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SERUM GAMMA-GLUTAMYL TRANSFERASE AS A METABOLIC BIOMARKER OF GLYCAEMIC DYSREGULATION IN DIABETES MELLITUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Diabetes mellitus is a major global metabolic disorder associated with increasing morbidity and mortality. Identification of inexpensive and accessible biomarkers for early glycaemic dysregulation remains clinically important. Serum gamma-glutamyl transferase (GGT), traditionally considered a hepatic enzyme marker, has recently been linked with oxidative stress, insulin resistance, and metabolic dysfunction.

Objective: To systematically evaluate and analyse the association between serum GGT levels and glycaemic dysregulation in patients with diabetes, prediabetes, and impaired fasting glucose.

Methods: A systematic review and meta-analysis was performed according to PRISMA 2020 guidelines. Electronic databases including PubMed, Scopus, Embase, Web of Science, and Cochrane Library were searched from inception until March 2025. Observational studies evaluating serum GGT levels in adults with diabetes, impaired fasting glucose, or prediabetes were included. Data extraction and quality assessment using the Newcastle–Ottawa Scale (NOS) were independently performed by reviewers. Random-effects meta-analysis was used to estimate pooled standardized mean differences with 95% confidence intervals.

Results: Seventeen observational studies involving 61,189 participants met eligibility criteria for qualitative synthesis, while nine studies were included in quantitative meta-analysis. Pooled analysis demonstrated a significant association between elevated serum GGT levels and impaired glycaemic status. Considerable heterogeneity was observed among studies ($I^2 = 98.81\%$). Subgroup analysis suggested a stronger association among obese individuals and Asian populations. Funnel plot assessment indicated possible publication bias.

Conclusion: Elevated serum GGT levels are significantly associated with impaired glucose metabolism and diabetes risk. GGT may serve as an inexpensive and easily available biomarker for early metabolic risk stratification. Further large-scale longitudinal studies are needed to establish causality and standardise clinical application.

KEYWORDS: Gamma-glutamyl transferase, diabetes mellitus, impaired fasting glucose, oxidative stress, insulin resistance, biomarker, meta-analysis.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) is the most common form and contributes to nearly 90–95% of all diabetes cases worldwide. Rapid urbanization, sedentary lifestyle, obesity, and unhealthy dietary habits have significantly increased the global burden of diabetes over recent decades. Diabetes is associated with major long-term complications including cardiovascular disease, nephropathy, neuropathy, retinopathy, and increased mortality. Therefore, early identification of metabolic abnormalities and reliable biomarkers has become increasingly important in reducing disease burden and improving preventive strategies [1,2].

Oxidative stress and chronic low-grade inflammation play an important role in the development of insulin resistance and progression of T2DM. Persistent oxidative stress impairs insulin signalling pathways and contributes to pancreatic beta-cell dysfunction, thereby worsening glycaemic control [3]. In recent years, liver enzymes have gained attention as possible markers of metabolic dysfunction because of their close relationship with obesity, non-alcoholic fatty liver disease (NAFLD), insulin resistance, and metabolic syndrome [4].

Gamma-glutamyl transferase (GGT) is a membrane-bound enzyme involved in glutathione metabolism and maintenance of intracellular antioxidant defence systems. Traditionally, serum GGT has been used as a marker of hepatobiliary disease and alcohol intake. However, growing evidence suggests that elevated GGT levels may also reflect oxidative stress, systemic inflammation, endothelial dysfunction, and metabolic abnormalities associated with diabetes [5]. Increased GGT activity may indicate enhanced oxidative stress burden and depletion of antioxidant mechanisms, which can contribute to impaired glucose metabolism and insulin resistance [6].

Several epidemiological and cohort studies have demonstrated a significant association between elevated serum GGT levels and impaired fasting glucose, prediabetes, metabolic syndrome, and T2DM. Gao et al. reported that elevated liver enzyme concentrations were closely associated with prediabetes in the Shanghai Diabetes Study II [7]. Similarly, Nguyen et al. in the Bogalusa Heart Study observed that increased liver enzymes were predictive of future development of prediabetes and T2DM in younger adults [8]. Hong et al. demonstrated that obesity-associated impaired fasting glucose showed stronger association in individuals with higher serum GGT levels [9].

Wu et al. found that serum GGT and uric acid levels were significantly associated with impaired fasting glucose among adults in Inner Mongolia, China [10]. Qin et al. also observed a relationship between elevated liver enzymes and impaired fasting glucose in both males and females [11]. Longitudinal studies by Shin et al. and Yu et al. further showed that elevated serum GGT levels independently predicted future risk of impaired fasting glucose and diabetes mellitus [12,13]. Apart from glycaemic dysfunction, elevated GGT has also been linked with obesity, NAFLD, metabolic syndrome, unhealthy dietary habits, and systemic inflammation, all of which contribute to diabetes risk [14–17]. Hassan et al. recently demonstrated that serum GGT and C-reactive protein act as biomarkers of oxidative stress in patients with T2DM [18]. These findings support the role of GGT as an integrative marker reflecting both hepatic and metabolic dysfunction.

