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Meta-analysis

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Effect of Vitamin D Deficiency on Gestational Diabetes Mellitus: A Meta-Analysis

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ABSTRACT

Background: Gestational diabetes mellitus increases the risk of a number of short-term and long-term health problems in both mother and baby. Some evidence states that one of the causes of gestational diabetes mellitus is vitamin D deficiency. This study aimed to estimate the magnitude of the influence of vitamin D deficiency on the incidence of gestational diabetes mellitus, through a meta-analysis of previous primary studies.
Subjects and Method: This was a systematic review and meta-analysis with the following PICO, population: pregnant women, intervention: vitamin D deficiency, comparison: no vitamin D deficiency, outcome: gestational diabetes mellitus. The articles used in this study were obtained from four databases, namely PubMed, Google Scholar, Science Direct, and Springer Link, using the search keys "Vitamin D Deficiency"[Mesh] OR "Vitamin D Deficiency"[tw] AND "Diabetes, Gestational" [Mesh] OR "Gestational Diabetes Mellitus"[tw] OR "Gestational Diabetes"[tw]. The included article is a full-text cohort study design from 2018 to 2022 and reports the adjusted odds ratio (aOR) in a multivariate analysis. The selection of articles is done using PRISMA flow diagrams. Articles were analyzed using the Review Manager 5.3 application.
Results: A total of 9 cohort studies involving 42,972 pregnant women from the continents of Asia, Australia and Europe were used in the meta-analysis. Pregnant women with vitamin D deficiency had a risk of gestational diabetes mellitus 1.87 times compared to those without vitamin D deficiency (aOR= 1.87; 95% CI= 1.27 to 2.75; p= 0.002).
Conclusion: Vitamin D deficiency increases the risk of developing gestational diabetes mellitus.

Keywords: vitamin D deficiency, gestational diabetes mellitus, pregnancy

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BACKGROUND

Non-Communicable Diseases (PTM) cause 41 million deaths each year, equivalent to 74% of all deaths globally. Every year, 17 million people die from PTM before the age of 70, 86% of these premature deaths occur in low- and middle-income countries. One of the targets of the SDGs (Sustainable Development Goals) is to reduce by one third the premature death rate due to PTM through prevention and treatment (SDGs target 3.4). One of main types of PTM is diabetes. There are 1.5 million deaths every year due to diabetes (WHO, 2022). One of classifications of diabetes according to the ADA (2016) is Gestational Diabetes Mellitus (DMG). Globally, the prevalence of DMG varies widely, largely due to different diagnostic criteria. The latest meta-analysis reports, the global prevalence of GDM is 14.7% based on the criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG), the most widely used screening method worldwide (Saeedi et al., 2021).

DMG increases the risk of a number of short-term and long-term maternal health problems. DMG is associated with antenatal depression, premature birth, pre-eclampsia, type 2 diabetes mellitus (DMT2) later in life and susceptibility to cardiovascular disease (CVD). DMG can also have short and long term consequences for the baby. Among them result in macrosomia and are usually born by caesarean section, increased risk of hypoglycemia, risk of stillbirth, high risk of obesity, DMT2, CVD, and related metabolic diseases (Plows et al., 2018). The magnitude of problems caused by DMG requires an analysis of risk factors in prevention efforts. Accumulating evidence suggests, vitamin D, a fat-soluble nutriaent, plays an important role in the development of DMG (Silva et al., 2017). There are several clinical risk factors for developing gestational diabetes mellitus.

Recent evidence suggests that vitamin D plays a role in glucose metabolism and insulin sensitivity. Vitamin D deficiency has been associated with abnormal glucose metabolism, decreased insulin release and insulin sensitivity, and increased insulin resistance caused by pancreatic beta cell dysfunction in pregnancy (Berridge, 2017). This theory is in line with the research of Al-Ajlan et al. (2018), of 515 Saudi women was found that there was a relationship between vitamin D deficiency and an increased risk of gestational diabetes mellitus with an OR of 2.90 (95% CI= 1.07 to 7.89). Likewise, Dwarkanath et al. (2019), found that vitamin D deficiency had a risk of increasing the incidence of gestational diabetes mellitus in pregnant women with an OR= 2.32 (95% CI= 1.10 to 4.91). However, in a study by Zhu et al. (2019) concluded that vitamin D deficiency in early pregnancy was not significantly associated with the risk of developing gestational diabetes mellitus with an aOR= 0.78 (95% CI= 0.54 to 1.11).

