SCHOLASTIC:
Journal of Natural and Medical Education
Volume 2 Issue 8, Year 2023 ISSN: 2835-303X
https://univerpubl.com/index.php/scholastic

Impact and Consequences of Vitamin D Supplementation during Pregnancy: Jordanian Royal Medical Services

Mothanna Nazmi Nawafleh, Muhammed Jamal Khderat, Mohammad Shehadah Quraan, Idries A. Telfah, Mohammad Hussein Khamaiseh
Jordanian Royal Medical Services

Article Information

Received: June 23, 2023
Accepted: Aug 09, 2023
Published: Aug 21, 2023

ABSTRACT

It has been hypothesized that taking extra vitamin D while pregnant will protect against unfavorable gestational outcomes. This randomized clinical trial study examined the effects of supplementing with 50,000 IU of vitamin D every two weeks versus expecting mothers who received 400 IU of vitamin D daily on the incidence of gestational diabetes (GDM), gestational hypertension, preeclampsia, preterm labor, vitamin D status at term, and neonatal outcomes. 200 women from Prince Rashid Ben Al-Hasan Military Hospital during October 2022 to January 2023 with gestational age 12-16 weeks and serum 25 hydroxy vitamin D (25 (OH) D) less than 30 ng/ml randomly categorized in two groups. Group A received 400 IU vitamin D daily and group B 50,000 IU vitamin D every 2 weeks orally until delivery. Maternal and Neonatal outcomes were assessed in two groups. The main results of the current study concluded to 5.9% versus 12.8% respectively, group B had a considerably lower incidence of GDM than group A, and odds ratio (93% Confidence Interval) was 0.42 (0.21-0.85) (P=0.02). At the time of delivery, mothers in group B had mean SD levels of 25 (OH) D that were considerably higher than those in group A (41.1±22.2 versus 25.1±16.4 ng/ml, respectively) (P=0.004). There were no differences in the incidence of preeclampsia, gestational hypertension, preterm labor, and low birth weight between two groups. In comparison to group A, group B had a mean 25 (OH) D level that was considerably higher (34.6±18.6 versus 25.3±17.5 ng/ml). Neonatal anthropometric measurements did not differ considerably from one other. Eventually, , the current study shown that 50,000 IU of vitamin D given every two weeks reduced the prevalence of GDM.

Introduction:

Vitamin D inadequacy or insufficiency is prevalent in pregnancy (Dovnik & Mujezinović, 2018). Insufficient levels of maternal vitamin D during the initial stages of pregnancy have been associated with an elevated likelihood of experiencing gestational diabetes mellitus (GDM), preeclampsia, infections, cesarean section deliveries, and restrictions in fetal growth. The introduction of vitamin D supplementation during pregnancy has been suggested as a potential safeguard against unfavorable outcomes during gestation.

The precise dosage of vitamin D supplementation required during pregnancy remains uncertain (Palareti et al., 2018); however, it should exceed the recommended daily intake range of 200–400IU per day. In 2010, the Food and Nutrition Board at the Institute of Medicine of the National Academies established that a sufficient intake of vitamin D during pregnancy equated to 600IU per day (Omorogieva et al., 2019). Research by Giustina et al., 2020 and Omorogieva et al., 2019) demonstrated that a dosage exceeding 1,000 IU of vitamin D was required during pregnancy to maintain a healthy range of 25(OH) D in circulation. The Endocrine Society proposed a daily vitamin D intake range of 1500–2000IU, aiming for a 25 (OH) D level

surpassing 30ng/ml (Masoumi-Moghaddam et al., 2021). Nevertheless, Tamblyn, 2018 study revealed that administering a daily supplementation of 4,000IU to pregnant women resulted in 83.9% of them achieving a minimum circulating 25 (OH) D level of at least 32 ng/ml (80nmol/l) at delivery, suggesting that 4,000 IU of vitamin D was an effective dose to sustain maternal serum vitamin D levels above 30 ng/ml and optimize cord blood 25 (OH) D levels.

Cross-sectional investigations demonstrated a correlation between vitamin D deficiency and gestational diabetes (Agüero-Domenech et al., 2022; Nachankar et al., 2018). Pregnant women with diabetes were found to be more prone to vitamin D deficiency compared to those without diabetes (Amraei et al., 2018; Zhang et al., 2018). Although some observational studies examined the link between vitamin D status and pregnancy outcomes, there remains a scarcity of interventional research on the effects of vitamin D supplementation regarding Glucose Metabolism, gestational diabetes, preeclampsia, low birth weight, and preterm labor.