Despite increasing evidence, the magnitude and consistency of the association between serum GGT and glycaemic dysregulation remain variable across studies because of differences in study design, population characteristics, obesity prevalence, alcohol consumption, and laboratory methods used for GGT estimation. Therefore, a systematic review and meta-analysis was conducted to comprehensively evaluate the relationship between serum gamma-glutamyl transferase levels and impaired glycaemic status in diabetes mellitus and related metabolic conditions.

METHODOLOGY

Methods

Study Design and Reporting Guidelines

This systematic review and meta-analysis was conducted to evaluate the association between serum gamma-glutamyl transferase (GGT) levels and glycaemic dysregulation in patients with diabetes mellitus, prediabetes, and impaired fasting glucose. The review methodology was developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

Literature Search Strategy

A comprehensive electronic literature search was carried out using the following databases:

- PubMed
- Scopus
- Embase
- Web of Science
- Cochrane Library

The search included studies published from database inception until March 2025. Only studies published in the English language were considered.

The search strategy was developed using combinations of Medical Subject Headings (MeSH) terms and free-text keywords with Boolean operators (“AND”, “OR”). The commonly used search terms included:

- “Gamma-glutamyl transferase”
- “GGT”
- “Diabetes mellitus”
- “Type 2 diabetes mellitus”
- “Prediabetes”
- “Impaired fasting glucose”
- “Blood glucose”
- “Insulin resistance”
- “Liver enzymes”

An example of PubMed search strategy was:

(“Gamma-glutamyl transferase” OR “GGT”) AND (“Diabetes mellitus” OR “Type 2 diabetes mellitus” OR “Prediabetes” OR “Impaired fasting glucose”)

Reference lists of relevant original articles and review papers were also manually screened to identify additional eligible studies.

Eligibility Criteria

Inclusion Criteria

Studies were included if they fulfilled the following criteria:

- Studies involving adults aged 18 years and above.
- Observational studies including cohort, cross-sectional, and case-control designs.
- Studies evaluating serum GGT levels in patients with diabetes mellitus, prediabetes, or impaired fasting glucose.
- Studies reporting quantitative association between serum GGT and glycaemic parameters.
- Studies published in peer-reviewed journals.
- Studies published in English language.

Exclusion Criteria
The following studies were excluded:
- Case reports, conference abstracts, editorials, letters, and narrative reviews.
- Animal or experimental studies.
- Studies without extractable quantitative outcome data.
- Studies evaluating only pharmacological interventions without baseline association analysis.
- Duplicate publications.

Study Selection
All retrieved articles were imported into Microsoft Excel and duplicate studies were removed. Three reviewers independently screened titles and abstracts for eligibility. Full-text articles of potentially relevant studies were then assessed in detail according to inclusion and exclusion criteria. Any disagreement between reviewers was resolved through discussion and consensus.
The overall study selection process was summarized using a PRISMA flow diagram.

Data Extraction
Data extraction was independently performed by two reviewers using a predesigned Microsoft Excel sheet. The following variables were extracted from eligible studies:
- Name of first author
- Year of publication
- Country of study
- Study design
- Sample size
- Participant characteristics
- Mean serum GGT levels
- Glycaemic outcome measures
- Effect estimates
- Confounding variables adjusted during analysis

Any discrepancy in extracted data was resolved by discussion between reviewers.

Quality Assessment
Methodological quality of included observational studies was assessed using the Newcastle–Ottawa Scale (NOS). The NOS evaluates studies based on three domains:
- Selection of study groups
- Comparability of groups
- Outcome assessment

Studies scoring:
- <5 stars were considered low quality
- 5–7 stars were considered moderate quality
- ≥8 stars were considered high quality

Quality assessment was independently carried out by two reviewers.

Statistical Analysis
Meta-analysis was performed using Stata version 13 software. Pooled standardized mean differences (SMDs) with 95% confidence intervals (CI) were calculated using a random-effects model because significant clinical and methodological heterogeneity was anticipated among studies.
Heterogeneity among included studies was assessed using:
- Cochran's Q test
- I^2 statistic
- Tau^2 statistic

An I^2 value greater than 50% was considered suggestive of substantial heterogeneity.
Publication bias was evaluated by visual inspection of funnel plots and Egger's regression test wherever applicable.
Subgroup analyses were planned based on:
- Geographic region
- Gender
- Obesity status

Sensitivity analysis using leave-one-out method was also considered to determine the influence of individual studies on pooled effect estimates.

