Research Article

Vitamin D Levels and Its Influence on Maternal Blood Glucose, Blood Pressure, and Fetal Weight: A Cross-Sectional Study

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Abstract

Objective: To examine the impact of maternal Vitamin D levels on blood sugar, blood weight, and fetal weight.

Methods: All maternity patients from two selected public primary health care in Semarang, Indonesia were selected in this study. Twenty-six pregnant women were analyzed for vitamin D serum. Maternity outcome then were evaluated for blood glucose, blood pressure and estimated fetal weight using ultrasonography.

Results: Our study found a normal range of vitamin D levels of pregnant women in Semarang followed by normal glucose level and systolic pressure. Pearson's correlation rank test for Vitamin D with estimated fetal weight, blood glucose, systolic blood pressure, and gestational ages as covariate showed a non-significant P value.

Conclusion: No significant correlation was found between maternal vitamin D level and blood glucose, blood pressure, or estimated fetal weight

Keywords: blood pressure, fetal weight, maternal blood glucose, vitamin D.

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INTRODUCTION

Vitamin D is a fat-soluble vitamin primarily obtained from sunlight exposure and several natural food sources, including liver, egg yolks, fatty fish, mushrooms, and fish liver oils. Calciferol, the general term for the two physiologically active forms of vitamin D, D_2 and D_3 undergoes similar metabolic processes. Both forms experience two hydroxylation steps: first in the liver to produce 25-hydroxyvitamin D and then in the kidney to form 1,25-dihydroxyvitamin D.[1] Vitamin D is required for numerous physiological processes, including the regulation of inflammation, free radicals, immune function, and cell division and proliferation. It also contributes to the prevention of infections, cancer, metabolic disorders such as diabetes, and thyroid dysfunction.[2]

Vitamin D insufficiency is a global concern, including among pregnant women. Maternal deficiency has been linked to increased risks of preeclampsia, infection, cesarean delivery, gestational diabetes mellitus, and fetal growth restriction. Vitamin D supplementation during pregnancy has therefore been recommended to prevent adverse outcomes.[3] Although the optimal intake during pregnancy remains uncertain, it is likely higher than the commonly suggested 200–400 IU per day. In 2010, the Institute of Medicine established 600 IU per day as the recommended intake for pregnant women.[4] Evidence also suggests that vitamin D requirements during pregnancy and lactation may be higher than previously assumed.[5] Studies have shown that daily supplementation exceeding 1000 IU may be necessary to maintain adequate circulating 25(OH)D concentrations.[6,7] The Endocrine Society therefore recommends 1500–2000 IU per day, with a target maternal serum 25(OH)D level above 30 ng/mL.[8] Hollis and colleagues subsequently

demonstrated that daily supplementation with 4000 IU resulted in 83.9% of pregnant women achieving at least 32 ng/mL at delivery, a level considered protective for maternal health.[9]

Several studies have proposed a potential link between low vitamin D levels and gestational diabetes.[10,11] Vitamin D insufficiency has also been observed to be more common among pregnant women with diabetes than among those without diabetes.[12,13] Likewise, low circulating vitamin D levels have been associated with a higher incidence of hypertensive disorders in pregnancy.[14] Beyond maternal risks, inadequate maternal vitamin D status may adversely affect fetal development. Adequate maternal 25(OH) D and calcium reserves are essential for fetal bone formation and mineralization, as calcium is actively transported across the placenta. Previous studies have shown a positive association between maternal serum $1,25(OH)_2D$ levels and calcium absorption during pregnancy.[15] Severe maternal calcium deficiency may result in neonatal rickets, hypocalcemia, and skeletal abnormalities.[16,17] Since the fetus relies primarily on maternal 25(OH) D, fetal serum concentrations are typically about 25% lower than those of the mother.[18]

In line with the evidence above, low maternal serum vitamin D levels may be associated with several adverse pregnancy outcomes. However, data on the effects of vitamin D supplementation on maternal and neonatal health remain limited. Only a small number of studies have explored the mechanisms through which vitamin D may influence glucose metabolism, hypertension, and fetal growth. Additionally, most investigations on vitamin D status and pregnancy outcomes have been observational. Therefore, the primary objective of this study was to evaluate the impact of maternal vitamin D levels on fetal weight, systolic blood pressure, and maternal blood glucose levels.