Various studies have been conducted to see the effect of vitamin D deficiency on an increased risk of gestational diabetes mellitus, but the results of these studies have not shown consistent results. The results of several primary studies that have been carried out need to be processed again to obtain a higher level of statistical significance. This data processing is carried out by focusing on statistical summaries aimed at drawing conclusions that are more valid and reliable through meta-analysis studies.Based on that background, the authors are interested in conducting research on the effect of vitamin D deficiency on the incidence of gestational diabetes mellitus in pregnant women. This study aimed to estimate the magnitude of the influence of vitamin D deficiency on the incidence of gestational diabetes mellitus, through a meta-analysis of previous primary studies.

SUBJECTS AND METHOD

1. Study Design

This was a systematic review and meta-analysis. Article searches were conducted using 4 databases, namely: Pubmed, Google Scholar, Science Direct, and Springer Link which were published in 2018-2022 using the following keywords: "Vitamin D Deficiency"[Mesh] OR "Vitamin D Deficiency"-[tw] AND "Diabetes, Gestational"[Mesh] OR

“Gestational Diabetes Mellitus”[tw] OR “Gestational Diabetes”[tw].

2. Steps of Meta-Analysis

The meta-analysis was carried out through 5 steps as follows:

1) Formulate research questions in the PICO (Population, Intervention, Comparison, Outcome) format and develop more specific inclusion and exclusion criteria.
2) Browse literature from several databases, including Pubmed, Google Scholar, Science Direct, and Springer Link.
3) Conduct a study quality assessment (Critical Appraisal) of primary research articles.
4) Combine results and analyze data with Revman 5.3 software.
5) Putting findings in context.

3. Inclusion Criteria

Inclusion criteria in this study included full paper articles with a cohort study design, articles published in 2018 to 2022, research subjects were pregnant women, outcome of gestational diabetes mellitus research, multivariate analysis with adjusted odds ratio (aOR) to measure the estimated effect.

4. Exclusion Criteria

Exclusion criteria in this study included statistical results reported in the form of bivariate analysis and articles not in English.

5. Operational Definition of Variables

Article research was carried out by considering the eligibility criteria determined using the PICO model. The population of this study were pregnant women, the intervention used was vitamin D deficiency, the comparison in this study was no vitamin D deficiency and the outcome was gestational diabetes mellitus.

Vitamin D deficiency is a deficiency of serum 25(OH)D (vitamin D) in the body (less than 30 ng/mL).

Gestational Diabetes Mellitus is a degree of glucose intolerance first diagnosed in the second or third trimester of pregnancy, which is not clear whether type 1 or type 2 diabetes is preexisting.

6. Study Instruments

The instrument in this study was an article on the effect of vitamin D deficiency on the risk of developing gestational diabetes mellitus. Assessment of study quality was carried out quantitatively and qualitatively using a cohort study checklist sourced from the Center for Evidence Based Management (CEBMa) (2014). The critical appraisal process is carried out by cross-sharing between 2 independent people to get valid results.

7. Data Analysis

Research articles were selected according to predetermined criteria, then the results of the research were analyzed based on variations between studies using the fixed effect model and random effect model using RevMan 5.3 software. which serves to calculate the overall OR value by describing the 95% Confidence Interval (CI) using the effects model and data heterogeneity.

RESULTS

A search for articles in this study was conducted using the PubMed, Google Scholar, Science Direct, and Springer Link databases with the keywords "Vitamin D Deficiency"[Mesh] OR “Vitamin D Deficiency” [tw] AND "Diabetes, Gestational"[Mesh] OR “Gestational Diabetes Mellitus”[tw] OR “Gestational Diabetes”[tw] in the period 2018-2022. The article review process can be seen in Figure 1. The initial search process yielded 2,417 articles, after screening the articles, 1,838 articles were found, with 28 of them meeting the requirements for further full-text review. A total of 9 articles that met the quality assessment were included in the quantitative synthesis using meta-analysis. The selected research articles came from three continents, namely 7 articles from Asia, 1 article from Australia and 1 article from Europe, can be seen in Figure 2.