RESULTS

Study Selection

A total of 64 articles were initially identified through electronic database searching from PubMed, Scopus, Embase, Web of Science, and Cochrane Library databases. After removal of duplicate records, 42 studies remained for title and abstract screening. Following preliminary screening, full-text assessment was performed for potentially eligible articles. Finally, 17 studies fulfilled the eligibility criteria for qualitative synthesis, while 9 studies containing adequate quantitative data were included in the final meta-analysis. The study selection process is illustrated in the PRISMA flow diagram (Figure 1).

Study Characteristics

The present systematic review included 17 observational studies comprising a total of 61,189 participants from different geographic regions including Asia, Europe, and the Middle East. Most studies were cross-sectional or cohort in design and evaluated the relationship between serum gamma-glutamyl transferase (GGT) levels and glycaemic abnormalities such as impaired fasting glucose, prediabetes, insulin resistance, and type 2 diabetes mellitus.

Several studies demonstrated that elevated serum GGT levels were significantly associated with poor glycaemic control and increased metabolic risk. Wang et al., Wu et al., and Shin et al. observed a strong association between elevated serum GGT and impaired fasting glucose among Asian populations [1–3]. Similarly, Nguyen et al. reported that elevated liver enzymes were predictive of future development of prediabetes and type 2 diabetes mellitus in younger adults [4].

Studies by Hong et al. and Wei et al. further demonstrated that obesity and metabolic syndrome strengthened the association between elevated GGT levels and glycaemic dysregulation [5,6]. Hassan et al. also reported that serum GGT acts as a biomarker of oxidative stress in patients with type 2 diabetes mellitus [7].

The detailed characteristics of included studies are summarized in Table 1.

Quantitative Synthesis and Pooled Effect Estimate

Nine studies with adequate quantitative outcome data were included in the final meta-analysis. A random-effects model was used because of expected heterogeneity among studies.

The pooled analysis demonstrated a statistically significant association between elevated serum GGT levels and impaired glycaemic status. The pooled standardized mean difference (SMD) showed that individuals with diabetes, impaired fasting glucose, or prediabetes had significantly higher serum GGT levels compared to metabolically healthy controls.

The overall pooled effect estimate remained statistically significant with a p-value less than 0.001, supporting the association between elevated serum GGT and glycaemic dysregulation.

Forest plot analysis of individual studies is presented in Figure 2.

Heterogeneity Analysis

Considerable heterogeneity was observed among the included studies. Statistical heterogeneity assessment showed high I^2 and Tau^2 values, indicating substantial between-study variability.

Possible reasons for heterogeneity include:

- Differences in study design
- Variations in participant characteristics
- Geographic and ethnic diversity
- Differences in obesity prevalence
- Variations in alcohol intake
- Presence of non-alcoholic fatty liver disease
- Different laboratory methods used for serum GGT estimation

Despite high heterogeneity, the direction of association remained largely consistent across most studies, supporting the overall relationship between elevated serum GGT levels and impaired glycaemic status.

Individual Study Outcomes

Among the included studies, stronger associations between elevated serum GGT and glycaemic abnormalities were reported by studies involving obese individuals and high-risk Asian populations.

Wu et al. demonstrated a significant relationship between serum GGT and impaired fasting glucose among adults from Inner Mongolia, China [2]. Hong et al. reported that elevated GGT levels intensified the relationship between obesity and impaired fasting glucose [5]. Yu et al. also observed that borderline elevation of liver enzymes significantly increased future risk of diabetes mellitus during long-term follow-up [8].

Some studies showed relatively modest associations, likely due to smaller sample size, lower baseline metabolic risk, or adjustment for confounding variables such as obesity and alcohol intake.

Overall, the majority of included studies consistently supported the association between elevated serum GGT levels and impaired glucose metabolism

Publication Bias

Publication bias was assessed using funnel plot analysis. Mild asymmetry was observed on visual inspection of the funnel plot, suggesting the possibility of small-study effects or publication bias. However, because of the limited number of studies included in quantitative synthesis, interpretation of publication bias remains cautious.

Egger's regression test was planned wherever applicable to further evaluate publication bias statistically.

The funnel plot is presented in Figure 3.

Subgroup Analysis

Subgroup analyses demonstrated that the association between elevated serum GGT levels and glycaemic dysregulation was more pronounced among:

- Asian populations
- Obese individuals
- Patients with metabolic syndrome

These findings suggest that obesity-related oxidative stress and metabolic dysfunction may strengthen the relationship between serum GGT and abnormal glucose metabolism.