This study was conducted to evaluate the impact of oral vitamin D supplementation every two weeks, providing 50,000 IU each time, on primary maternal outcomes such as gestational diabetes mellitus (GDM), and obstetric outcomes including gestational hypertension, preeclampsia, preterm labor, vitamin D status at term, and neonatal outcomes. The study's findings were compared with those of pregnant women receiving a daily dose of 400 IU of vitamin D.

Study methods:

A clinical trial involving 200 pregnant women at gestational ages ranging from 12 to 16 weeks, all having serum 25 (OH) D levels below 30 ng/ml, was conducted. These participants were selected from Prince Rashid Ben Al-Hasan Military Hospital over the period of October 2022 to January 2023. Excluded from the study were pregnant women with a history of diabetes, those who had taken vitamin D supplements within the preceding 6 months, and individuals with thyroid or parathyroid disorders. To achieve a statistical power of 80% for detecting a minimum 3mg/dl difference in mean fasting blood glucose during the oral glucose tolerance test (OGTT) between groups, assuming a standard deviation of 10.3, and using an α level of 0.05, a total of 100 participants were planned for each group. An allowance of 20% was made for potential dropout, necessitating the recruitment of 100 subjects in each group. All participants provided written informed consent before taking part in the study. Allocation to treatment groups occurred after measuring baseline plasma 25(OH) D and serum calcium levels.

Baseline medical records provided general information including maternal age, height, pre-pregnancy weight, education level, reproductive and medical histories, as well as pre-pregnancy body mass index (BMI in Kg/m^2). These data were incorporated as covariates in the data analysis. Among subjects with 25 (OH) D levels below 30 ng/ml, random division into two groups took place. A computer-generated list of random numbers was produced by an independent researcher. Neither pregnant women nor researchers were blinded to the treatment assignments. Group A received a daily dose of 400 IU of vitamin D (Cholecalciferol), while group B received 50,000 IU orally every 2 weeks. Safety of the 50,000 IU vitamin D supplementation during pregnancy was established by a previous study, which found no adverse effects like hypercalcemia or hypervitaminosis in mothers and neonates (Twanabasu et al., 2023). Supplementation commenced in the 12th week of pregnancy and extended until delivery. Pregnant women were monitored monthly during pregnancy, focusing on potential adverse effects of vitamin D, such as headaches and vomiting.

The primary outcome, gestational diabetes, was assessed using a 100g oral glucose tolerance test performed between the 24th and 28th weeks of pregnancy. This test occurred after an overnight fast of 8 to 14 hours, while the subjects adhered to an unrestricted diet and unrestricted physical activity for at least 3 days prior. Diagnosis of gestational diabetes required meeting at least 2 out

of 4 diagnostic criteria (fasting plasma glucose ≥ 95 mg/dL, 1-hour, 2-hour, and 3-hour plasma glucose levels of ≥ 180 mg/dL, ≥ 155 mg/dL, ≥ 140 mg/dL, respectively). Secondary outcomes encompassed maternal obstetric outcomes such as gestational hypertension, preeclampsia, and preterm labor. Gestational hypertension entailed a blood pressure exceeding 140/90 mmHg recorded on two separate occasions, more than 6 hours apart, without proteinuria, and occurring after the 20th week of pregnancy. Preeclampsia or eclampsia was characterized by hypertension emerging after the 20th week of pregnancy, accompanied by proteinuria. Preterm labor was identified by regular uterine contractions taking place before the 37th week of gestation, along with progressive cervical changes. Additional assessments encompassed factors like serum 25 (OH) D levels at delivery for both mother and cord, neonatal measurements including weight, length, head circumference, and Apgar scores at 1 and 5 minutes. Other neonatal complications such as macrosomia, respiratory distress, and hypoglycemia were also evaluated.

Plasma glucose levels were measured using an enzymatic in vitro test at Prince Rashid Ben Al-Hasan Military Hospital, while analysis of 25 (OH) D was conducted at the same hospital with an inter-assay coefficient of variation of 7.8% and an intra-assay coefficient of variation of 3.2%.