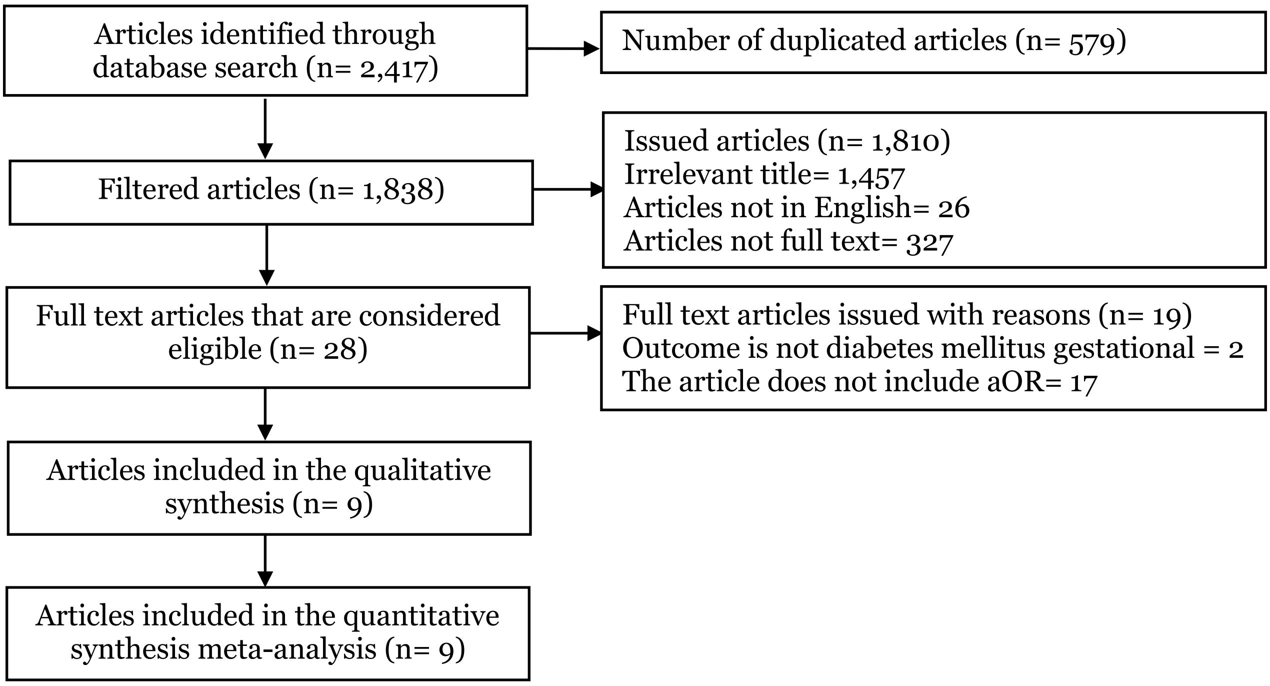

Figure 1. PRISMA flow diagram of the effect of vitamin D deficiency on the incidence of gestational diabetes mellitus

Figure 2. Map of the effect of vitamin D deficiency on gestational diabetes mellitus

Table 1, the researcher conducted an assessment of the quality of the study (critical appraisal). The nine articles that have been obtained from several data-bases need to be assessed to determine the quality of the articles before being used as material for meta-analysis. This research was conducted using a critical assessment checklist from a cohort study sourced from the Center for evidence based management (CEBMa) (2014). This assessment consists of 12 question criteria with each given a score of 2 = yes, 1 = don't know, and 0 = no answer, then added up. The results of assessment have been carried out, obtained 5 articles with a total score of 24, namely Cin et al. (2022), Eggemoen et al. (2018), Li et al. (2020), Luo et al. (2022), Shao et al. (2019). In addition, there are 4 articles with a total score of 23, namely Al-Ajlan et al. (2018), Dwarkanath et al. (2019) and Iqbal et al. (2020), and Mosavat et al. (2021).