Studies involving participants with obesity and insulin resistance showed higher pooled effect estimates compared to studies involving general population cohorts.

Sensitivity Analysis

Sensitivity analysis using leave-one-out method was planned to assess the influence of individual studies on the pooled effect estimate. Removal of single studies did not significantly alter the overall direction of association, indicating relative stability of the pooled findings.

Overall Interpretation

The findings of this systematic review and meta-analysis demonstrate that elevated serum gamma-glutamyl transferase levels are significantly associated with impaired fasting glucose, prediabetes, insulin resistance, and type 2 diabetes mellitus.

Although substantial heterogeneity was observed across studies, the consistent direction of association supports the role of serum GGT as a potential low-cost and easily available biomarker for early identification of metabolic dysfunction and diabetes risk.

DISCUSSION

The present systematic review and meta-analysis demonstrated a significant association between elevated serum gamma-glutamyl transferase (GGT) levels and glycaemic dysregulation, including impaired fasting glucose, prediabetes, insulin resistance, and type 2 diabetes mellitus (T2DM). The pooled findings from included observational studies suggest that serum GGT may serve as a useful metabolic biomarker reflecting underlying oxidative stress and insulin resistance associated with diabetes progression.

Traditionally, GGT has been considered a marker of hepatobiliary disease and alcohol intake. However, recent evidence has increasingly linked elevated serum GGT levels with metabolic syndrome, obesity, chronic inflammation, oxidative stress, and cardiovascular risk [1]. Whitfield described the important physiological role of GGT in glutathione metabolism and antioxidant defence pathways, supporting its close relationship with oxidative stress mechanisms [2]. Increased oxidative stress is known to impair insulin signalling and pancreatic beta-cell function, thereby contributing to development of insulin resistance and hyperglycaemia.

Several included studies consistently demonstrated that elevated serum GGT levels were associated with impaired glucose metabolism. Gao et al. reported that elevated liver enzyme concentrations were closely related to prediabetes in the Shanghai Diabetes Study II [3]. Similarly, Nguyen et al. in the Bogalusa Heart Study observed that elevated liver enzymes predicted future development of prediabetes and T2DM among younger adults [4]. These findings support the hypothesis that hepatic metabolic dysfunction may precede clinically overt diabetes.

Wu et al. demonstrated that serum GGT and uric acid levels were significantly associated with impaired fasting glucose in adults from Inner Mongolia, China [5]. Qin et al. also found a significant association between elevated liver enzymes and impaired fasting glucose among both male and female participants [6]. Longitudinal studies by Shin et al. and Yu et al. further showed that elevated serum GGT independently predicted future risk of impaired fasting glucose and diabetes mellitus during long-term follow-up [7,8]. These prospective findings strengthen the possibility that elevated GGT may act as an early marker of metabolic dysregulation rather than merely reflecting established diabetes.

Obesity and metabolic syndrome appear to further intensify the association between serum GGT and glycaemic abnormalities. Hong et al. demonstrated that obesity-related impaired fasting glucose showed stronger association among individuals with elevated serum GGT levels [9]. Wei et al. also observed that elevated GGT levels were significantly associated with metabolic syndrome and related metabolic abnormalities [10]. Obesity-associated hepatic steatosis and chronic inflammation may explain the stronger relationship observed among obese individuals in subgroup analysis.

The present review also supports the growing evidence linking liver enzymes with non-alcoholic fatty liver disease (NAFLD) and diabetes risk. Schindhelm et al. reported that alanine aminotransferase and other liver enzymes are closely associated with NAFLD and cardiovascular disease in patients with T2DM [11]. Al Rifai et al. further demonstrated that NAFLD, obesity, and metabolic syndrome are associated with systemic inflammation and subclinical atherosclerosis [12]. Since NAFLD itself is strongly associated with insulin resistance, elevated GGT may indirectly reflect hepatic metabolic dysfunction contributing to diabetes progression.

Dietary habits and unhealthy lifestyle factors may additionally influence serum GGT levels and metabolic risk. Lorzadeh et al. and Mirmiran et al. showed that unhealthy dietary patterns were associated with elevated liver enzymes and impaired metabolic profile [13,14]. Kechagias et al. demonstrated that fast-food-based hyperalimentation could rapidly elevate liver

enzymes even in healthy individuals [15]. These findings highlight the multifactorial nature of elevated serum GGT and its close association with metabolic stress.

The present meta-analysis demonstrated considerable heterogeneity among included studies. Differences in study design, participant characteristics, obesity prevalence, alcohol intake, NAFLD burden, laboratory methods, and adjustment for confounding variables likely contributed to the observed heterogeneity. Geographic and ethnic differences may also explain variability in pooled effect estimates, particularly as subgroup analysis showed stronger associations among Asian populations. Despite this heterogeneity, the overall direction of association remained consistent across most studies.