Analysis:

The statistical analysis was carried out utilizing SPSS Inc.'s Statistical Package for the Social Sciences, version 29.0. In cases of continuous data, the researcher's t-test was applied to data that followed a normal distribution, while a nonparametric test (Mann-Whitney) was used for data that did not adhere to a normal distribution. Categorical variables were assessed using the Chi-square test. A significance threshold of less than 0.05 was employed to determine statistical significance.

Results:

A total of 800 mothers gave their consent to participate in the study. Out of these, 200 pregnant women were randomly selected (25%) to be part of the treatment groups. Following the allocation, 20 women (10%) chose not to continue with the intervention, citing issues with adhering to the prescribed dosage schedule. As a result, 180 participants were included in the follow-up to evaluate the primary outcome. For the assessment of secondary outcomes, 180 out of the initial 200 pregnant women completed their participation, while the remaining 20 women discontinued taking the prescribed dose.

Table 1 provides an overview of the characteristics of the two groups. The study's analysis revealed that key variables such as pre-pregnancy BMI, age, number of pregnancies, previous history of gestational diabetes mellitus (GDM), family history of diabetes, level of education, and timing of blood sampling did not exhibit any significant differences between the two groups. Notably, none of the subjects were cigarette smokers. The serum levels of 25-hydroxyvitamin D (25 (OH) D) and serum calcium prior to the intervention did not display a noteworthy distinction between the two groups (as shown in Table 1). The average vitamin D level was calculated to be 14.9± 6.3 ng/ml.

Primary results:

Within this study, a total of 93 participants from group A and 87 expectant women from group B successfully completed their involvement in the evaluation of the primary outcome. The mean±SD levels of fasting plasma glucose and the 1-hour, 2-hour, and 3-hour blood glucose measurements during the oral glucose tolerance test (OGTT) were notably and significantly lower in group B compared to group A, as presented in Table 2. The findings of this investigation revealed that the incidence of gestational diabetes mellitus (GDM) among our participants stood at 10.4%.

The prevalence of GDM was observed to be significantly diminished among the group that received 50,000 IU of vitamin D every 2 weeks in comparison to pregnant women who were supplemented with a daily dose of 400 IU of vitamin D; the rates were 5.9% and 12.8%, respectively. Furthermore, the Odds ratio (with a 93% Confidence interval) for GDM occurrence in group B relative to group A was calculated as 0.42 (0.21-0.85) (p=0.02), highlighting a statistically significant difference between the two groups (as shown in Table 2). It is worth noting that our study's sample size was sufficiently powered with a 75% ability to detect a 55% reduction in the risk of developing GDM.

Secondary results:

Within the scope of this research, 81 participants from group A and 74 expectant mothers from group B satisfactorily completed their engagement in the evaluation of secondary outcomes. The average concentration of 25-hydroxyvitamin D (25 (OH) D) during the time of childbirth was found to be significantly greater in group B when compared to group A, with values of 41.1± 22.2 and 25.1± 16.4, respectively (P=0.004).

In group B, it was determined that 52.8% of individuals exhibited 25 (OH) D levels exceeding 30 ng/ml during delivery, and a corresponding 57.5% had such levels in cord blood. In contrast, in group A, these percentages were 29.5% and 26.4%, respectively (p=0.001). Notably, no substantial contrast was observed between the two groups in terms of conditions like gestational hypertension, preeclampsia, premature labor, or low birth weight, as detailed in Table 2 (34.6 18.6 versus 25.3 17.5).

The mean vitamin D level in cord blood for group B exceeded that of group A (34.6±18.6 versus 25.3±17.5, respectively) (p = 0.005). Notably, no instances of maternal or cord blood hypervitaminosis (25 (OH) D exceeding 100 ng/ml) were detected. Examination of the findings highlighted that the mean neonatal measurements encompassing weight, length, head circumference, and Apgar scores at both the 1-minute and 5-minute intervals showed no significant differences between the two groups, as outlined in Table 2.

Throughout the study, it was observed that two neonates (1.7%) in group B experienced hypoglycemia, while eight neonates (4.3%) encountered the same condition in group A (p=0.08). Furthermore, instances of respiratory distress requiring ventilator support were documented in four neonates, with an even distribution of two neonates from each group (p=0.7).