Table 1. Critical appraisal checklist for cohort studies in meta-analysis

Primary Study	Criteria of Questions												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Al-Ajlan et al. (2018)	2	2	2	1	2	2	2	2	2	2	2	2	23
Cin-Aslan et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Dwarkanath et al. (2019)	2	2	2	1	2	2	2	2	2	2	2	2	23
Eggemoen et al. (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24
Iqbal et al. (2020)	2	2	2	1	2	2	2	2	2	2	2	2	23
Li et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24
Luo et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Mosavat et al. (2021)	2	2	2	1	2	2	2	2	2	2	2	2	23
Shao et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24

Description of the question criteria:

1 = Does the research address a clearly focused question/problem?
2 = Is the cohort research method (study design) appropriate to answer the research question?
3 = Are there enough research subjects to establish that the findings did not occur by chance?
4 = Was cohort selection based on objective and validated criteria?
5 = Is the cohort representative of the defined population?
6 = Was the follow-up done in sufficient time?
7 = Are the outcome criteria objective and unbiased?
8 = Are objective and validated measurement methods used to measure outcomes?
9 = Are effect sizes practically relevant?
10 = Is there a confidence interval given?
11 = Have confounding factors been taken into account?
12 = Can the results be applied to your research?

Description of the answer score:

0 = No
1 = Hesitant
2 = Yes

Table 2 shows that 9 articles from cohort studies as evidence of the linkage of the effect of vitamin D deficiency on the risk of developing gestational diabetes mellitus. Primary studies that met the specified criteria totaled 9 cohort research articles, with 7 articles from the continent of Asia (1 from Saudi Arabia, 1 from Turkey, 2 from India, 3 from China), 1 article from the continent of Australia (Western Australia), and 1 articles from continental Europe (Norway) involving a total sample of 42,972.

Table 2. Table 2. Summary of primary cohort study articles in the meta-analysis (N= 42,972)

Author (year)	Country	Sample size	P	I	C	O
Al-Ajlan et al. (2018)	Saudi Arabia	515	Pregnant mother	serum 25(OH)D <50 nmol/L	Sufficient vitamin D	GDM
Cin-Aslan et al. (2022)	Turkey	889	Pregnant mother	serum 25(OH)D <20 ng/mL	Sufficient vitamin D	GDM
Dwarkanath et al.(2019)	India	392	Pregnant mother	serum 25(OH)D <50 nmol/L	Sufficient vitamin D	GDM
Eggemoen et al. (2018)	Norway	745	Pregnant mother	serum 25(OH)D <50 nmol/L	Sufficient vitamin D	GDM
Iqbal et al. (2020)	India	290	Pregnant mother	serum 25(OH)D <50 nmol/L	Sufficient vitamin D	GDM
Li et al. (2020)	China	34,417	Pregnant mother	serum 25(OH)D 25-50 nmol/L	Sufficient vitamin D	GDM
Luo et al. (2022)	China	1,516	Pregnant mother	serum 25(OH)D <50 nmol/L	Sufficient vitamin D	GDM
Mosavat et al. (2021)	Western Australia	890	Pregnant mother	serum 25(OH)D 30-49 nmol/L	Sufficient vitamin D	GDM
Shao et al. (2019)	China	3,318	Pregnant mother	serum 25(OH)D <20 ng/mL	Sufficient vitamin D	GDM

Table 3 displays the value of the adjusted odds ratio (aOR), the lower limit and upper limit of the confidence interval for each article used in the study. The selection of articles in this study took into account articles that had controlled for confounding factors. According to Murti (2018), confounding factor is mixing the estimation of the relationship between exposure and the disease being studied, by other factors that are related, both to disease and exposure.

Table 3. Adjusted Odds Ratio (aOR) data on the effect of rotavirus vaccine on the incidence of diarrhea (N= 17,840)

Author (Year)	aOR	95%CI	
		Lower Limit	Upper Limit
Al-Ajlan et al. (2018)	2.90	1.07	7.89
Cin-Aslan et al. (2022)	10.60	2.82	39.76
Dwarkanath et al. (2019)	2.32	1.10	4.91
Eggemoen et al. (2018)	1.1	0.69	1.60
Iqbal et al. (2020)	2.31	1.14	4.91
Li et al. (2020)	1.023	0.95	1.09
Luo et al. (2022)	1.224	0.79	1.89
Mosavat et al. (2021)	12.52	1.27	23.75
Shao et al. (2019)	2.19	1.16	4.14

