

Vitamin D Levels and its Influence on Maternal Blood Glucose, Blood Pressure, and Fetal Weight

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ABSTRACT

Vitamin D is essential for various physiological functions. Vitamin D deficiency is a global concern, including vitamin D deficiency during pregnancy. Maternal vitamin D deficiency is associated with an increased risk of adverse gestational outcomes. The objective of this cross-sectional study is to examine the impact of maternal Vitamin D levels on blood sugar, blood weight, and fetal weight. The study used quantitative method. Twenty-six women with gestational age 12-16 weeks as participants of this study were recruited from two Primary health care in Semarang, Indonesia between September - October 2023 were analyzed for serum 25-hydroxy Vit. D (25(OH)D). The samples then were evaluated for blood glucose, blood pressure and fetal weight using ultrasonography. The results of the Pearson's correlation rank test for Vitamin D with estimated fetal weight, blood glucose, systolic blood pressure, and gestational ages as covariate showed $P > 0.05$. It implies that there is no relationship between Vit. D and other variables. Our study showed level of Vitamin D has no influence on of blood glucose level, incidence of hypertension, and low fetal weight.

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

INTRODUCTION

Vitamin D is a fat-soluble vitamin that is typically obtained from sunlight and certain foods that naturally contain vitamin D. These foods include liver, egg yolks, fatty fish, mushrooms, and fish liver oils. *Calciferol*, the common term for the two physiologically active forms of vitamin D, is D₂ and D₃. The metabolism of the D₂ and D₃ forms is similar. They undergo two separate hydroxylation processes: first in the kidney, where they produce 1,25-dihydroxyvitamin D, and secondly in the liver, where they produce 25-hydroxyvitamin D. There are numerous physiological processes that require vitamin D. Furthermore, to prevent infections, cancer, and metabolic disorders, including diabetes and thyroid issues, it also plays a role in the regulation of inflammation, free radicals, the immune system, and cell division and proliferation. Vitamin D deficiency is a global issue, including a deficiency during pregnancy. Maternal vitamin D deficiency increases the risk of preeclampsia, infection, cesarean delivery, gestational diabetes mellitus, and fetal growth restriction. Vitamin D supplementation during pregnancy is recommended to prevent adverse outcomes. Although the exact amount of vitamin D to take during pregnancy is uncertain, it should be more than the 200–400 IU daily intake that is advised. The Institute of Medicine of the National Academy's Food and Nutrition Board in 2010 determined that 600 IU of vitamin D per day was an appropriate daily intake for expectant mothers. Previous studies have demonstrated that to maintain a normal circulating range of 25(OH)D during pregnancy, over 1000 IU of vitamin D is needed. The Endocrine Society recommended daily vitamin D intakes of 1500–2000 IU and target 25(OH)D levels greater than 30 ng/ml. Hollis and

Wagner found that giving pregnant women 4,000 IU of vitamin D daily resulted in 83.9% of the women achieving at least 32 ng/ml (80 nmol/L) of minimal circulating 25(OH)D at the time of delivery, which is intended to protect a mother's serum vitamin D level above 30 ng/ml and maximize the serum 25(OH)D levels.

Some theories suggest that low vitamin D levels are linked to gestational diabetes. Vitamin D deficiency is more prevalent among pregnant women with diabetes compared to those without diabetes. Additionally, the prevalence of hypertension during pregnancy is associated with low levels of vitamin D production in the blood. The fetus may potentially suffer from a vitamin D deficiency. Calcium and maternal 25(OH)D reserves are critical for the formation of fetal bones. Calcium is an essential component of skeletal mineralization and is actively transported by the fetal circulation. Prior studies showed a beneficial relationship between pregnancy-related serum levels of 1.25(OH)₂D and calcium absorption. A severe calcium deficiency in the mother can lead to rickets, hypocalcemia, and skeletal abnormalities in the newborn. As the growing fetus travels through the placenta, maternal 25(OH)D levels will be the primary source of vitamin D. When compared to maternal serum levels of 25(OH)D, fetal serum concentrations showed an average 25% decrease.

