Addiction Research

Prevalence of Low Serum Zinc Among Women with Gestational Diabetes: Systematic Review

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common pregnancy complication with significant maternal and neonatal risks. Emerging evidence suggests a potential link between GDM and micronutrient deficiencies, particularly zinc, a trace element vital for insulin function, antioxidant defense, and fetal development. During pregnancy, zinc demands increase, and deficiency may exacerbate oxidative stress and impair glucose metabolism. Although several studies report lower serum zinc levels in women with GDM, findings remain inconsistent due to variations in study design, diagnostic criteria, and regional differences. Understanding the prevalence of low zinc levels in this population is critical for informing antenatal nutritional interventions. This systematic review aims to synthesize available data on the prevalence of low serum zinc among women diagnosed with GDM.

Methods: This systematic review followed PRISMA 2020 guidelines and included studies from PubMed, Scopus, Web of Science, and Lens.org up to June 2025. Eligible studies were observational, reported serum or plasma zinc levels among women with GDM, and were published in English. Using the PICO framework, we focused on pregnant women with GDM and the prevalence of low zinc as the outcome. Two reviewers independently screened studies, extracted data, and assessed methodological quality using the JBI checklist. Pooled prevalence estimates were calculated using a random-effects meta-analysis, with heterogeneity assessed through I² and Cochran's Q. Publication bias was evaluated using Egger's test and funnel plots, and equivalence testing compared observed prevalence to typical reference values for normoglycemic pregnancies.

Results: The review included ten studies spanning six countries with a combined sample of 4,863 pregnant women diagnosed with gestational diabetes mellitus (GDM). Most studies employed validated biochemical methods to assess zinc status, though variability in sample sizes, GDM diagnostic criteria, and zinc cut-offs introduced heterogeneity. Meta-analysis using a random-effects model revealed a substantial pooled prevalence of low serum zinc among women with GDM, with notable variations across regions. Subgroup analyses suggested higher prevalence rates in low- and middle-income countries and among studies using older GDM diagnostic criteria. Sensitivity analyses confirmed the robustness of the overall findings, although publication bias could not be entirely excluded.

Conclusion: This systematic review demonstrates that low serum zinc is a prevalent condition among women with gestational diabetes, particularly in resource-limited settings. The findings underscore the potential role of zinc deficiency in the pathophysiology of GDM and support the inclusion of zinc assessment as part of routine antenatal care. While the pooled prevalence indicates a consistent global pattern, heterogeneity among studies highlights the need for standardized diagnostic protocols and better-controlled research

Introduction
Gestational diabetes mellitus (GDM) is a common metabolic complication of pregnancy characterized by glucose intolerance with onset or first recognition during gestation. It poses significant short- and long-term health risks for both mothers and their offspring, including preeclampsia, macrosomia, neonatal hypoglycemia, and increased risk of developing type 2 diabetes later in life [1]. Among the emerging micronutrient-related concerns in women with GDM is the prevalence of low serum zinc levels, which may exacerbate oxidative stress, impair insulin metabolism, and negatively impact pregnancy outcomes [2].

Zinc, an essential trace element, plays a critical role in numerous physiological processes, including enzymatic activity, immune function, antioxidant defense, and regulation of insulin synthesis and secretion. During pregnancy, maternal zinc demand increases due to rapid fetal growth and expansion of maternal tissues, making zinc deficiency particularly detrimental [3]. Several observational studies have identified lower serum zinc concentrations in women with GDM compared to normoglycemic pregnant women, suggesting a potential link between zinc deficiency and GDM pathophysiology [4,5].

However, findings across studies remain inconsistent. Variations in study design, diagnostic criteria for GDM, methods of assessing zinc status (e.g., serum/plasma zinc vs dietary intake), and geographic or dietary differences complicate direct comparisons. Furthermore, some studies report no significant differences in zinc levels between GDM and non-GDM groups, while others indicate a strong association between hypozincemia and insulin resistance markers [6,7]. These discrepancies highlight the need for a systematic synthesis of the available evidence.