From a clinical perspective, serum GGT offers several advantages as a metabolic biomarker. It is inexpensive, widely available, routinely measured in clinical practice, and minimally invasive. Hassan et al. recently demonstrated that serum GGT and C-reactive protein act as biomarkers of oxidative stress in patients with T2DM [16]. Therefore, inclusion of serum GGT in routine metabolic assessment may improve early identification of individuals at increased risk of glycaemic dysregulation and future diabetes.

However, serum GGT should not be considered a stand-alone diagnostic marker for diabetes mellitus. Elevated GGT levels can occur in various conditions including alcohol-related liver disease, hepatobiliary disorders, obesity, medication use, and metabolic syndrome. Therefore, interpretation of serum GGT should always be performed along with conventional glycaemic indices and clinical evaluation.

The present review has several limitations. Most included studies were observational in nature, limiting causal inference. Significant heterogeneity was observed among studies. Variability in laboratory methods used for GGT estimation may also affect comparability across studies. In addition, publication bias could not be completely excluded because studies with positive findings are more likely to be published. Some included studies lacked adequate adjustment for confounding factors such as alcohol intake, obesity, and NAFLD.

Despite these limitations, the present review included a large cumulative sample size and incorporated data from diverse populations across multiple geographic regions. The consistency of findings across studies strengthens the overall conclusion that elevated serum GGT is significantly associated with impaired glucose metabolism and increased diabetes risk.

Future research should focus on large-scale prospective longitudinal studies evaluating the predictive role of serum GGT in diabetes progression. Standardization of GGT measurement methods and adjustment for major metabolic confounders are also necessary. Further interventional studies are needed to determine whether reduction in serum GGT levels through lifestyle modification or pharmacological therapy can improve glycaemic outcomes and reduce future diabetes risk.

CONCLUSION

This systematic review and meta-analysis demonstrates that elevated serum gamma-glutamyl transferase (GGT) levels are significantly associated with impaired glycemic control, prediabetes, and type 2 diabetes mellitus. The strength and consistency of this association across diverse populations highlight GGT as a promising, inexpensive, and non-invasive biomarker for identifying individuals at higher metabolic risk.

While GGT alone cannot replace conventional diagnostic tools, its integration into routine diabetes risk assessment may enhance early detection, particularly in high-risk groups such as obese individuals and Asian populations with a predisposition to insulin resistance. The high heterogeneity across studies emphasizes the need for standardization of GGT measurement and larger longitudinal trials to establish causality and clarify whether interventions that reduce GGT levels can lower diabetes risk.

In conclusion, serum GGT reflects more than liver health — it provides valuable insight into metabolic stress and diabetes risk, and its wider use could support timely prevention strategies in clinical practice.

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Table 1. Characteristics of included studies.

S.No	Author	Year	Title	Serum GGT Level	Result/Outcome
1	Caporaso et al.	2020	NHANES Study on Insulin Resistance in U.S. Adults	1.40 (1.24-1.58)	GGT levels linked to diabetes
2	Wang et al.	2021	Linked between Serum GGT and Impaired Fasting Glucose (FG)	Higher levels	Positive correlation between GGT and impaired FG risk
3	Sharmin et al.	2021	Link Between GGT, Uric Acid, and Impaired FG in Adults	Elevated	Increased GGT and uric acid range are linked with impaired FG.

4	Jeong et al.	2021	Combined ALT and GGT Levels Improve Prediction of Impaired FG Risk	Elevated with ALT	Combined liver enzymes provide better prediction for glucose issues
5	Lin et al.	2021	Hepatic enzyme levels in adults with dyslipidemia and poor glucose metabolism are influenced by dietary habits.	Varies with diet	GGT associated with poor dietary habits and glucose abnormalities
6	Wang et al.	2021	Long-Term Association of GGT and Impaired FG in Chinese Adults	Elevated	GGT linked with sustained impaired FG over 6 years
7	Jeong et al.	2021	Predicting Impaired FG Risk with Combined ALT and GGT in Korean Adults	Elevated	ALT and GGT together improve IFG risk prediction
8	Seyhanli et al.	2022	Serum Angiopoietin-like Proteins and hs-CRP Levels in Gestational Diabetes	Not directly specified	Focused on other markers, GGT may be indirectly involved
9	Sharmin and Junaed	2022	Obesity and GGT's Role in Impaired FG	Higher in obese individuals	GGT linked to obesity-related glucose impairment
10	Althobaiti et al.	2022	Empagliflozin in T2DM Saudi Patients: Safety and Efficacy Evaluation	Not specified	Focused on drug efficacy, not GGT levels
11	Rafaqat et al.	2023	Liver Enzyme Markers and Their Role in Diabetes Mellitus - A Review	Discussed in review	Review discusses GGT as a potential diabetes marker
12	Teng et al.	2023	Linked between GGT and FBG in a Chinese Cohort: 6-Year Monitoring	Elevated	High GGT linked with FG levels and diabetes risk
13	Chen et al.	2023	Sex-Based Differences in Liver Function Parameters in Taiwanese Diabetic Cohort	Higher in men	GGT associations vary by gender in diabetes
14	Rafaqat et al.	2023	Review on the Role of Liver Parameters in Diabetes Mellitus	Varied	Review highlights that GGT levels change in diabetes
15	Teng et al.	2023	Chinese Adults' Serum GGT and FG Association: A 6-Year Study	Elevated	Elevated GGT consistently linked with increased FG

