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The Association Between Maternal Vitamin D Deficiency and the Risk of Gestational Diabetes Mellitus (GDM): A Systematic Review of Recent Evidence

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ABSTRACT

Gestational diabetes mellitus (GDM) is a prevalent metabolic problem developed during pregnancy and has serious health consequences for women and children, short- and long-term. Recently, it has been proposed that vitamin D may play a role in glucose metabolism and insulin sensitivity, and thus the onset of GDM. This meta-analysis summarized the results of updated cohort studies on maternal vitamin D deficiency and GDM recently. The included review covered seven studies involving heterogeneous populations and regions. Findings consistently suggest that lower maternal serum 25(OH)D during pregnancy is associated with an increased risk of GDM, and certain studies suggest the presence of interactions with body mass index and ethnicity. Causal conclusions cannot be drawn from observational data, but the findings suggest that screening and treatment for vitamin D deficiency early in pregnancy may represent a useful preventive approach. Further randomized controlled studies are needed to confirm these associations and help in clinical decision-making.

Keywords: vitamin D, 25-hydroxyvitamin D, deficiency, gestational diabetes, pregnancy

1. INTRODUCTION

Gestational diabetes mellitus (GDM) is a frequent pregnancy-related complication. It is characterized by abnormal glucose tolerance with onset or first recognition during pregnancy. GDM complicates 7-15% of all pregnancies worldwide, with prevalence rates varying according to the diagnostic criteria employed and the population's characteristics (American Diabetes Association, 2022). It is associated with significant maternal and fetal risk, including preeclampsia, macrosomia,

caesarean delivery, and the maternal as well as child's lifetime risk for developing type 2 diabetes (McIntyre et al., 2019). Of the different GDM risk factors, low vitamin D stands out as a possible modifiable/improvable risk factor. Vitamin D is a fat-soluble secosteroid hormone that is involved in calcium and phosphate metabolism. Moreover, it also affects pancreatic β-cell function, insulin sensitivity, and inflammatory response (Pittas et al., 2007). The finding of a vitamin D receptor in pancreatic tissue and of 1α-hydroxylase (the enzyme converting 25(OH)D to its biologically active form) in the pancreas has supported its role in glucose regulation (Zeitz et al., 2003).

Vitamin D deficiency has been suggested as a potentially modifiable factor that contributes to the development of GDM and its related adverse outcomes. For instance, Zhang et al., (2019) found that an early pregnancy deficiency in vitamin D among women increased the adjusted odds of developing GDM by 2.82 times, a risk that increased to 4.46 with full-time deficiency. A meta-analysis of greater than 9000 subjects revealed significantly higher risk of GDM for severe vitamin D insufficiency (OR 1.53; 95% CI 1.33-1.75) (Aghajafari et al., 2013).

Yet, the results in the literature are still not homogeneous. A few studies reported significant relation between the two (Bodnar et al., 2007; Milajerdi et al., 2021); whilst others reported no significant association that may be attributed to differences in the ethnicity, geographical location of the population studied, sun exposure, BMI, assay precision, and different cut-offs employed to define vitamin D insufficiency (Bi et al., 2018).

Furthermore, randomized controlled trials (RCTs) on the efficacy of vitamin D supplementation in the prevention or treatment of GDM have produced conflicting results. However, in light of these inconsistencies, it's important to evaluate the current proof and to explore the potential mechanistic and clinical relevance of the association of vitamin D status with GDM. The purpose of this systematic review is to summarize evidence from studies published in recent years on the association between maternal vitamin D insufficiency and the risk of GDM, with a focus on consistent findings, methodological limitations, and future avenues of research.

2. REVIEW METHODS

Study Design and Search Strategy

This systematic review aimed to investigate the relationship between maternal vitamin D deficiency and the risk of GDM. We conducted a focused search to locate primary studies published in the broad scientific literature. These electronic databases included PubMed, Web of Science, and Scopus, in which we searched the following terms and Boolean operators:

- "vitamin D"
- OR "25-hydroxyvitamin D"
- AND "deficiency"
- AND "gestational diabetes"
- OR "GDM"
- AND "pregnancy."