METHODS

A cross-sectional study was conducted among pregnant women in public primary health care in Semarang, Central Java, Indonesia between September – October 2023. This study have been approved by Ethical Committee of Sultan Agung Islamic University (No.29/KEPK-RSISA/II/2025).

A purposive sampling methods were used in this study to select public primary health care in Semarang. Of all 37 public primary health care in Semarang, two were selected to reflect urban and rural area. All pregnant women from two selected public primary health care were included in the study as long as not met the exclusion criteria, including, women with thyroid or parathyroid disorders, pregnant women with diabetes history, and those individuals who have consumed *Vit. D* supplements within previous six months. All agreed participants were given an informed consent to enrolled in this study.

Vitamin D levels were measured using Enzyme Linked Immunosorbent Assay (ELISA) for 25(OH) D using blood serum samples taken from patients on their visit to the primary healthcare according to manufacture protocol (DuoSet® ELISA, R&D System, Mineapolis, USA). From the same serum, glucose levels were analyzed using Glucose Assay reagent (Sigma Aldrich, Merck, Darmstadt, Germany) according to manufacture protocol.

To asses the correlation between vitamin D levels and clinical outcome of pregnant women, blood pressure was measure twice on a resting condition using standardized sphygmomanometer (Rudolf Riester GmbH, Jungingen, Germany). Estimated fetal weight was measured using ultrasonography (Philips, Eindhoven, The Netherlands) operated by single obstetrician.

Statistical analysis was conducted using SPSS Statistics version 17.0 (SPSS Inc., Chicago, Illinois, USA). The appropriate correlation test was selected based on data distribution: Pearson's correlation coefficient was used for normally distributed data, while Spearman's rank correlation coefficient was applied to non-normally distributed data. A two-tailed p-value less than 0.05 ($p < 0.05$) was considered to indicate statistical significance.

RESULTS

We recruited twenty-six pregnant women in two public primary health care in Semarang, including Puskesmas Lebdosari and Puskesmas Mijen. The participants average was 28.08 ± 5.67 years old. Gestational age was predominantly in the third semester (53.8%), with a mean of 27.21 ± 10.21 weeks, measured by ultrasonography and operate by obstetrician/gynecologist. The average Body Mass Index (BMI) of participants was 25.84 ± 4.32 kg/m2, with most classified as normal weight (42.3%), followed by overweight (30.8%), obese (19.2%), and underweight (7.7%). Mean vitamin D levels were 23.56 ± 3.57 ng/ml, indicating values within the normal range. Blood

glucose levels averaged 146.42 ± 32.13 mg/dl, while the estimated fetal weight, measured by ultrasonography, had a mean of 1333.57 ± 111.33 grams. As seen in the table 1, the results of normality test obtained P>0.05, so the data can be tested using the parametric correlation test.

The study involved twenty-six pregnant women. The subject's attributes are shown in the following table.

Table 1. Research Characteristics Data

Characteristics	n	%	Mean	Tests of Normality
Age, mean± SD			28.08± 5.67	0.91
Gestational Age (trimester),				0.49
First				
Second	3	11.5		
Third	9	34.6		
(weeks)	14	53.8	27.21± 10.21	
Body Mass Index (Kg/m²)				
Underweight	2	7.7	25.84 ± 4.32	0.73
Normal weight	11	42.3		
Overweight	8	30.8		
Obesity	5	19.2		
Vit. D levels (ng/dl)			23.56± 3.57	0.86
Blood Glucose levels (mg/dl)			146.42± 32.13	0.2101
Systolic Blood Pressure			119.06± 16.95	0.62
Estimated Fetal Weight			1333.57± 1111.33	0.34