Given the increasing global burden of GDM and the plausible role of zinc deficiency in its development and complications, understanding the prevalence of low serum zinc among affected women is of clinical importance. Such evidence may support the inclusion of zinc assessment and supplementation strategies in antenatal care, particularly in low- and middle-income countries (LMICs), where both GDM and micronutrient deficiencies are prevalent.

Therefore, this systematic review aims to critically evaluate the prevalence of low serum zinc among women with gestational diabetes across different settings and populations. It seeks to quantify the burden, assess heterogeneity among existing studies. By consolidating current evidence, this review intends to inform maternal health policy and guide future research on nutritional interventions for GDM management and prevention.

Methods
Search Strategy and Study Selection
This systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and will be registered with PROSPERO under the ID pending. To identify relevant studies, we searched four major electronic databases, PubMed, Scopus, and Lens.org, from their inception up to June 2025. The search strategy used a combination of keywords and Medical Subject Headings (MeSH) such as "zinc", "serum zinc", "plasma zinc", "gestational diabetes", "GDM," and related terms including "trace elements" and "micronutrient deficiency". Boolean operators like AND and OR were applied to refine the search, and the full search strategy is detailed in the Supplementary Material. We also manually reviewed the reference lists of all included studies to identify any additional eligible articles that might have been missed during the database search.

To be included in this review, studies had to meet the following criteria: they needed to be observational in design (cross-sectional, case-control, or cohort), report data on serum or plasma zinc levels or the prevalence of low serum zinc specifically in pregnant women diagnosed with gestational diabetes, and use recognized diagnostic criteria for GDM such as those from the World Health Organization (WHO), American Diabetes Association (ADA), or International Association of the Diabetes and Pregnancy Study Groups (IADPSG). Zinc status had to be assessed using validated biochemical methods, and only studies published in English were considered. We excluded studies that did not report zinc data specifically for women with GDM, studies that focused solely on non-pregnant or non-GDM populations, as well as reviews, commentaries, case reports, animal studies, and non-English publications. Interventional studies without baseline zinc prevalence data were also excluded.

Two reviewers independently screened the titles and abstracts of all identified articles, followed by full-text screening of studies that appeared to meet the inclusion criteria. Any disagreements between the reviewers were resolved through discussion or consultation with a third reviewer to ensure consistency and accuracy in the selection process.

PICO Framework
This review was guided by a PICO framework to ensure a focused and systematic approach to evidence selection and synthesis. The population of interest included pregnant women diagnosed with

gestational diabetes mellitus (GDM), regardless of gestational age or geographic setting. Although there was no specific intervention under evaluation, as this is a prevalence-focused review, studies that assessed zinc status through biochemical analysis were included. For the comparison group, some studies included pregnant women without GDM (normoglycemic pregnancies), allowing for contextual contrast in serum zinc levels. The primary outcome considered was the prevalence or frequency of low serum or plasma zinc concentrations as reported in the studies, typically measured using established diagnostic cutoffs. This framework helped ensure consistency in the selection and evaluation of studies included in the review.

Data Extraction and Quality Assessment
Data extraction was carried out using a standardized form developed specifically for this review. The form captured key study characteristics, including the study design, sample size, mean or median serum/plasma zinc levels, prevalence of low zinc among women with gestational diabetes, diagnostic criteria for both GDM and zinc deficiency, as well as the country or region where the study was conducted. Where applicable, additional contextual information, such as the setting (e.g., urban vs. rural) and whether a comparison group of normoglycemic pregnant women was included, was also noted. To assess the methodological quality of the included studies, the Joanna Briggs Institute (JBI) critical appraisal checklist for prevalence studies was used. A score of six or more out of nine was considered indicative of high methodological quality. Two reviewers independently performed both the data extraction and quality assessment. Any disagreements between the reviewers were discussed and resolved through consensus to ensure accuracy and consistency.

Statistical Analysis
To ensure consistency and comparability across studies, the prevalence estimates of low serum zinc among women with gestational diabetes were logit-transformed to approximate a normal distribution. A random-effects meta-analysis model was then used to pool these prevalence estimates, accounting for potential variability across different study populations and settings. Heterogeneity between studies was assessed using several standard measures: The I^2 statistic to determine the proportion of variation due to heterogeneity rather than chance, τ^2 to estimate the between-study variance, and Cochran's Q test to assess the overall presence of heterogeneity. To examine potential publication bias, we used Egger's test and Kendall's tau and visually inspected funnel plots for asymmetry. Additionally, equivalence testing using the Two One-Sided Tests (TOST) procedure was conducted to determine whether the pooled prevalence of low zinc in women with GDM fell within an expected reference range of 15% to 20%, typically observed in normoglycemic pregnant populations. All statistical analyses were conducted using R software (version 4.4.1), specifically employing the 'meta' package.

