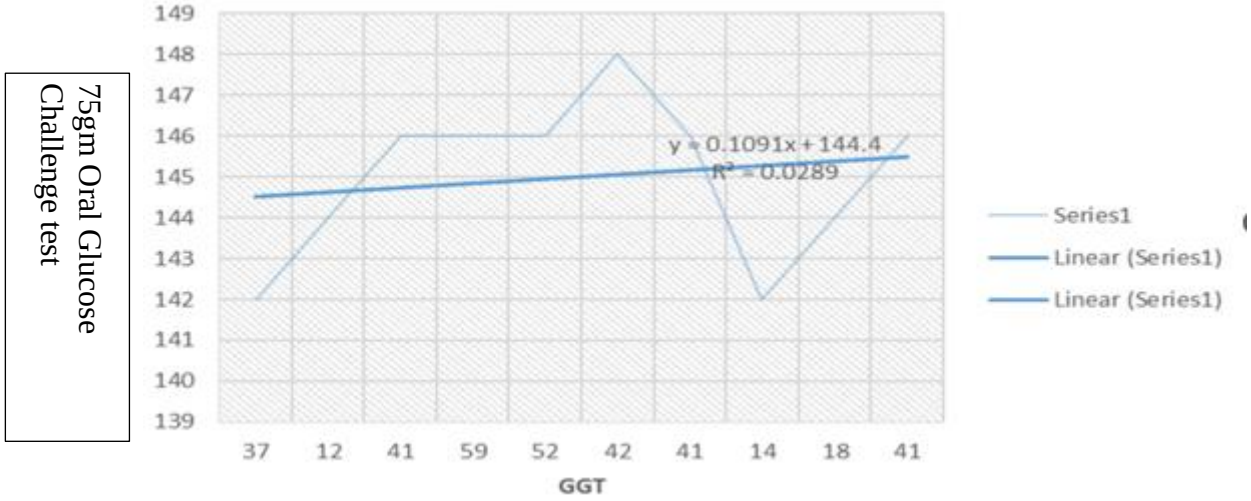
|---|---|---|---|---|---|---|
| Total | 165 | 82.50 | 35 | 17.50 | 200 | 100.00 |
| p value | 0.0001*** | | | | | |

This study demonstrated a significant association between elevated early pregnancy GGT levels and the later development of gestational diabetes mellitus (GDM). Among 35 women with GGT >23 U/L, 7 (3.5%) developed GDM, while only 4 (2%) out of 165 with GGT ≤23 U/L developed it. The results suggest that higher GGT levels in early pregnancy may be predictive of GDM. The association was statistically significant with a p-value of 0.0001.

**Fig: 1** Association between GGT at 6-14 weeks and 75gm Oral Glucose Challenge test




Above graph shows the association between 75gm Oral Glucose Challenge test by DIPSI method and GGT by linear regression curve. R squared indicates how well the model fits the data. In this graph a value of 0.0289 indicates that there is weak direct relationship between serum GGT and 75gm Oral Glucose Challenge test.

**Table 4: Distribution of cases according to Fasting 75g 2 hr OGTT according to IADPSG**

| Fasting 75g 2 hr OGTT according to IADPSG | Total | |
|---|---|---|
| | No. | % |
| Positive | 3 | 1.5 |
| Negative | 197 | 98.5 |
| Total | 200 | 100.00 |

In this study of 200 pregnant women, the fasting 75g 2-hour OGTT was conducted according to the IADPSG criteria. The results showed that 3 participants (1.5%) tested positive for gestational diabetes mellitus (GDM), while the remaining 197 participants (98.5%) had negative results. This indicates a low prevalence of GDM when screened using the IADPSG method in this cohort.

