



Vitamin D and Gestational Diabetes Mellitus: A Literature Review

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is one of public health concerns that can increase risk of harmful pregnancy outcome. Diabetes in pregnancy often associated with vitamin D level, it means that lack of vitamin D in pregnancy could raise the risk of gestational diabetes.

Objective: To describe the vitamin D blood level and pregnancy-related gestational diabetes incidence.

Methods: This literature review was taken from PubMed and Science Direct database. Screening of reviewed article based on inclusion and exclusion criteria.

Results: Seven articles that had been reviewed said pregnancy with gestational diabetes mellitus had lower 25(OH)D serum level than in non GDM group. The proportion of pregnant women which are sufficient of vitamin D is very low.

Conclusion: Pregnancy-related low vitamin D levels are linked to an elevated risk of gestational diabetes mellitus. Sufficient vitamin D levels are protective against GDM.

Keywords: Vitamin D deficiency, gestasional diabetes mellitus, pregnancy

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a pregnancy complication that is found to have glucose tolerance disorders, for example hyperglycaemia that is first identified during pregnancy.¹ According to the International Diabetes Federation (IDF), the prevalence of GDM in the world is 14% and an estimated 21.1 million live births are affected by hyperglycaemia during pregnancy, with about 80.3% caused by GDM.² GDM is one of the major causes of mortality and morbidity for both mothers and fetuses globally.³ The prevalence of GDM in Asia is estimated to be around 11.5%.⁴ In Indonesia, the prevalence of GDM ranges from 1.9% to 3.6% of pregnancies.⁵

Gestational diabetes mellitus has become a public health problem that has increased in recent years.⁶ In a short period of time, GDM increases the risk of adverse pregnancies outcome, and in the long term, it increases a mother's risk of developing diabetes type 2 and various cardiometabolic disorders in her offspring.⁷ Maternal complications associated with GDM include abortion, hypertension in pregnancy, preeclampsia, polyhydramnios, and also premature delivery.⁸ Effects on babies from mothers suffering from gestational diabetes include macrosomia, shortness of breath, intrauterine growth restriction (IUGR), and fetal death.⁹

As a fat-soluble vitamin, vitamin D has two types such as ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃).¹⁰ The

important role of vitamin D is to maintain calcium homeostasis and bone metabolism, can modulate congenital and adaptive immune functions, cardiovascular functions as well as proliferation and differentiation of keratinocytes.¹¹ In addition, vitamin D can also play a role in preventing diabetes and low levels of vitamin D correlate with the pathological conditions of pregnancy including gestational diabetes.¹² Globally, vitamin D deficiency generally occurs in about 54% of pregnancies.¹³ In Indonesia, the prevalence of pregnant women suffering from vitamin D deficiency is 99.6%, thus increasing the risk of GDM.⁵ The body of an individual with a severe vitamin D deficiency has a correlation to less exposure to sunlight.¹⁴ Vitamin D deficiency that occurs during pregnancy leads to increase insulin resistance and decrease in insulin secretion. This condition can affect glucose intolerance up to postpartum.¹⁵

GDM high concentrations of vitamin D in pregnant women in studies are reported to reduce the risk of developing GDM.¹⁶ The aim of this review literature is to discuss the description of serum vitamin D levels with the incidence of gestational diabetes, given that vitamin D deficiency is still very common in pregnant women.

METHODS

This research is a literature review that uses article searching taken from two database sources PubMed and ScienceDirect using keywords "vitamin D" OR "25(OH)D" OR

“vitamin D level” AND “gestational diabetes mellitus”. The inclusion criteria in the literature review are articles published from 2018 to 2023, articles in English, full-text articles, and study design articles using cohort, case-control, and cross sectional. While the exclusion criteria in this review are duplicate articles, research is not done on humans, and is irrelevant to the title and abstract.

The articles that have been obtained are screened using the PRISMA scheme. (*Preferred Reporting Items for Systematic Reviews & Meta-Analysis*) and can be found in Figure 1.

and inclusion criteria. The following article synthesizes data to discuss the description of vitamin D levels associated with gestational diabetes mellitus (Table 1).

Gestational diabetes mellitus is a condition of pregnant women who have diabetes and are first detected during the second or third trimester of pregnancy.² In addition, gestational diabetes mellitus is also characterized by failure to compensate for insulin secretion in response to increased insulin resistance during pregnancy.¹⁵ Vitamin D deficiency is linked to the incidence of diabetes in pregnancy.