The forest plot in Figure 3 shows that there is an effect of vitamin D deficiency on the incidence of gestational diabetes mellitus. Pregnant women with vitamin D deficiency had a risk of developing gestational diabetes mellitus 1.87 times compared to those without vitamin D deficiency, and this effect was statistically significant (aOR= 1.87; 95% CI= 1.27 to 2.75; p= 0.002). Forest plots show very large variation in effect estimates between studies with heterogeneity of study data showing I^2 = 77%; p= 0.002, so that the interpretation of the results of the calculation of the average effect estimate is carried out using a random effect model approach

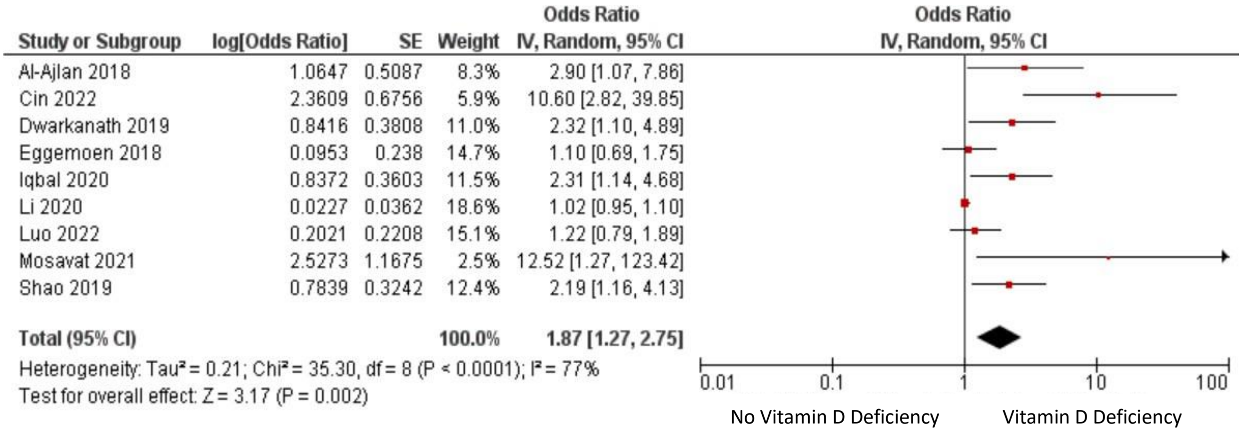

Figure 3. Forest plot of the effect of vitamin D deficiency on the incidence of gestational diabetes mellitus

Figure 4 shows a funnel plot with an asymmetric distribution of effect estimates, where 6 plots are on the right and 3 plots on the left. This indicates publication bias. Bias also occurs from an imbalance between the distances between studies on both the right and left sides of the funnel plot. Publication bias in this study overstates the true effect (over-estimation), because the distribution of effect estimates is more to the right of the vertical line and the average effect estimate in the forest plot is also to the right of the null hypothesis vertical line. The plot on the left side of the graph has a standard error between 0 to 0.5 and the plot on the right has a standard error between 0 to 1.5.

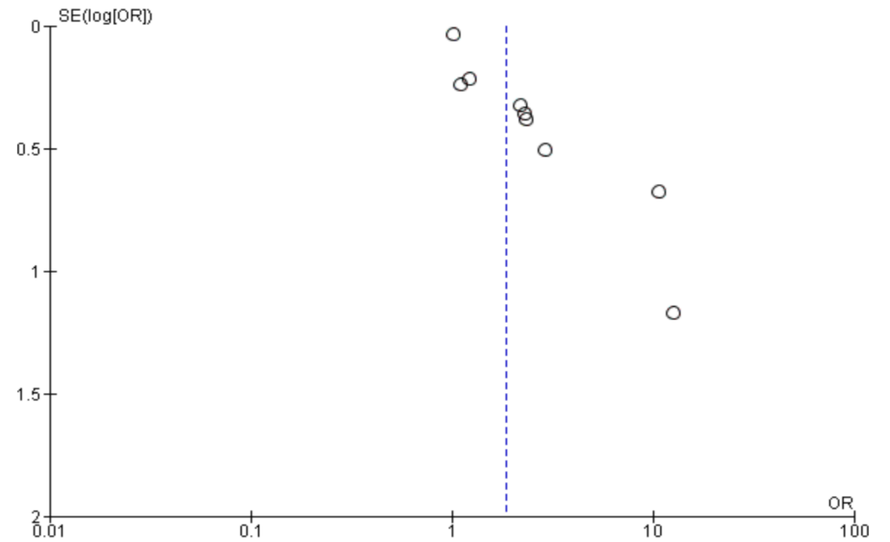

Figure 4. Funnel plot of the effect of vitamin D deficiency on the incidence of gestational diabetes mellitus