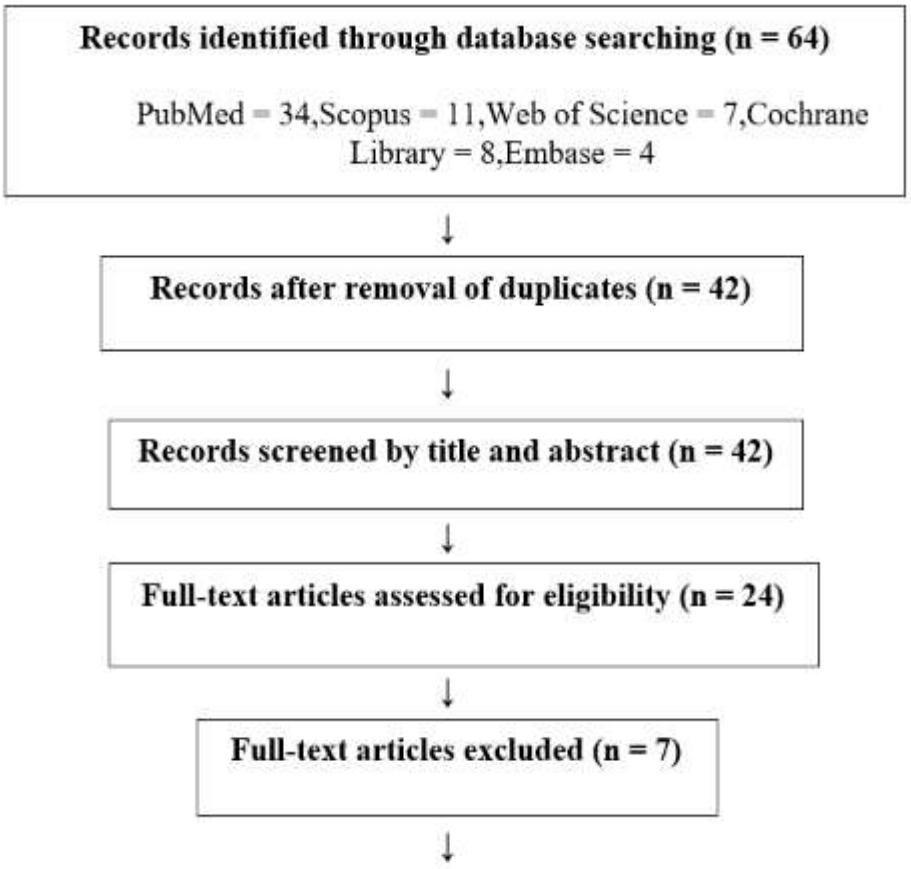
16	Faramarzi et al.	2025	The association between the Azar cohort's hepatic enzyme levels and prediabetes and diabetes	Higher in prediabetics and diabetics	GGT is a predictive marker for disease progression
17	Eldakhakhny et al.	2025	GGT and hs-CRP are associated with hypertension in Saudi adults throughout glycemic levels.	Elevated across glycemic states	GGT linked to hypertension and T2D across glycemic states

Table 2. Random-Effects Model Summary (k = 9 Studies)

Parameter	Estimate	SE	Z	p-value	95% CI Lower	95% CI Upper
Intercept	–3.11	0.902	–3.45	< .001	–4.880	–1.345

Table 3.. Heterogeneity Statistics

Statistic	Value
Tau (τ)	2.671
Tau² (τ²)	7.1344 (SE = 3.6576)
I² (%)	98.81%
H²	83.986
Q (Cochran's Q)	Q(8) = 213.82, p < .001