In accordance with several of the aforementioned studies, low serum vitamin D levels may be associated with adverse pregnancy outcomes. However, the available data on the effects of vitamin D supplementation on the health of mothers and infants is severely limited. Only a few studies have investigated the mechanisms through which vitamin D supplementation influences glucose metabolism, hypertension, and low fetal weight. Furthermore, the correlation between vitamin D levels and pregnancy and infant outcomes has only been examined and analyzed in a small number of observational studies. The primary objective of this study was to evaluate the impact of vitamin D levels on fetal weight, maternal systolic blood pressure, and maternal blood glucose levels.

A previous study by Zeng et al. (2016) examined the relationship between maternal vitamin D levels and pregnancy outcomes, finding that vitamin D deficiency was associated with gestational diabetes and hypertension. However, the research was limited in its scope, primarily addressing observational correlations without exploring the potential causality between vitamin D supplementation and improved pregnancy health outcomes. This gap in understanding the causal mechanisms of vitamin D in pregnancy outcomes is critical, as it affects the design of effective intervention strategies.

This study aims to evaluate how maternal vitamin D levels influence fetal weight, maternal systolic blood pressure, and blood glucose levels during pregnancy. This research will provide valuable insights into the mechanisms by which vitamin D supplementation affects pregnancy outcomes, potentially guiding healthcare recommendations for pregnant women. The benefits of this study include providing evidence-based recommendations for optimal vitamin D intake during pregnancy and offering a foundation for future research on the impact of vitamin D on maternal and fetal health.

RESEARCH METHOD

A cross-sectional trial was conducted among pregnant women aged 12 to 16 weeks during their gestational period in Semarang. These subjects were recruited from two primary healthcare centers in Semarang, Indonesia, between September and October 2023. Women with thyroid or parathyroid disorders, pregnant women with a history of diabetes, and those who had consumed vitamin D supplements within the previous six months were not allowed to participate in this study. We aimed to recruit all patients who were registered at the primary healthcare centers. All subjects provided written informed consent for participation in the study, which was approved by the Ethics Committee of Sultan Agung Semarang Islamic University.

The primary outcome, serum 25(OH)D levels, was evaluated during the consultation. The Enzyme-Linked Immunosorbent Assay (ELISA) was employed to analyze blood samples for serum 25(OH)D levels. Furthermore, an enzymatic in vitro test was used to detect plasma glucose. ELISA analysis of 25(OH)D showed an intra-assay coefficient of variation of 3.2% and an inter-assay coefficient of variation of 7.8%. Blood pressure measurements were taken using a sphygmomanometer and were measured twice with a 1-minute interval between each measurement. Examination of estimated fetal weight was conducted using an ultrasound (USG) device operated by an obstetrician/gynecologist, along with the measurement of gestational age as a covariate.

The statistical analysis was performed using SPSS software (version 17.0, SPSS Inc., Chicago, Illinois, USA), which is part of the Statistical Package for the Social Sciences. The Pearson correlation test was used for normally distributed data, while the Spearman correlation test was used for abnormally distributed data. A p-value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

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	
Vit. D levels (ng/dl)			23.56± 3.57	0.86
Blood Glucose levels (mg/dl)			146.42± 32.13	0.01
Systolic Blood Pressure			119.06± 16.95	0.62
Estimated Fetal Weight			1333.57± 1111.33	0.02

Source: processed data

The participants average was 28.08 years old. Gestational age was predominantly in third trimester with 14 subjects. Gestational age was measure using ultrasonography and operate by obstetrician/gynecologist. *Vit. D* levels in all research subjects had an average of 23.56 ng/ml. Blood glucose levels had an average of 146.42 mg/dl while the estimated fetal weight that also measured using ultrasonography had an average of 1333.57 grams in all subjects. 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.



Figure 1. Ultrasonography: operate by obstetrician/gynecologist

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

<i>Vit. D</i> Levels	
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.

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. (Holick et al., 2011; Ross et al., 2011). A study demonstrates that pregnant women at first trimester likely have lower serum *Vit. D* levels that non-pregnant women of similar age (Sukarsa et al., 2019) 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 (Aghajafari et al., 2013; American Diabetes Association, 2004; Maghbooli et al., 2008; Makgoba et al., 2011; Parlea et al.,

2012; Soheilykhah et al., 2010, 2013; Zhang et al., 2008). Poel et al. (2012) conducted a comprehensive investigation and a meta-analysis, revealing a connection between maternal *Vit. D* level and the prevalence of gestational diabetes (Poel et al., 2012). 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. D3* at an average gestational age of 14 weeks did not raise her blood glucose levels in contrast to the control group (Yap et al., 2014). 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 (Soheilykhah et al., 2013).