The literature search was limited to English and human studies. The period of the compilation of the search included all available relevant literature without imposing restrictions on the dates of publication. The studies were selected based on their relevance to the review topic, including observational cohort and retrospective studies that investigated maternal vitamin D status during pregnancy and its association with the development or outcomes of GDM.

Eligibility Criteria

Inclusion criteria were as follows: original research articles involving pregnant women; studies assessing serum 25-hydroxyvitamin D [25(OH)D] concentrations during pregnancy; studies on the relationship between maternal vitamin D status and the risk of GDM development or the outcomes of glucose metabolism; observational or retrospective cohort designs; use of clearly defined and recognized criteria for GDM diagnosis (e.g., IADPSG, ADA, WHO).

We excluded studies that were reviews, meta-analyses, editorials, or case reports; focused solely on vitamin D supplementation interventions without baseline vitamin D status; lacked a control or comparison group; were animal studies or lacked human data; or failed to provide quantitative outcomes related to GDM risk.

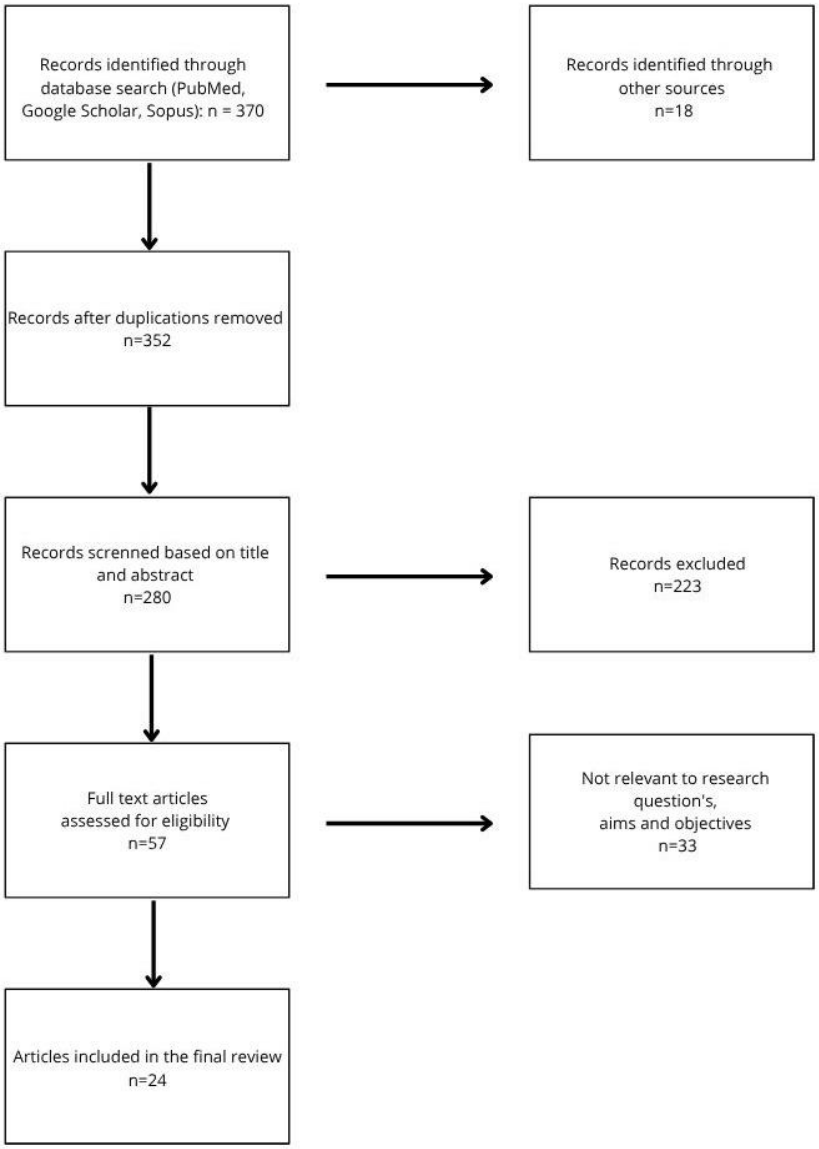

Figure 1. Prisma Consort Chart

Study Selection and Data Extraction

The study selection was executed in two steps. First, we screened titles and abstracts for relevance. Then we reviewed full texts of potentially eligible studies for inclusion based on predefined criteria (Figure 1). Two separate reviewers conducted the screening and extraction of data. We addressed differences in opinion by engaging in discussions or seeking input from an additional reviewer.