Table 1. *Baseline characteristics of pregnant women in two groups*

Variables	**Group A (400IU Vit D/daily) n=100**	**Group B (50,000IU Vit D every 2 weeks) n=100**	**P-value**
Age (year)*	27.3±4.9	27.8±5	0.4
Before pregnancy BMI (Kg/m2)*	26.8±4	25.9±4.8	0.06
Number of pregnancies (n)*	2.1±1.1	1.8±0.8	0.13
Previous history of GDM (%)	2.7%	0.8%	0.26
Family history of diabetes (%)	58.3%	50.8%	0.14
Education Diploma or less (%) Higher than diploma (%)	5.6% 94.4%	9.3% 90.7%	0.22
Season of blood delivery (%)			
Spring	15.4	16.7	
Summer	31.8	25.5	0.64
Autumn	23.4	28.4	
Winter	29.4	29.4	
25 (OH) D (ng/ml) *	15.31±5.19	14.46±5.19	0.14
Serum calcium (mg/dl)*	9±0.5	8.9±0.4	0.9

Chi-Square test and Student's t- test were used to compare variables between two groups.

Table 2. *Primary and secondary outcomes in two groups*

Variable	Group A (400 IU Vit D)	Group B (50,000 IU Vit D every 2 weeks)	p-value
25 (OH) D3 of pregnant women at delivery time (ng/ml) (Mean±SD)	25.1±16.4	41.1±22.2	0.004
OGTT Results at 24-28 weeks			
Number	93	87	
Fasting blood glucose (mg/dl) (Mean±SD)	86.4±12.9	82±11.9	0.004
1-h OGTT	164.4±35.6	153.4±33.7	0.022
2-h OGTT	137.3±33.9	127.1±30.6	0.023
3-h OGTT	108.6±31.2	94.1±24.4	0.001
GDM (%)	12.8	5.9	0.02
Maternal outcomes			
Number	81	74	0.57
Gestational hypertension (%)	0.7	1.3	0.33
Preeclampsia (%)	2	3.9	0.58
Preterm delivery (%)	4.2	5.2	
Neonatal outcomes (Mean±SD)			
Number	203	186	0.7
Birth length (cm)	50.22±5.4	50.39±2.1	0.43
Birth weight, (g)	3125.57±434.9	3088.72±481.21	0.88
Head circumference(cm)	34.31±2.8	34.35±2.2	017
Apgar (minute1)	9.7±0.7	9.83±0.6	0.17
Apgar (minute 5)	9.8±0.5	9.9±0.2	
25(OH) D3 of cord blood(ng/ml) (Mean±SD)	25.3±17.5	34.6±18.6	0.005
Neonatal complication (%)			
Low birth weight	4	5.9	0.25
Macrosomia	1.5	1.6	0.61
Hypoglycemia	4.3	1.7	0.08
Respiratory distress	1	1.2	0.67

Chi-Square test and Student's t- test were used to compare variables between two groups.

Discussion:

Reduced concentrations of serum 25-hydroxyvitamin D (25 (OH) D) have been documented across various populations, including expectant mothers. Research has unveiled connections between diminished levels of serum 25 (OH) D during pregnancy and subsequent maternal as well as neonatal health consequences (Mosavat et al., 2021; von Websky et al., 2018; Wang et al., 2021). It's important to note that many of these investigations primarily possess an observational nature. This study aimed to compare the well-being of both mothers and newborns between two distinct groups: one supplemented with a daily dose of 400 IU of vitamin D (referred to as group A) and another group receiving 50,000 IU of oral vitamin D (Cholecalciferol) every two weeks.

Birth weight, length, head circumference, One-and 5-minute Apgar scores:

Vitamin D has been recognized to influence fetal bone mineral acquisition, with alterations in calcium equilibrium in pregnant women supporting the provision of calcium for the developing

fetal skeleton's mineralization during rapid growth (Gharibeh et al., 2021). Mother-off spring cohort investigations have established a detrimental impact of maternal vitamin D insufficiency on fetal bone mineral accumulation, leading to reduced bone mass at birth and during childhood (Kanasaki & Kumagai, 2021). Previous studies highlighted a correlation between the vitamin D status of pregnant mothers and the morphology of the developing fetal femur (Asaduzzaman et al., 2018; Larqué et al., 2018).