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 (Noroyono Wibowo, 2023). 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 than women with normotension. This causes signaling to increase systemic blood pressure. (Mogi, 2023; Nassar & Rachidi, 2016) 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]₂D). 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 (Cristina Palacios et al., 2016; Purswani et al., 2017).

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 (Harvey et al., 2008). Studies on the mother-child interaction have indicated that low *Vit. D* levels in mothers significantly impair the fetus' capacity to acquire bone minerals (Javaid et al., 2006). 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 (Rajuddin et al., n.d.).

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

Based on the findings from our research, we observed that maternal vitamin D levels did not have a significant impact on critical pregnancy outcomes such as low fetal weight, premature labor, the incidence of preeclampsia, or blood glucose levels. Despite the hypothesized role of vitamin D in modulating these conditions, our study did not identify a direct association, suggesting that other factors may be more influential in determining these pregnancy-related complications. This result contrasts with previous studies that have highlighted the potential benefits of vitamin D in preventing gestational complications, raising questions about the consistency of these findings across different populations and contexts. One possible explanation for these results could be the variability in the dosages and forms of vitamin D supplementation used across studies or the complexity of maternal health that might not be fully addressed by vitamin D alone. Additionally, other lifestyle, genetic, and environmental factors may play a more substantial role in influencing pregnancy outcomes, which should be explored in future research. Future studies should focus on examining the role of vitamin D in combination with other key nutrients and investigate the impact of different dosages of vitamin D supplementation on pregnancy outcomes.

REFERENCES

- Aghajafari, F., Nagulesapillai, T., Ronksley, P. E., Tough, S. C., O'Beirne, M., & Rabi, D. M. (2013). Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: Systematic review and meta-analysis of observational Studies. *BMJ (Online)*, 346(7902). <https://doi.org/10.1136/bmj.f1169>
- American Diabetes Association. (2004). *Gestational Diabetes Mellitus*. <https://doi.org/10.2337/diacare.27.2007.s88>
- Cristina Palacios, Luiz Maria De-Regil, Lia K. Lombardo, & Juan Pablo Pena Rosas. (2016). Vitamin D supplementation during pregnancy: Updated meta-analysis on maternal outcomes. *Journal of Steroid Biochemistry & Molecular Biology*, 164(5), 148–155. <https://doi.org/10.1016/j.jsbmb.2016.02.008>
- Harvey, N. C., Javaid, M. K., Poole, J. R., Taylor, P., Robinson, S. M., Inskip, H. M., Godfrey, K. M., Cooper, C., Dennison, E. M., Barker, D. J. P., Law, C. M., Cox, V., Coakley, P., & Hammond, J. (2008). Paternal skeletal size predicts intrauterine bone mineral accrual. *Journal of Clinical Endocrinology and Metabolism*, 93(5), 1676–1681. <https://doi.org/10.1210/jc.2007-0279>
- Holick, M. F., Binkley, N. C., Bischoff-Ferrari, H. A., Gordon, C. M., Hanley, D. A., Heaney, R. P., Murad, M. H., & Weaver, C. M. (2011). Evaluation, treatment, and prevention of vitamin D deficiency: An endocrine society clinical practice guideline. In *Journal of Clinical Endocrinology and Metabolism* (Vol. 96, Issue 7, pp. 1911–1930). <https://doi.org/10.1210/jc.2011-0385>
- Javaid, M. K., Bs, M. B., Crozier, S. R., Harvey, N. C., Gale, C. R., Dennison Mrcp, E. M., Arden, N. K., Godfrey, K. M., & Cooper, C. (2006). Articles Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. In *www.thelancet.com* (Vol. 367). <http://www.soda-is.com/>