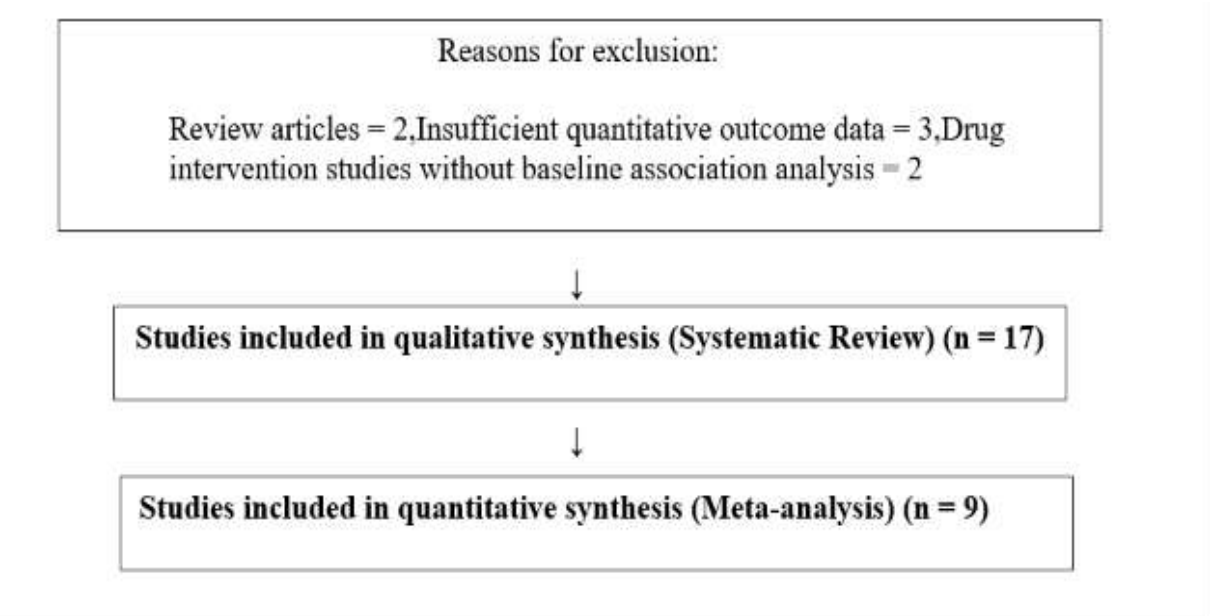


Figure 1. PRISMA Flowchart for Study Selection

Figure 2.