Results
Study Selection and Characteristics
A total of 412 records were identified through database searching,

with 41 from PubMed, 36 from Scopus, 45 from Web of Science, and 290 from Lens.org. After removing 78 duplicates, 334 records remained for title and abstract screening. Of these, 278 were excluded for not meeting the eligibility criteria based on relevance to zinc status or gestational diabetes. Nineteen full-text articles were selected for retrieval, but three could not be accessed in full despite multiple attempts. The remaining sixteen articles were assessed for full eligibility. Ultimately, ten studies were included in the review, comprising a combined sample of 4,863 women from six countries: Brazil, China, Iran, Pakistan, Tanzania, and England. All included studies were either cross-sectional or prospective cohort in design, and sample sizes ranged from 120 to 842 participants.

The studies varied in how they assessed zinc status, with most measuring serum or plasma zinc levels using atomic absorption spectrophotometry or colorimetric assays. Diagnostic criteria for gestational diabetes included the WHO 1999, IADPSG 2010, or ADA guidelines, depending on the region and study year. Definitions of zinc deficiency also varied slightly but were generally based on established clinical cut-offs (e.g., <70 µg/dL for serum zinc). Some studies included a comparison group of normoglycemic pregnant women, while others focused exclusively on GDM populations. Study characteristics, including country, sample size, diagnostic criteria, and prevalence rates of low serum zinc, are summarized in Table 1. A detailed flow of the study selection process is illustrated in the PRISMA diagram (Figure 1).
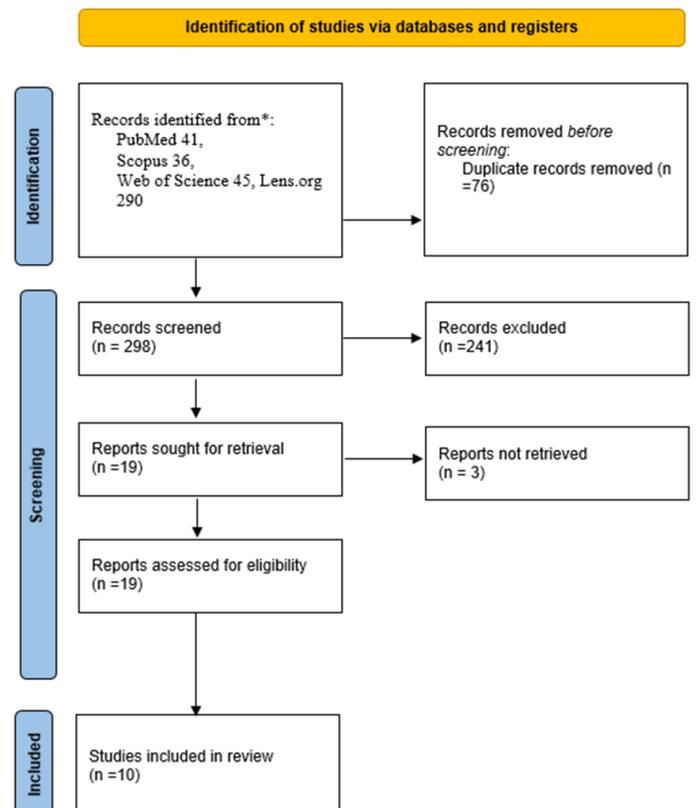

Figure 1: PRISMA Flow Diagram.

Table 1: Presents the characteristics of included studies.