DISCUSSION

This systematic review and meta-analysis study combines several primary studies regarding the effect of vitamin D deficiency on the incidence of gestational diabetes mellitus. The independent variable analyzed was vitamin D deficiency. The dependent variable in this study was gestational diabetes mellitus. This systematic review and meta-analysis of several primary studies suggests an epidemiological study design with a larger sample size from several countries thus providing a basis for concluding that vitamin D deficiency has a statistical effect on the incidence of gestational diabetes mellitus.

This systematic review and meta-analysis study used primary research that controlled for confounding factors indicated by the inclusion requirements of the study, namely multivariate analysis and the reported statistical results were adjusted odds ratio (aOR). According to Murti (2018), confounding factor is mixing the estimation of the relationship between exposure and disease which is examined by other factors that are related, both to disease and exposure. Confounding factors influencing the relationship or effect of exposure to disease occurrence were estimated by studies to be dissimilar to the actual relationship or effect in the target population, or to invalid (incorrect) study results.

This study uses articles with an observational study design, namely cohorts. Primary studies that met the criteria totaled 9 research articles consisting of 7 articles from the continent of Asia, 1 article from the continent of Australia, and 1 article from the continent of Australia involving a total sample of 42,972. The population taken from several regions and the instruments used in various articles form heterogeneity.

The results of the systematic review and meta-analysis studies that have been conducted show that pregnant women with vitamin D deficiency have a risk of gestational diabetes mellitus 1.87 times compared to those without vitamin D deficiency (aOR= 1.87; 95% CI= 1.27 to 2.75; p=0.002). This research is in line with Wang et al. (2019) in a meta-analysis study which stated that vitamin D deficiency was associated with a high risk of developing DMG (OR= 1.15; 95% CI= 1.07 to 1.23) with p<0.001. Results of a meta-analysis study by Amraei et al. (2018) also stated that vitamin D deficiency in pregnant women had an effect on an increased risk of developing DMG (OR= 1.18; 95% CI= 1.01 to 1.35) with p<0.001. Likewise with Milajerdi et al. (2021) stated that there was a relationship between vitamin D deficiency and the risk of developing DMG (OR= 1.26; 95% CI= 1.13 to 1.41) with evidence of significant heterogeneity (I^2= 71.3%; p<0.001).

A possible mechanism related to the relationship between vitamin D and gestational diabetes mellitus is that the direct effect of vitamin D on the performance of pancreatic β cells has a regulatory effect on the circulating rate of glucose in the blood which is channeled through the linkage of 1.25 (OH)2D3 to vitamin D recipients in pancreatic β cells. Glucose stimulates the expression of insulin receptors and the enzyme 25-hydroxyvitamin D-1-α-hydroxylase and increases insulin response to transfusion (Vaidya and Williams, 2012). Since Vitamin D is also known to regulate extracellular calcium, low levels of Vitamin D can lead to inadequate intracellular cytosolic calcium, which is required for insulin-mediated intracellular processes and glucose regulation (El-Lithy et al., 2014).

Vitamin D directly works with its receptors in the nucleus of pancreatic β cells to regulate the secretion of glucose-regulating hormones (Bellan et al., 2014). Vitamin D also influences insulin-mediated intracellular glucose metabolism by acting on intracellular calcium regulatory mechanisms (Seshadri et al., 2011). A significant association has been found between serum vitamin D concentrations and low levels of inflammation, which has been recognized as a risk factor for diabetes (Haidari et al., 2016). Vitamin D deficiency increases the inflammatory response through the NF-kB pathway by regulating p-p65/RelB in pancreatic tissue (Wang et al., 2019). Excessive Ca2+ and reactive oxygen species (ROS) in β cells that occur in vitamin D deficiency, result in cell death and diabetes (Berridge, 2017).