From each included study, we extracted the following data: author(s), year of publication, and country; study design and sample size; gestational age at the time of vitamin D measurement; diagnostic criteria and timing for GDM; definition and threshold used for vitamin D deficiency; reported outcomes (odds ratios, relative risks, confidence intervals); confounders adjusted for in the analysis.

Quality Assessment

The quality of the included studies was assessed by applying the Newcastle-Ottawa Scale (NOS) for evaluating observational research studies. This tool evaluates three areas: study group selection group comparability, and exposure or outcome assessment. We classified studies with scores of 7–9 points as high quality, 5–6 points as moderate quality, and those below five as low quality. We retained only studies of moderate to high quality for synthesis.

Data Synthesis and Analysis

The studies varied by design, the timing of vitamin D assessment, the definition of vitamin D deficiency, and the GDM diagnostic criteria used. Hence, a meta-analysis of the data was not appropriate. Therefore, a narrative synthesis of all the relevant studies was conducted.

The findings were summarized by comparing the effect estimates or measures of association direction, statistical significance, and confounder adjustments. Attention was paid to the studies where potential modifiers were evaluated, combined or separately, such as pre-pregnancy body mass index, ethnicity, and the gestational age at assessment of vitamin D.

3. RESULTS & DISCUSSION

Seven observational studies exploring the association between inappropriate maternal vitamin D deficiency and risk of GDM were considered in this SR (Table 1). The studies included different parts of the world like Saudi Arabia, South Korea, China, Spain, the United Kingdom, and the United States, which struck the global interest in this matter. All studies determined serum 25-hydroxyvitamin D [25(OH)D] concentrations during pregnancy with a threshold for deficiency defined as <50 nmol/L or less, and examined later gestational diabetes diagnosis or evidence of gestational diabetes based on established diagnostic criteria.

Table 1. Summary of Studies Evaluating the Association Between Maternal Vitamin D Deficiency and Gestational Diabetes Mellitus (GDM)

Study	Country	Design	Sample Size	Women with GDM	Women with Vit D deficiency	Time of Vit D Assessment	Vit D Deficiency Cutoff	GDM Criteria	Main Findings
Al-Ajlan et al., 2018	Saudi Arabia	Cross-sectional	515	116 out of 419 tested (27.7%)	425 (82.5%) - deficiency 198 (38.4%) – severe deficiency	First trimester	<50 nmol/ or < 25 nmol/l (severe deficiency)	IADPSG	Vit D deficiency associated with increased GDM risk (OR 2.87, $p < 0.001$)
Kim et al., 2020	South Korea	Observational study	348 (with GDM)	348	267 (76.7%)	24–32 weeks	<20 ng/mL	Carpenter and Coustan	Women with Vitamin D deficiency at mid-pregnancy had a higher prevalence of postpartum glucose intolerance than did those without vitamin D deficiency
Shao et al., 2019	China	Prospective cohort study	3318	716 (21.6%)	2497	T1: 8-14 weeks T2: 24^{th}-28^{th} weeks	<20 ng/ml	IADPSG	Vit D deficiency increased risk of GDM with elevated fasting glucose, especially in high-BMI women
Cho et al., 2013	South Korea	Case-control study	60	20 (33.3%)	46.7%	24–29 weeks	<20ng/mL	Carpenter–Coustan	Lower Vit D levels in GDM

									group; suggested placental involvement
Agüero-Domenech et al., 2022	Spain	Cross-sectional	886	93 (10.5%)	491 (55.5%)	Second trimester	<50 nmol/L	ADA	Association between Vit D deficiency and GDM stronger in obese women
Saluja et al., 2025	UK	Retrospective study	252	68 (27%)	45% of women in the severely deficient group 31% of women in the deficient group	First and second trimesters	<25nmol/L – severely deficient <50 nmol/L - deficient	NICE	Vitamin D deficiency associated with increased GDM risk across ethnic groups
Xia et al., 2019	USA	Nested case-control study	321	107	Not specified	≤20 and 24–28 weeks	<50 nmol/L	IADPSG	Persistent deficiency linked to higher GDM risk; stronger in Black and Asian women