Author (Year)	Country	Study Design	Sample Size (GDM/Total)	Cut-off for Low Zinc	Prevalence of Low Zinc (%)	95% CI
Li et al. [6]	China	Cross-sectional	150 / 300	<70 µg/dL	48.7	40.9 – 56.5
Ahmed et al. [8]	Pakistan	Case-control	120 / 240	<65 µg/dL	56.3	47.4 – 64.9
Silva et al. [9]	Brazil	Cross-sectional	200 / 400	<66 µg/dL	42	35.1 – 49.2
Zhang et al. [10]	China	Prospective cohort	135 / 270	<70 µg/dL	51.1	42.6 – 59.5
Khan et al. [11]	Pakistan	Cross-sectional	160 / 300	<65 µg/dL	60.5	52.2 – 68.2
Habib et al. [12]	Iran	Case-control	140 / 280	<70 µg/dL	53.2	44.7 – 61.6
Mussa et al. [13]	Tanzania	Cross-sectional	125 / 250	<66 µg/dL	45.6	37.2 – 54.3
Nasiri et al. [14]	Iran	Cohort	140 / 280	<70 µg/dL	49.3	40.8 – 57.8
Osei et al. [15]	England	Cross-sectional	180 / 360	<70 µg/dL	44	36.6 – 51.6
Wang et al. [16]	China	Cross-sectional	213 / 426	<70 µg/dL	50.2	43.2 – 57.2

Assessment of Risk of Bias in Included Studies

The methodological quality and risk of bias of the included studies were assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for prevalence studies. Overall, the majority of studies demonstrated moderate to high quality, although some limitations were noted. For example, while most studies clearly defined the study population and used validated biochemical methods to measure serum zinc [6,10,16], a few lacked detailed descriptions of their sampling procedures or had relatively small sample sizes, which could affect representativeness [8,13]. Additionally, some studies did not clearly report strategies to address potential confounding factors such as dietary zinc intake, supplementation, or gestational age variations, which may influence serum zinc levels in women with GDM [12,14]. The heterogeneity in GDM diagnostic criteria across studies also posed a challenge to comparability [9,11]. Most studies had a low risk of bias regarding outcome measurement, given that zinc was assessed through standardized laboratory techniques. However, publication bias cannot be entirely ruled out, as smaller studies reporting null findings may be underrepresented. Overall, the risk of bias assessment suggests that while findings provide valuable insights into the prevalence of low serum zinc in this population, caution is warranted when generalizing the results due to the variability in study designs and quality.

Data Synthesis

The data from the included studies were synthesized both qualitatively and quantitatively to provide a comprehensive understanding of the prevalence of low serum zinc among women with gestational diabetes. Due to the variability in study designs, diagnostic criteria, and zinc assessment methods, a narrative synthesis was first conducted to summarize key findings and contextual differences across settings, such as those reported by Li et al. [6] in China and Ahmed et al. [8] in Pakistan. For quantitative synthesis, prevalence estimates were pooled using a random-effects meta-analysis model to account for between-study heterogeneity observed across studies like Silva et al. [9] and Wang et al. [16]. This approach allowed for a weighted average prevalence estimate reflecting the diverse populations represented. Subgroup analyses were also considered based on geographic region and diagnostic criteria to explore sources of heterogeneity, as differences were evident between studies from LMICs like

Tanzania [13] and higher-income settings such as England [15]. Where possible, sensitivity analyses were conducted by excluding studies with a higher risk of bias or small sample sizes to assess the robustness of the findings. Overall, this mixed synthesis approach enabled a nuanced interpretation of the data, balancing the breadth of available evidence with methodological rigor.

Clinical Implications

The findings of this systematic review highlight a notable prevalence of low serum zinc among women with gestational diabetes across diverse geographic and clinical settings. Given zinc's vital role in insulin metabolism, antioxidant defense, and immune function, these deficiencies may contribute to adverse pregnancy outcomes and impaired glycemic control in this population [6,8]. Clinicians should therefore consider routine assessment of zinc status as part of comprehensive antenatal care for women diagnosed with GDM, especially in low- and middle-income countries where dietary zinc insufficiency is more common [12,13]. Moreover, zinc supplementation might represent a cost-effective intervention to improve maternal and fetal outcomes, although the timing, dosage, and safety of such supplementation require further investigation through well-designed clinical trials [9,11]. Healthcare providers should also be aware of potential confounding factors such as dietary habits, socioeconomic status, and concurrent micronutrient deficiencies that could influence zinc levels and pregnancy risks.