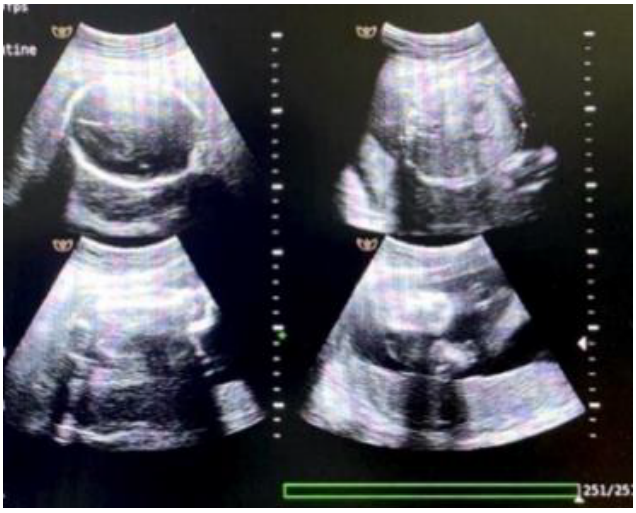

Figure 1. Ultrasonography: operate by obstetrician/gynecologist

Table 2. Correlation Analysis Vit. D levels and other variables

Vit. D Levels	*P-value*
Blood Glucose	0.703
Systolic Blood Pressure	0.405
Gestational Age	0.955
Estimated Fetal Weight	0.84

Note: Pearson's Correlation Rank Test, significance p<0,05

The Pearson's correlation rank test results for *Vit. D* with estimated fetal weight, blood glucose, systolic blood pressure, and gestational ages showed a value of P>0.05. Statistically, it means that there is no correlation between *Vit. D* and other variables.

DISCUSSION

In obstetrics and gynecology aspect, *Vit. D* is considered as crucial in sustaining pregnant women's health and treating illnesses. As previously stated, the Endocrine Society suggests 30 ng/ml of *Vit. D* for pregnant woman, whilst The Established of Pharmaceutical proposes 20 ng/ml.[4,8]. A study demonstrates that pregnant women at first trimester likely have lower serum *Vit. D* levels that non-pregnant women of similar age.[19] within this study the average serum *Vit. D* level among all participants was recorded at 23.56 ng/ml. While this concentration is in line with the Institute of Medicine standards, it falls short of the Endocrine Society's suggested criteria. Insufficient levels of 25(OH)D in the serum have been associated to several adverse pregnancy results, including gestational diabetes, preeclampsia, and the birth of children categorized as undersized for their gestational age.[12,13,20–25] Previous researchers conducted a comprehensive investigation and a meta-analysis, revealing a connection between maternal vitamin D levels and the prevalence of

gestational diabetes. [26] A recent research study has indicated that pregnant women who received 50,000 IU of *Vit. D* every two weeks exhibited a reduced risk of developing gestational diabetes compared to those who received 400 IU daily. Nevertheless, some research indicates that giving the mother a daily dosage of 5000 IU of *Vit. D*3 at an average gestational age of 14 weeks did not raise her blood glucose levels in contrast to the control group.[27] Furthermore, research revealed that providing 50,000 IU of *Vit. D* every two weeks to expectant mothers beginning at week 12 and continuing until delivery significantly lowered insulin resistance.[20]

During a normal pregnancy, an increase in RAS activation causes increased quantities of renin and angiotensin I and II to be released into the blood. Renin, angiotensin I, and II circulation levels were lower in PE than in a typical pregnancy. However, in response to stimuli, the autoantibody against angiotensin II and the plasma receptor for renin were both activated.[2] 1.25 (OH)2D can decrease the transcription of the renin gene through a mechanism that depends on the VDR, and PE patients have higher plasma levels of active renin that women with normotension. This causes signaling to increase systemic blood pressure.[28,29] After entering the circulation, *Vit. D* is hydrolyzed in the liver to produce 25-hydroxy*Vit. D* (25[OH] D), which then gets transformed by the kidneys to 1,25-dihydroxy*Vit. D* (1.25[OH]D). The fetus absorbs *Vit. D* from the mother in the active form, 1.25 (9OH)2D. The failure of 1.25(OH)2D synthesis and the consequences on blood pressure control induced by injury to the kidney and placenta's blood vessel cells causes blood pressure to increase.[15,30]