Based on the results of these studies, pregnant women need to meet the adequacy of vitamin D in the body. Adequate levels of vitamin D have the potential to improve glucose homeostasis. Many epidemiological studies suggest that serum 25(OH)D levels above 30 ng/ml may have the additional health benefit of reducing diabetes risk. Guidelines for minimal vitamin D intake in pregnant women are a minimum daily requirement of 600 IU/day during pregnancy (Holick et al., 2011), although evidence indicates the need for additional supplementation to reduce the risk of GDM.

Vitamin D supplementation during pregnancy is advised to prevent adverse pregnancy outcomes and vitamin D deficiency in both mother and baby. Vitamin D supplementation of 4000 IU/day is more effective in reducing vitamin D deficiency in pregnant women and increasing serum levels of 25(OH)D in mothers and neonates compared to 2000 IU/day and 400 IU/day (Nausheen et al., 2021). Adequacy of vitamin D before 20 weeks of gestation is a protective factor against gestational diabetes mellitus (Yue and Ying, 2020).

The advantage of this study is that the sample size is larger than the primary studies used, thereby providing a basis for concluding that vitamin D deficiency has a statistical effect on the incidence of gestational diabetes mellitus. However, the researcher realizes that there are limitations to this research, namely publiccation bias shown in the funnel plot results and search bias because it only uses four databases.

AUTHOR CONTRIBUTION

The DH is the principal researcher who selects topics, searches for and collects research data. EPP and BM analyzed data and reviewed research documents.

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The study was self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

REFERENCES

ADA (2016). Position Statement: Standards of Medical Care in Diabetes. Diabetes Care. 39.

Al-Ajlan A, Al-Musharaf S, Fouda MA, Krishnaswamy S, Wani K, Aljohani NJ, Al-Serehi A, et al. (2018). Lower vitamin D levels in Saudi pregnant women are associated with higher risk of developing GDM. BMC Pregnancy Childbirth. 18(1). doi: 10.1186/s12884-018-1723-3.

Amraei M, Mohamadpour S, Sayehmiri K, Mousavi SF, Shirzadpour E, Moayeri A. (2018). Effects of Vitamin D Deficiency on Incidence Risk of Gestational Diabetes Mellitus: A Systematic Review and Meta analysis. Frontiers in endocrinology. 9 (7) doi: 10.3389/fendo.2018.00007.

Bellan M, Guzzaloni G, Rinaldi M, Merlotti E, Ferrari C, Tagliaferri A, Pirisi M, et al (2014). Altered glucose metabolism rather than naive type 2 diabetes mellitus (T2DM) is related to vitamin D status in obesity. Cardiovasc Diabetol. 13.

Berridge MJ (2017). Vitamin D deficiency and diabetes. Biochem J. 474: 1321–32. doi: 10.1042/BCJ20170042.

Cin-Aslan NN, Yalçin M, Yardimci H (2022). Vitamin D deficiency during the first trimester of pregnancy and the risk of developing gestational diabetes mellitus. J Obstet Gynecol Neonatal Nurs. 51(5): 526-535. doi: 10.1016/j.jogn.2022.06.038.

Dwarkanath P, Vinotha P, Thomas T, Joseph S, Thomas A, Shirley G, Sheela CN, et al. (2019). Relationship of Early Vitamin D Concentrations and Gestational Diabetes Mellitus in Indian Pregnant Women. Front Nutr. 6. doi: 10.3389/fnut.2019.00116.

Eggemoen ÅR, Waage CW, Sletner L, Gulseth HL, Birkeland KI, Jenum AK (2018). Vitamin D, Gestational Diabetes, and Measures of Glucose Metabolism in a Population-Based Multiethnic Cohort. J Diabetes Res. doi: 10.1155/2018/8939235.

El-Lithy A, Abdella RM, El-Faissal YM, Sayed AM, Samie RM (2014). The relationship between low maternal serum Vitamin D levels and glycemic control in gestational diabetes assessed by HbA1c levels: An observational cross-sectional study. BMC Pregnancy Childbirth. 14: 1-6.

Haidari F, Zakerkish M, Karandish M, Saki A, Pooraziz S (2016). Association between serum Vitamin D level and glycemic and inflamematory markers in non-obese patients with type 2 diabetes. Iran J Med Sci. 41.

Holick MF (2017). The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord. 18: 153–165. doi: 10.1007/s11154-017-9424-1.