**Table 5: Relation between mean GGT and development of gestational diabetes mellitus**

| Presence of gestational Diabetes Mellitus | No of women | Mean GGT IU/L | SD | t value | p value |
|---|---|---|---|---|---|
| Gestational Diabetes Mellitus | 3 | 41.33 | 0.58 | 5.250 | 0.0001*** |
| Normal | 197 | 16.90 | 8.04 | | |

This study found that women who developed GDM had significantly higher mean GGT levels (41.33 IU/L) compared to those without GDM (16.90 IU/L). The difference was statistically highly significant (t = 5.250, p = 0.0001). These findings

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suggest that elevated GGT in early pregnancy may serve as a strong predictive marker for GDM.

## DISCUSSION

In our study conducted at a tertiary care center in Northwestern Rajasthan, the prevalence of GDM was relatively low—only 1.5% (3 out of 200 pregnant women). In contrast. In our study, the age distribution among GDM and non-GDM participants revealed no statistically significant association (p = 1.000). Most women with GDM were younger than 30 years, and there were no GDM cases among women over 30 years of age, which is somewhat contrary to norms as older age is often considered a risk factor for GDM. This result is inconsistent with several largescale cohort studies. For instance, Wu et al. (2023) in BMC Medicine demonstrated that women aged above 30 had a markedly higher risk of developing GDM, with a clear age-related trend in liver enzyme markers and glucose intolerance [8].

In our study, primigravida women showed a slightly higher GDM prevalence (1%) compared to multigravida women (0.5%), though this was not statistically significant (p = 0.958). This is contrary to findings by Sridhar et al. (2014), who demonstrated that multigravidas, especially those with prior GDM or adverse pregnancy outcomes, had an elevated risk [9]. Our observed that all GDM cases were diagnosed between 12–14 weeks gestation, indicating a statistically significant association (p = 0.0001). This supports the potential utility of early screening. Consistent with this, Kim et al. (2014) supported early biochemical screening (before 14 weeks) in high-risk women for timely intervention [10]. The analysis showed that all GDM cases occurred in overweight or obese women, with a strong statistical association (p = 0.0001). Song et al. (2022) also concluded that BMI is an independent predictor of GDM, regardless of other metabolic parameters [11]. Our data aligns robustly with these findings and emphasizes the role of pre-pregnancy weight management in preventing GDM. This study's most significant finding was the association between elevated GGT (>23 U/L) in early pregnancy and GDM development (75gm Oral Glucose Challenge Test by DIPSI method >140 mg/dL) later in pregnancy, with high statistical significance (p = 0.0001). Kong et al. (2018) found similar results, asserting that GGT levels in mid-pregnancy directly correlated with later GDM diagnosis[12]. Our analysis showed that mean GGT levels in GDM women were significantly higher (41.33 IU/L) than in non-GDM women (16.90 IU/L), with strong significance (p = 0.0001). Ghosh et al. (2015) similarly reported mean GGT values above 35 IU/L in GDM patients, demonstrating the enzyme's diagnostic relevance [13].

## CONCLUSION

The observational data from this study indicated that while demographic factors such as age and gravidity had no significant association with gestational diabetes mellitus (GDM), certain clinical and biochemical parameters were strongly correlated with its development. GDM was observed exclusively in women between 12–14 weeks of gestation, highlighting a critical window for early detection (p = 0.0001). A higher body mass index (BMI), particularly in overweight and obese women, was significantly associated with the occurrence of GDM (p = 0.0001), emphasizing the role of body weight as a modifiable risk factor. Additionally, elevated serum gamma-glutamyl transferase (GGT) levels (>23 U/L) in early pregnancy were significantly linked to GDM development later in gestation. Women with GGT levels ranging from 26.9–74 U/L had a GDM prevalence of 13.63%, whereas none with levels ≤26.8 U/L developed the condition. The mean GGT level in GDM-positive women was 41.33 IU/L, significantly higher than 16.90 IU/L in GDM-negative women. These findings suggest that both elevated early GGT and high BMI are reliable early predictors of GDM, supporting their use in first-trimester screening protocols for timely risk identification and intervention.

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