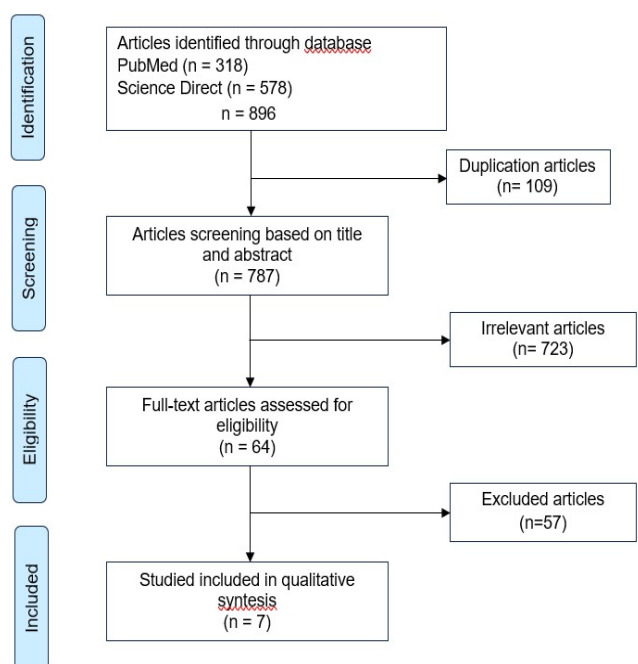


Figure 1. PRISMA scheme article searching

RESULTS AND DISCUSSION

According to the results of the search and screening of articles from the databases PubMed and Science Direct, the researcher obtained 7 articles that match the exclusion

Nu	Author, Year	Country	Title	Study Design	Sample	Results
1	Cheng et al. 2022	China	Maternal vitamin D status in early pregnancy and its association with gestational diabetes mellitus in Shanghai: a retrospective cohort study	Cohort	7816 pregnant women	The risk of gestational diabetic melitus decreases when the concentration of 25(OH)D \geq 20 ng/mL, whereas the concentrations of 25(OH) D \geq 30 ng/mL significantly decrease the risk of gestational diabetes mellitus compared with concentration of 25(OH)D $<$ 20 ng/mL ($p=0.01$).
2	Al-Ajlan et al. 2018	Saudi Arabia	Lower vitamin D levels in Saudi pregnant women are associated with higher risk of developing GDM	Cohort	515 pregnant women	The risk of GDM is significantly higher in the vitamin D deficiency group (OR:2.87;CI:1.32-6.25; $p=0.008$)
3	Xia et al. 2019	USA	Vitamin D status during in pregnancy and the risk of gestational diabetes mellitus: a longitudinal study in a multiracial cohort	Nested Case-control	107 GDM group 214 control group	Vitamin D deficiency levels $<$ 50 nmol/L at 10-14 weeks of pregnancy are significantly associated with an increased risk of GDM (OR=2.82, 95% CI: 1.15-6.93). Pregnant women who have a persistent deficiency at 10-14 and 15-26 weeks of pregnancy have a 4.46 times higher risk of developing GDM (OR=4.46, 95% CI: 1.15-17.3)
4	Yang et al. 2021	China	Vitamin D status and vitamin D deficiency risk factors among pregnancy of Shanghai in China	Cross-sectional	953 pregnant women	Women with gestational diabetes have lower levels of vitamin D than those without GDM group ($p=0.02$). Decreased vitamin D levels during pregnancy increase the risk of GDM.
5	Dwarkanath et al. 2019	India	Relationship of early vitamin D concentrations and gestational diabetes mellitus in Indian pregnant women	Cohort	392 pregnant women	Higher prevalence of GDM was found in the quartile group of pregnant women of the 1st trimester with the lowest plasma vitamin D levels compared to the other three quartile groups ($p=0.033$)

6	Yaqiong et al. 2020	China	Study on the levels of 25(OH)D, inflammation markers and glucose and fat metabolism indexes in pregnant women of Han nationality in Jiangsu province with gestational diabetes mellitus	Cross-sectional	110 GDM group 100 control group	Serum levels of 25(OH)D in the GDM group were significantly lower than in the control group ($p < 0.001$). Increased risk of developing GDM is associated with serum 25(OH)D levels.
7	Iqbal et al. 2020	India	Serum Vitamin D levels and gestational diabetes mellitus: analysis of early pregnancy cohort from a teaching hospital of Kashmir Valley	Cohort	290 pregnant women	Serum vitamin D levels < 30 nmol/L were found to be significantly higher in the gestational diabetes group ($p < 0.05$). Maternal vitamin D deficiency has been responsible to an increased risk of GDM in Khasmiri pregnant women.