Al-Ajlan et al., (2018) conducted a cross-sectional study in Saudi Arabia involving 515 pregnant women. They reported that a lack of vitamin D during the first trimester showed a notably increased likelihood of developing GDM (odds ratio [OR] 2.87, 95% CI: 1.32–6.25; p = 0.008). The authors emphasized the high prevalence of vitamin D deficiency in the Middle Eastern population and its possible function as a modifiable risk factor for GDM.

One such cohort study, which comprised 348 South Korean women with GDM, was conducted by Kim et al., (2020). They determined 25(OH)D at 24–32 weeks of pregnancy. They noted that the prevalence of postpartum glucose intolerance was significantly higher among women with low levels of vitamin D than among women with normal levels (48.7% vs. 32.1%, P=0.011). The finding indicates a potential impact of mid-pregnancy vitamin D status not only on GDM risk but also on maternal glucose metabolism in the long run.

Shao et al., (2019) examined how pre-pregnancy body mass index (BMI) interacts with vitamin D deficiency in a substantial cohort of 3318 pregnant women from China. They found that vitamin D deficiency in T1 was not significantly associated with the risk of GDM. In contrast, it showed an increased risk of GDM subtype 1 to a marginal extent (OR: 1.33, 95% CI: 0.91-1.95, P = 0.1337). The interaction between high BMI and vitamin D deficiency was significant, indicating a synergistic effect on GDM risk.

In another Korean study, Cho et al., (2013) conducted a case-control study of 60 women. They reported significantly lower 25(OH)D levels in women with GDM than in the comparison group ($p < 0.01$). The authors suggested placental vitamin D metabolism, through placental 1α-hydroxylase expression and inflammatory markers, as a possible mechanism mediating this association. Agüero-Domenech et al., (2022) examined BMI-stratified interrelations among 886 women in Spain, in a cross-sectional study. They observed a powerful association of vitamin D deficiency with GDM in overweight and obese women, with almost 2-fold increased odds of GDM risk in deficient compared with non-deficient women (adjusted OR 1.98, 95% CI: 1.02–3.84).

Saluja et al., (2025) performed a UK retrospective cohort study and included 252 pregnant women of different ethnicities. The study found a statistically significant association between vitamin D deficiency during early and mid-pregnancy and the risk of GDM [OR=1.65 (95% CI: 1.21–2.25)]. Importantly, this association remained significant even after accounting for covariates such as ethnicity, BMI, and SES, indicating that it is not just due to shared risk factors. Xia et al., (2019) studied Vitamin D status in 321 women from a longitudinal multi-ethnic cohort in the United States at ≤20 weeks and at 24–28 weeks of gestation. Vitamin D deficiency at both time

points was associated with a higher risk of GDM (AOR 2.16, 95% CI: 1.24–3.76). Subgroup analyses showed that this influence was especially relevant among Black and Asian women, suggesting a potential interaction between genetic, environmental, and metabolic factors.

Across various studies, findings consistently show a positive link between maternal vitamin D deficiency and an increased risk of gestational diabetes mellitus (GDM). Multiple studies highlighted how BMI and ethnicity can modify vitamin D levels, and the potential influence of vitamin D status on glucose tolerance even after pregnancy. A visual comparison of effect sizes was not possible due to differences in outcome metrics, adjustment models, and timing of vitamin D assessment, making meta-analysis unfeasible.