Iqbal S, Malik M, Bano G (2020). Serum Vitamin D levels and gestational diabetes mellitus: analysis of early pregnancy cohort from a teaching hospital of Kashmir Valley. J Family Med Prim Care. 9(8):4323-4328. doi: 10.4103/jfmpc.jfmpc_900_20

Li H, Ma J, Huang R, Wen Y, Liu G, Xuan M, Yang L, et al. (2020). Prevalence of vitamin D deficiency in the pregnant women: an observational study in Shanghai, China. Arch Public Health. 78. doi: 10.1186/s13690-020- 00414-1.

Luo C, Li Z, Lu Y, Wei F, Suo D, Lan S, Ren Z, et al (2022). Association of serum vitamin D status with gestational diabetes mellitus and other laboratory parameters in early pregnant women. BMC Pregnancy Childbirth. doi: 10.1186/s12884-022-04725-9.

Milajerdi A, Abbasi F, Mousavi SM, Esmaillzadeh A (2021). Maternal vitamin D status and risk of gestational diabetes mellitus: A systematic review and meta-analysis of prospective cohort studies. Clin Nutr. 40(5): 2576-2586. doi: 10.10 16/j.clnu.2021.03.037.

Mosavat M, Arabiat D, Smyth A, Newnham J, Whitehead L (2021). Second-trimester maternal serum vitamin D and pregnancy outcome: The Western Australian Raine cohort study. Diabetes Res Clin Pract.

175. doi: 10.1016/j.diabres.2021.1-08779.

Murti B (2018). Principles and Methods of Epidemiological Research (5th ed.). Master's Program of Public Health, Universitas Sebelas Maret.

Nausheen S, Habib A, Bhura M, Rizvi A, Shaheen F, Begum K, Iqbal J, et al (2021). Impact evaluation of the efficacy of different doses of vitamin D supplementation during pregnancy on pregnancy and birth outcomes: a randomised, controlled, dose comparison trial in Pakistan. BMJ Nutrition, Prevention & Health. doi: 10.1136/bmjnph-2021-000304.

Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH (2018). The Patho-physiology of Gestational Diabetes Mellitus. Int J Mol Sci. 19(11): 3342. doi: 10.3390/ijms1-9113342.

Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D (2021). Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. Diabetes Res Clin Pract. 172. doi: 10.1016/-j.diabres.2020.108642.

Seshadri KG, Tamilselvan B, Rajendran A (2011). Role of vitamin D in Diabetes. J Endocrinol Metab. 1.

Shao B, Mo M, Xin X, Jiang W, Wu J, Huang M, Wang S, et al. (2019). The interaction between prepregnancy BMI and gestational vitamin D deficiency on the risk of gestational diabetes mellitus subtypes with elevated fasting blood glucose. Clin Nutr. 39(7):2265-2273. doi: 10.1016/j.clnu.2019.10.015.

Silva-Zolezzi I, Samuel TM, Spieldenner J (2017). Maternal nutrition: opportunities in the prevention of gestational diabetes. Nutr Rev. 75. doi: 10.1093/nutrit/nuw033.

Vaidya A, Williams JS (2012). Vitamin D and insulin sensitivity: can gene association and pharmacogenetic studies of the vitamin d receptor provide clarity? Metab Clin Exp 61: 759–61. doi:10.1016/j. metabol.20-11.12.009.

Wang W, Zhang J, Wang H, Wang X, Liu S (2019). Vitamin D deficiency enhances insulin resistance by promoting inflammation in type 2 diabetes. Int J Clin Exp Pathol. 12: 1859e67.

WHO (2022). Noncommunicable disease. World Health Organization.

Yue CY, Ying CM (2020). Sufficience serum vitamin D before 20 weeks of pregnancy reduces the risk of gestational diabetes mellitus. Nutr Metab (Lond). doi: 10.1186/s1298-6-020-00509-0.

Zhu B, Huang K, Yan S, Hao J, Zhu P, Chen Y, Ye A, Tao F (2019). VDR Variants rather than Early Pregnancy Vitamin D Concentrations Are Associated with the Risk of Gestational Diabetes: The Ma'anshan Birth Cohort (MABC) Study. J Diabetes Res. doi: 10.1155/20-19/8313901.