This condition emerges as a consequence of vitamin D which is key to regulating liver metabolism, development of the Langerhans islet pancreas, oxidative stress, blood calcium levels, and immune system that can trigger the onset of gestational diabetes mellitus.¹³

Vitamin D deficiency includes risk factors for gestational diabetes mellitus. Low levels of vitamin D are risk factor for insulin resistance and glucose tolerance disorders. If there is an increase in vitamin D nutritional status during pregnancy then it is significantly associated with a decrease in incidence of gestational diabetes. A cross-sectional study by Yang et al. found that the vitamin D levels of 953 pregnant women in Shanghai, China, included 303 (31.8%) with severe vitamin D deficiency, 388 (40.7%) with vitamin D deficiency, 239 (239) with vitamin D insufficiency (25.1%), and only 23 (2.4%) with vitamin D sufficiency.¹⁷

In Saudi Arabia, the highest incidence rate of gestational diabetes is compared to a direct vitamin D deficiency. Pregnant women who have a concentration of 25(OH)D <50 nmol/L are classified as deficient in vitamin D whereas a level of 25(OH)D >50 nmol/L is defined as vitamin D sufficient. In the study by Al-Ajlan et al reported 425 pregnant women (82.5%) in the first trimester experienced vitamin D deficiency. In the second trimester, out of the 419 pregnant women who had vitamin D deficiency underwent an OGTT examination and 116 (27.7%) of them were diagnosed with gestational diabetes mellitus.

There is a correlation between vitamin D status and the incidence of gestational diabetes mellitus, this can be seen from the increased risk of developing GDM by 2.87 times higher in the vitamin D deficiency group compared to the non-vitamin D deficiency group.¹⁸ A study by Xia et al also showed persistent vitamin D deficiency in early to mid-pregnancy has a 4.46 times higher risk of gestational diabetes.¹⁹

There are a number of mechanisms for linking low levels of vitamin D to predisposition to gestational diabetes mellitus. Vitamin D plays an important role in modulating the function of pancreatic beta cells and their secretion through the binding of the active form of vitamin D in circulation with the vitamin D receptors of the beta cell and regulating the calcium balance between pools in extracellular and intracellular.²⁰ The active form of vitamin D metabolite 1,25(OH)₂D can inhibit the production and action of inflammatory cytokines, thereby reducing systemic inflammation and triggering the lifespan of pancreatic beta cells.¹⁹ Vitamin D can also trigger insulin sensitivity by stimulating expression of insulin receptors and increasing insulin responsibility for glucose transport. Furthermore, vitamin D is known to be involved in the regulation of extracellular calcium, with low vitamin D levels leading to insufficient intracellular cytosol calcium, which is required in intracellular activities mediated by insulin and glucose regulation.²¹

In recent years, more research has shown that vitamin D is involved in various

aspects of human health, particularly chronic diseases. Vitamin D deficiency can be associated with disorders glucose tolerance and the action of insulin secretion. The study by Yaqiong et al revealed that the gestational diabetic group had significantly lower serum 25(OH)D levels than the control group. Therefore, low levels of 25(OH)D have been linked to an increased risk of diabetes mellitus during pregnancy.²² Other studies also show that serum vitamin D levels of the GDM group are significantly lower compared to non-GDM.¹⁷ A cohort study conducted by Cheng et al also showed that low levels of maternal serum vitamin D were found in the GDM group while the maternal group with adequate levels of vitamin D showed a small proportion.¹⁶

Study by Iqbal et al obtained positive correlation that low concentrations of vitamin D in early pregnancy have a high risk of developing gestational diabetes. Based on quartile data, the lowest vitamin D quartile (≤ 23.6 nmol/L) had a higher proportion of gestational diabetes than higher levels of vitamin D quartile. A cohort study by Dwarkanath et al also showed that higher prevalence of gestational diabetes mellitus was found in early pregnancy with the lowest total plasma vitamin D levels in the quartile group (≤ 23.6 nmol/L) compared to the other three quartile groups.²⁰

Maternal vitamin D levels ≥ 20 ng/mL as significant protective factor against incidence of gestational diabetes.¹⁶ In pregnant women it is recommended to perform a serum vitamin D test when first antenatal care and resumed

in the second trimester. It has a beneficial effect on maternal and newborn mortality and morbidity.²¹ Studies by Xia et al found that testing for vitamin D in the first trimester of pregnancy helped identify the risk of developing gestational diabetes in pregnant women. High-risk pregnancies such as gestational diabetes mellitus, vitamin D supplementation may be considered to be given during pregnancy as a preventive effort against GDM and to maintain 25(OH)D levels above 20 ng/mL.^{16,19}

CONCLUSION

Risk factors for gestational diabetes due to vitamin D deficiency. Pregnancy with diabetes is associated with low serum vitamin D levels. Sufficiency of vitamin D levels is a preventable cause of gestational diabetes. Testing for vitamin D levels in the blood is necessary during the first antenatal care and the second trimester of pregnancy as an attempt at early detection of diabetes in pregnant women. The author hopes that there will be research ahead that focuses on the role of vitamin D supplementation in reducing the risk of gestational diabetes.

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CONFLICT OF INTEREST

The researcher in the writing of this review literature has no conflict of interest with the other parties.

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