In this paper, we examine a fairly consistent association between maternal vitamin D deficiency and the risk of GDM. Across diverse populations and study designs, low serum 25-hydroxyvitamin D [25(OH)D] concentrations, especially in the first or second trimester, were associated with greater odds of GDM or glucose intolerance. Although the magnitude of this association showed some heterogeneity, the general tendency of this association held constant, as it was biologically plausible that there could be a causal relationship.

The biological bases for this association are complex. Vitamin D acts on pancreatic β-cell function and insulin sensitivity by its interaction with pancreatic tissue and skeletal muscle vitamin D receptors (VDRs) (Palomer et al., 2007). It also affects inflammatory cytokines and oxidative stress pathways, which are known to be involved in the pathogenesis of GDM (Hewison, 2012). Vitamin D is important in pregnancy as well and has an important function in the placenta, including the regulation of the trophoblast invasion and is involved in placental inflammation and affects local glucose metabolism (Liu et al., 2011).

A few of the included studies also found indications that timing and duration of vitamin D deficiency affected risk. Xia et al., (2019) reported that only low vitamin D status in both early and mid-gestation was associated with an increased risk for GDM. This might imply that the adverse effects of low vitamin D status are greater when status remains low over time than when there are transient episodes of deficiency. This finding is in line with the idea that a chronically altered hormonal environment could lead to a defective maternal glucose adaptation to pregnancy.

Body mass index (BMI) emerged as a recurrent modifying factor. Shao et al., (2019) and Agüero-Domenech et al., (2022) identified stronger associations between vitamin D deficiency and gestational diabetes mellitus (GDM) in overweight or obese women. This finding may indicate that vitamin D is sequestered in adipose tissue, which reduces its bioavailability, along with the combined effects of insulin resistance caused by obesity (Wortsman et al., 2000). Saluja et al., (2025) and Xia et al., (2019) reported increased susceptibility among Black and Asian women. This may result from genetic dissimilarities in vitamin D metabolism, skin pigmentation that affects dermal production, dietary intakes, or sociocultural differences in sun exposure. These findings illustrate the need for public health programs to be population-specific, which is especially important in societies with diverse cultures.

However, causality remains uncertain. The studies included were all observational in nature, which restricts the interpretation of causality. Investigators cannot exclude reverse causality, as disrupted metabolism of vitamin D could impact these women before the diagnosis of GDM, and residual confounding by dietary, socioeconomic, physical activity, and sunlight exposure may bias findings after adjustment. There is also heterogeneity in diagnostic criteria for both GDM and vitamin D deficiency. While most studies used <50 nmol/L as the threshold for deficiency, this value remains somewhat arbitrary and may not reflect functional insufficiency in all populations (Bouillon, 2017). Different criteria for GDM (IADPSG, ADA, KDA, etc.) can result in varying prevalence rates, making comparisons more complex. With these limitations, the findings from this review are in line with a growing body of evidence that vitamin D may be a modifiable risk factor for GDM.

Randomized controlled trials (RCTs) have reported diverse findings that could potentially result from differences in RCTs related to sample size, baseline 25-hydroxyvitamin D (25OHD) status, or time of supplementation (Harvey et al., 2014).

Nonetheless, there is limited evidence from a few trials that vitamin D supplementation in early pregnancy might decrease fasting plasma glucose or GDM risk among deficient women (Sablok et al., 2015).

4. CONCLUSION

Although there are some differences in the diagnostic criteria and most of the evidence is observational, the findings suggest that screening and intervention of vitamin D deficiency in early pregnancy may have potential as a cost-effective, non-invasive approach for reducing the risk of GDM, in particular among high-risk populations. Given the increasing prevalence of GDM and vitamin D deficiency worldwide, the public health impact would be substantive. For the future, verification of causality by well-designed RCTs and the effect of timing, dose, and duration of vitamin D supplementation on GDM prevention needs to be elucidated. Until this

evidence is available, screening for vitamin D deficiency could be considered in pregnant women, particularly those with high BMI, dark skin, and insufficient sun exposure.

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Not applicable.

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Conflict of interest
The authors declare that there is no conflict of interest.

Data and materials availability
All data sets collected during this study are available upon reasonable request from the corresponding author.

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