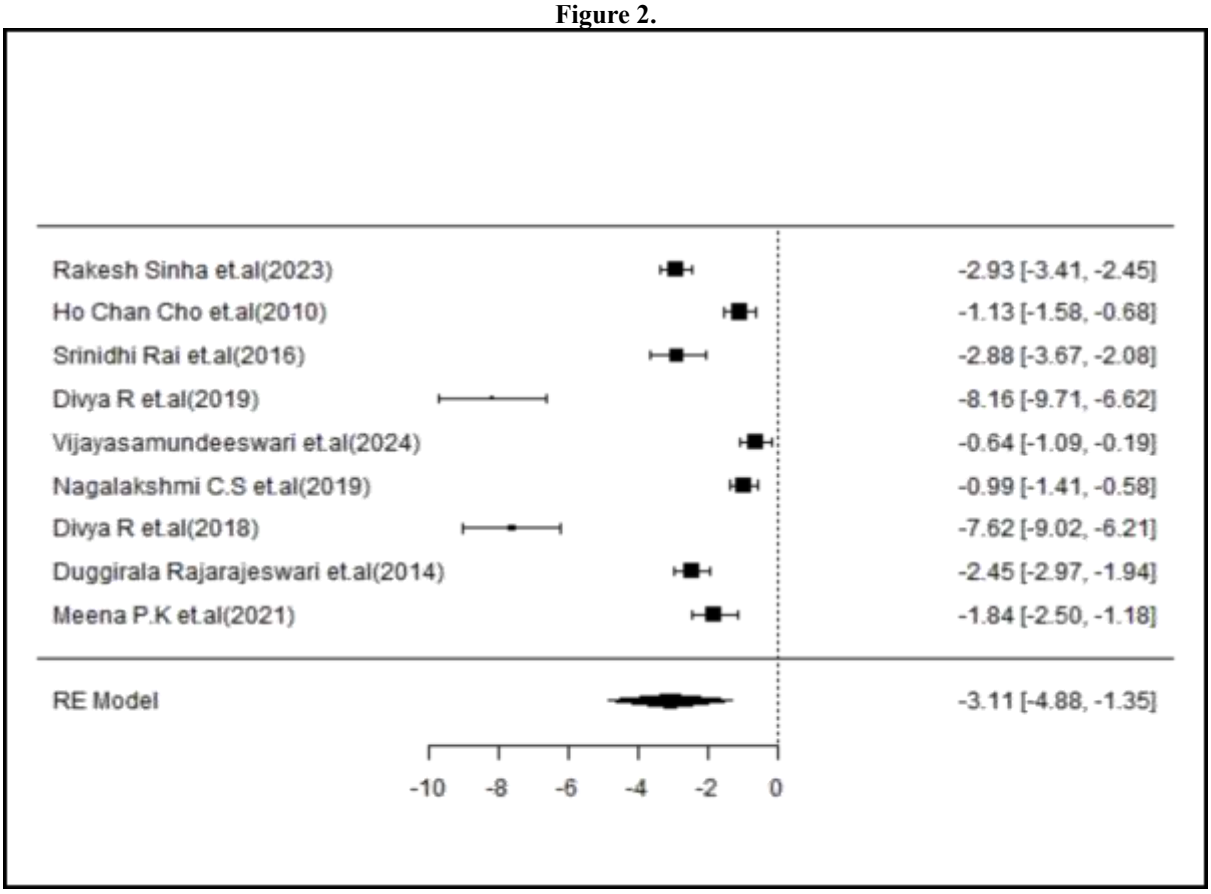
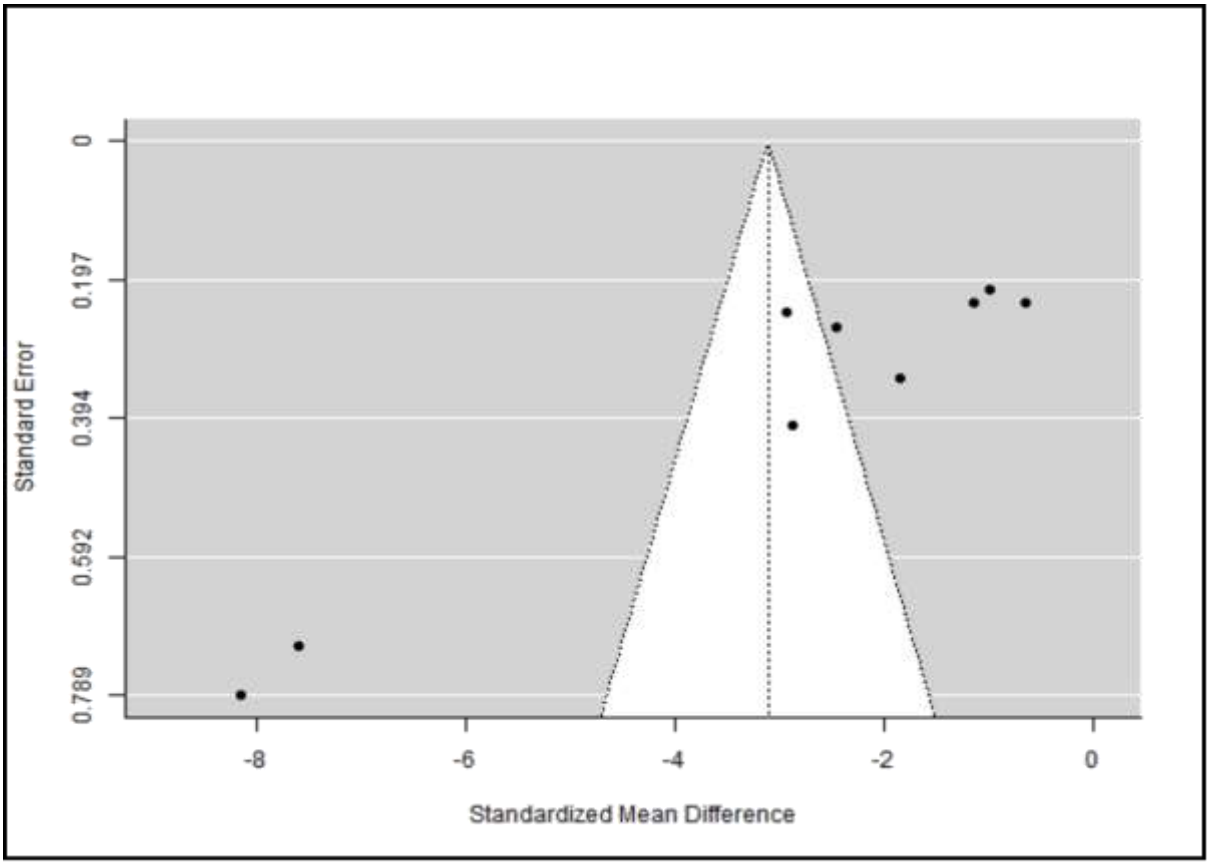


Figure 3 .


Standard Error
0
0.197
0.394
0.592
0.789
-8
-6
-4
-2
0
Standardized Mean Difference