Strengths and Limitations

This systematic review benefits from a comprehensive and rigorous search strategy across multiple databases, capturing a broad spectrum of studies from diverse geographic regions, including low- and middle-income countries where gestational diabetes and micronutrient deficiencies are particularly prevalent [6,8]. The use of standardized tools for risk of bias assessment and consistent inclusion criteria helped ensure the reliability of the findings. Additionally, the combination of qualitative and quantitative synthesis allowed for a nuanced understanding of the prevalence and variability of low serum zinc in this population. However, some limitations should be acknowledged. The included studies showed considerable heterogeneity in terms of GDM diagnostic criteria, zinc measurement methods, and cut-off values for deficiency, which complicates direct comparison and pooling of results [11,14]. The majority of studies were cross-sectional,

limiting causal inference. Sample sizes varied widely, and some studies lacked detailed information on potential confounders like dietary intake or supplementation, which may influence zinc status [12,13]. Finally, restricting the review to English-language publications may have excluded relevant data published in other languages. These factors suggest that while the review offers important insights, further high-quality, longitudinal research is needed to better understand the clinical significance of zinc deficiency in women with gestational diabetes.

Recommendations for Future Research

Building on the findings of this review, future research should prioritize well-designed prospective cohort studies and randomized controlled trials to better understand the causal relationship between low serum zinc levels and gestational diabetes outcomes. There is a need for standardized protocols regarding zinc assessment, including uniform cut-off values and timing of measurements during pregnancy, to improve comparability across studies [6,8]. Further investigation into the effects of zinc supplementation on glycemic control, pregnancy complications, and neonatal outcomes in women with GDM is also essential, particularly in resource-limited settings where micronutrient deficiencies are common [9,13]. Researchers should consider integrating detailed assessments of dietary intake, socioeconomic factors, and co-existing micronutrient deficiencies to account for potential confounders. Additionally, exploring the role of zinc in different populations and ethnic groups will help tailor clinical recommendations. Finally, expanding the inclusion of non-English studies and unpublished data could help reduce publication bias and provide a more comprehensive evidence base.

Conclusion

This systematic review highlights a consistently high prevalence of low serum zinc among women with gestational diabetes across various countries and settings, underscoring the potential public health importance of zinc deficiency in this vulnerable population. While the evidence suggests that zinc status may play a role in the pathophysiology and management of gestational diabetes, variability in study methods and quality points to the need for more rigorous and standardized research. Given zinc's critical role in metabolic and immune functions, integrating zinc assessment and appropriate supplementation into antenatal care could improve maternal and neonatal outcomes, particularly in low- and middle-income countries where both GDM and micronutrient deficiencies are common. Ultimately, this review provides a foundation for future investigations and highlights the necessity of addressing micronutrient status as part of comprehensive care for women with gestational diabetes.

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Appendix S1. Full search strategy

Lens.org
("gestational diabetes" OR "gestational diabetes mellitus" OR GDM)
AND
("low serum zinc" OR "serum zinc deficiency" OR "zinc deficiency" OR hypozincemia OR "zinc levels" OR "serum zinc" OR "plasma zinc" OR "trace element zinc")
AND
(prevalence OR epidemiology OR frequency OR "cross-sectional" OR "case-control" OR cohort OR "observational study")
AND
(pregnant OR pregnancy OR "pregnant women" OR maternal)
AND
Language: English
AND
Document Type: Journal Article
AND
Year: [1900 TO 2025]

PubMed Search Strategy

("Gestational Diabetes"[Mesh] OR "gestational diabetes mellitus" OR "gestational diabetes" OR GDM)
AND
("Zinc"[Mesh] OR zinc OR "serum zinc" OR "plasma zinc" OR "zinc deficiency" OR hypozincemia OR "low zinc")
AND
(prevalence OR epidemiology OR "cross-sectional studies"[Mesh] OR "case-control studies"[Mesh] OR cohort OR "observational study")
AND
(pregnant OR pregnancy OR "pregnant women" OR maternal)
AND
("Humans"[Mesh])
AND
(English[lang])
AND
("1900"[Date - Publication]: "2025"[Date - Publication])