It is commonly known that *Vit. D* affects the development of fetal bone mineral and that changes in a woman's calcium homeostasis during pregnancy increasing the amount of calcium available for the mineralization of the quickly expanding fetal skeleton.[31] Studies on the mother-child interaction have indicated that low *Vit. D* levels in mothers significantly impair the fetus' capacity to acquire bone minerals.[32] The study, which included 39 pregnant women, found that the neonate's *Vit. D* levels were connected to maternal concentrations throughout the third trimester but had no association with the newborn's birth weight.[33]

Our results did not align with those of some earlier research. This study is observational, like the majority of research on *Vit. D* levels in expectant mothers. Consequently, it is typically challenging to achieve a uniform distribution of data. Numerous previous investigations have shown diverse and perhaps conflicting findings. This is caused by a variety of circumstances, including the lifestyle, education, and background of expectant mothers. We believe this to be the underlying cause of our study's findings. More homogeneous individuals and an examination of the research subjects' backgrounds and lifestyles are required for future studies.

CONCLUSION

According to our research, low fetal weight, premature labor, preeclampsia incidence, and blood glucose levels are all unaffected by *Vit. D* levels.

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REFERENCES

1. De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database Syst Rev. 2016;(1):CD008873. doi:10.1002/14651858.CD008873.pub3
2. Wibowo N. The existing facts regarding the level of vitamin D in pregnant women in Indonesia. Indones J Obstet Gynecol. 2023;11(3): 128-9. doi:10.32771/inajog.v11i3.2116
3. De-Regil LM, Palacios C, Ansary A, Kulier R, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database Syst Rev. 2012;(2):CD008873. doi:10.1002/14651858.CD008873.pub2
4. Ross AC, Taylor CL, Yaktine AL, Del Valle HB, editors. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC. National Academies Press. 2011. doi:10.17226/13050
5. Hollis BW, Wagner CL. Assessment of dietary vitamin D requirements during pregnancy and lactation. Am J Clin Nutr. 2004;79(5):717–26. doi:10.1093/ajcn/79.5.717
6. Vieth R, Chan PC, MacFarlane GD. Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level. Am J Clin Nutr. 2001;73(2):288–94. doi:10.1093/ajcn/73.2.288
7. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. Am J Clin Nutr. 2003;77(1):204–210. doi:10.1093/ajcn/77.1.204

8. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911–30. doi:10.1210/jc.2011-0385
9. Hollis BW, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: Double-blind, randomized clinical trial of safety and effectiveness. J Bone Miner Res. 2011;26(10):2341–57. doi:10.1002/jbmr.463
10. Clifton-Bligh RJ, McElduff P, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. Diabet Med. 2008;25(6):678–84. doi:10.1111/j.1464-5491.2008.02422.x
11. Lau SL, Gunton JE, Athayde NP, Byth K, Cheung NW. Serum 25-hydroxyvitamin D and glycated haemoglobin levels in women with gestational diabetes mellitus. Med J Aust. 2011;194(7):334–7. doi:10.5694/j.1326-5377.2011.tb03000.x
12. Soheilykhah S, Mojibian M, Rashidi M, Rahimi-Saghand S, Jafari F. Maternal vitamin D status in gestational diabetes mellitus. Nutr Clin Pract. 2010;25(5):524–7. doi:10.1177/0884533610379851
13. Maghbooli Z, Hossein-Nezhad A, Karimi F, Shafaei AR, Larijani B. Correlation between vitamin D3 deficiency and insulin resistance in pregnancy. Diabetes Metab Res Rev. 2008;24(1):27–32. doi:10.1002/dmrr.737
14. Karmia HR, Fadhillah T. The low level of serum 1,25-dihydroxyvitamin D3 and calcium in preeclampsia women and its impact on maternal outcomes. Indones J Obstet Gynecol. 2023;11(4):228-34. doi:10.32771/inajog.v11i4.1931
15. Purswani JM, Gala P, Dwarkanath P, Larkin HM, Kurpad A, Mehta S. The role of vitamin D in pre-eclampsia: a systematic review. BMC Preg Childbirth. 2017;17(1):231. doi:10.1186/s12884-017-1408-3
16. Pérez-López FR, Pasupuleti V, Mezones-Holguin E, et al. Effect of vitamin D supplementation during pregnancy on maternal and neonatal outcomes: a systematic review and meta-analysis of randomized controlled trials. Fertil Steril. 2015;103(5):1278–84.e4. doi:10.1016/j.fertnstert.2015.02.019
17. Kovacs CS. Bone metabolism in the fetus and neonate. Pediatr Nephrol. 2014;29(5):793–803. doi:10.1007/s00467-013-2461-4
18. Karras SN, Wagner CL, Castracane VD. Understanding vitamin D metabolism in pregnancy: From physiology to pathophysiology and clinical outcomes. Metabolism. 2018;86:112–23. doi:10.1016/j.metabol.2017.10.001
19. Sukarsa RA, Budi RS, Purwara BH, Syam HH, Sadikin H. Differences of vitamin D level in non-pregnant reproductive age women and first trimester pregnant women. Indones J Obstet Gynecol. 2019;7(4):271-6. doi:10.32771/inajog.v7i4.998
20. Soheilykhah S, Mojibian M, Moghadam MJ, Shojaoddiny-Ardekani A. The effect of different doses of vitamin D supplementation on insulin resistance during pregnancy. Gynecol Endocrinol. 2013;29(4):396–9. doi:10.3109/09513590.2012.752456
21. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care. 2004;27(Suppl 1):S88–S90. doi:10.2337/diacare.27.2007.s88
22. Zhang C, Qiu C, Hu FB, et al. Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes mellitus. PLoS One. 2008;3(11):e3753. doi:10.1371/journal.pone.0003753
23. Makgoba M, Nelson SM, Savvidou M, Messow CM, Nicolaides K, Sattar N. First-trimester circulating 25-hydroxyvitamin D levels and development of gestational diabetes mellitus. Diabetes Care. 2011;34(5):1091–3. doi:10.2337/dc10-2264
24. Parlea L, Bromberg IL, Feig DS, Vieth R, Merman E, Lipscombe LL. Association between serum 25-hydroxyvitamin D in early pregnancy and risk of gestational diabetes mellitus. Diabet Med. 2012;29(7):e25–e32. doi:10.1111/j.1464-5491.2011.03550.x
25. Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies. BMJ. 2013;346:f1169. doi:10.1136/bmj.f1169
26. Poel YHM, Hummel P, Lips P, Stam F, van der Ploeg T, Simsek S. Vitamin D and gestational diabetes: a systematic review and meta-analysis. Eur J Intern Med. 2012;23(5):465–9. doi:10.1016/j.ejim.2012.01.007
27. Yap C, Cheung NW, Gunton JE, et al. Vitamin D supplementation and the effects on glucose metabolism during pregnancy: a randomized controlled trial. Diabetes Care. 2014;37(7):1837–44. doi:10.2337/dc14-0155
28. Nassar K, Rachidi W. Vitamin D and pre-eclampsia. Gynecol Obstet (Sunnyvale). 2016;6(6):389. doi:10.4172/2161-0932.1000389
29. Mogi M. Renin-angiotensin system in the placenta of women with preeclampsia. Hypertens Res. 2023;46(9):2243–4. doi:10.1038/s41440-023-01356-1
30. Palacios C, De-Regil LM, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation during pregnancy: updated meta-analysis on maternal outcomes. J Steroid Biochem Mol Biol. 2016;164:148–55. doi:10.1016/j.jsbmb.2016.02.008
31. Harvey NC, Javaid MK, Poole JR, et al. Paternal skeletal size predicts intrauterine bone mineral accrual. J Clin Endocrinol Metab. 2008;93(5):1676–81. doi:10.1210/jc.2007-0279
32. Javaid MK, Crozier SR, Harvey NC, et al. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. Lancet. 2006;367(9504):36–43. doi:10.1016/S0140-6736(06)67922-1
33. Rajuddin R, Moulina DH, Yeni CM, Nora H. The role of vitamin D in pregnant women in birth weight of neonates. Indones J Obstet Gynecol. 2023;11(2):130-5. doi:10.32771/inajog.v11i2.2092