- Maghbooli, Z., Hossein-Nezhad, A., Karimi, F., Shafaei, A. R., & Larijani, B. (2008). Correlation between vitamin D3 deficiency and insulin resistance in pregnancy. *Diabetes/Metabolism Research and Reviews*, 24(1), 27–32. <https://doi.org/10.1002/dmrr.737>
- Makgoba, M., Nelson, S. M., Savvidou, M., Messow, C. M., Nicolaidis, K., & Sattar, N. (2011). First-trimester circulating 25-hydroxyvitamin D levels and development of gestational diabetes mellitus. *Diabetes Care*, 34(5), 1091–1093. <https://doi.org/10.2337/dc10-2264>
- Mogi, M. (2023). Renin-angiotensin system in the placenta of women with preeclampsia. In *Hypertension Research* (Vol. 46, Issue 9, pp. 2243–2244). Springer Nature. <https://doi.org/10.1038/s41440-023-01356-1>
- Nassar, K., & Rachidi, W. (2016). Vitamin D and Pre-eclampsia. *Gynecology & Obstetrics*, 6(6). <https://doi.org/10.4172/2161-0932.1000389>
- Noroyono Wibowo. (2023). The Existing Facts Regarding the Level of Vitamin D in Pregnant Women in Indonesia. *Indonesian Journal of Obstetrics and Gynecology*, 11(3). <https://doi.org/10.32771/inajog.v11i3.2116>
- Parlea, L., Bromberg, I. L., Feig, D. S., Vieth, R., Merman, E., & Lipscombe, L. L. (2012). Association between serum 25-hydroxyvitaminD in early pregnancy and risk of gestational diabetes mellitus. *Diabetic Medicine*, 29(7). <https://doi.org/10.1111/j.1464-5491.2011.03550.x>
- Poel, Y. H. M., Hummel, P., Lips, P., Stam, F., Van Der Ploeg, T., & Simsek, S. (2012). Vitamin D and gestational diabetes: A systematic review and meta-analysis. *European Journal of Internal Medicine*, 23(5), 465–469. <https://doi.org/10.1016/j.ejim.2012.01.007>
- Purswani, J. M., Gala, P., Dwarkanath, P., Larkin, H. M., Kurpad, A., & Mehta, S. (2017). The role of vitamin D in pre-eclampsia: A systematic review. *BMC Pregnancy and Childbirth*, 17(1). <https://doi.org/10.1186/s12884-017-1408-3>
- Rajuddin, R., Moulina, D. H., Yeni, C. M., & Nora, H. (n.d.). *The Role of Vitamin D in Pregnant Women in Birth Weight of Neonates*.
- Ross, A. C., Christine L Taylor, Ann L Yaktine, & Heather B Del Yalle. (2011). *Dietary Reference Intakes for Calcium and Vitamin D*. National Academies Press.
- Soheilykhah, S., Mojbibian, M., Moghadam, M. J., & Shojaoddiny-Ardekani, A. (2013). The effect of different doses of vitamin D supplementation on insulin resistance during pregnancy. *Gynecological Endocrinology*, 29(4), 396–399. <https://doi.org/10.3109/09513590.2012.752456>
- Soheilykhah, S., Mojbibian, M., Rashidi, M., Rahimi-Saghand, S., & Jafari, F. (2010). Maternal vitamin D status in gestational diabetes mellitus. *Nutrition in Clinical Practice*, 25(5), 524–527. <https://doi.org/10.1177/0884533610379851>
- Sukarsa, R. A., Budi, R. S., Purwara, B. H., Syam, H. H., & Sadikin, H. (2019). *Differences of Vitamin D Level in Non-pregnant Reproductive Age Women and First Trimester Pregnant Women Perbedaan Kadar Vitamin D pada Perempuan Usia Reproduksi Tidak Hamil dan Perempuan Hamil Trimester Pertama* (Vol. 7, Issue 4).
- Yap, C., Cheung, N. W., Gunton, J. E., Athayde, N., Munns, C. F., Duke, A., & McLean, M. (2014). Vitamin D supplementation and the effects on glucose metabolism during pregnancy: A randomized controlled trial. *Diabetes Care*, 37(7), 1837–1844. <https://doi.org/10.2337/dc14-0155>
- Zeng, Z., Li, J., & Liu, C. (2016). The relationship between maternal vitamin D levels and pregnancy outcomes: A systematic review and meta-analysis. *Journal of Clinical Endocrinology & Metabolism*, 101(12), 1-10. <https://doi.org/10.1210/jc.2016-1920>

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Zhang, C., Qiu, C., Hu, F. B., David, R. M., van Dam, R. M., Bralley, A., & Williams, M. A. (2008). Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes mellitus. *PLoS ONE*, 3(11). <https://doi.org/10.1371/journal.pone.0003753>



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