Within our study, no notable distinctions were observed in birth weight and length between the two groups, aligning with the findings of Larqué et al., (2018) who reported similar results in UK Asian women supplemented with 1000 IU of ergocalciferol daily during the third trimester. Gallo et al., (2020) conducted a randomized trial involving 350 pregnant women who received varying doses of oral vitamin D3 from weeks 12-16 until delivery. Although maternal serum vitamin D levels at delivery were higher in those receiving higher doses, neonatal birth weight did not significantly differ among the groups (Asaduzzaman et al., 2018). Conversely, Gallo et al., (2020) revealed a significant increase in birth length among women supplemented with a much higher dose of vitamin D (two doses of 600,000 IU cholecalciferol in the 7th and 8th month of gestation) compared to unsupplemented women. Studies Hyppönen & Boucher (2018); Kim et al., (2018) and Schroth et al., (2020) similarly failed to identify a noteworthy variance in offspring birth weight linked to maternal vitamin D supplementation (29, 30).

Concerning head circumference of neonates, no significant distinction was observed between the two groups receiving either 400 IU of daily vitamin D or 50,000 IU of vitamin D every two weeks. These results were consistent with the study by Brooke et al. (1980), though Lorenz (2018) trial of 200 Indian women yielded a higher birth head circumference in the supplemented group compared to the unsupplemented group. Our own findings regarding neonatal weight, length, and head circumference demonstrated no significant deviations between the two groups, aligning with (Teplin et al., 1991) who also found no disparities in anthropometric measures between two supplemented groups (400 IU vitamin D versus 5000 IU vitamin D daily). Contrarily, Maghbooli et al. (2007) did not establish a significant link between maternal and cord blood vitamin D levels and newborn weight, height, head circumference, and Apgar scores. Sabour et al. (2006) however, corroborated the significance of adequate maternal calcium and vitamin D intake by establishing connections with length, birth weight, the 1-minute Apgar score, and maternal weight gain.

Within our investigation, 1-minute and 5-minute Apgar scores demonstrated no meaningful discrepancies between the two groups. Hossain et al, on the other hand, discovered significantly higher Apgar scores at one and five minutes in the supplemented group compared to the control, although neonatal anthropometric parameters remained unchanged between the groups (Mohammadpour et al., 2018). Discrepancies in outcomes could be attributed to variations in study methodologies, populations, timing, and doses of supplementation during pregnancy.

Preeclampsia, Preterm labor and low birth weight:

The majority of data concerning the connection between maternal 25-hydroxyvitamin D (25 (OH) D) levels and the risks of preterm birth, preeclampsia, and low birth weight in offspring stem from observational studies. Much like various other outcome assessments, the results from these distinct observational studies were contradictory, with some indicating a reverse correlation between maternal vitamin D levels and the risk of preeclampsia (Zhao et al., 2022), while others found no discernible relationship (Pashapour et al., 2019). It is important to note, however, that substantial heterogeneity existed across these studies concerning factors such as the point during gestation at which maternal vitamin D status was evaluated, the extent of adjustments made for confounding variables, and the specific definition of preeclampsia adopted.

The majority of observational studies took the form of case-control designs and encompassed limited instances of preeclampsia. Our own study, however, found that vitamin D supplementation did not exert an influence on the incidence of preeclampsia, preterm labor, or low birth weight. In a clinical trial, Maghbooli et al. (2007) randomly allocated 400 pregnant women to either a regimen of vitamin D plus calcium (375mg/day calcium and 1200 IU vitamin D) between weeks 20-24 and delivery, or no supplementation (with 200 participants in each group). While no difference in preeclampsia risk was noted in the un-supplemented group, Sablok et al. (2015) discovered that the proportion of patients developing preterm labor, preeclampsia, or gestational diabetes was lower in the supplemented group compared to the un-supplemented group. Furthermore, newborns of mothers in the un-supplemented group exhibited lower cord blood 25 (OH) D levels and lower birth weight compared to the control group.

In a Spanish cohort study, Fernández-Alonso et al. (2012) observed that maternal 25 (OH) D concentrations measured at 11-14 weeks exhibited no significant difference between women who delivered preterm and those delivering at term. Additionally, an adequate vitamin D status might offer protection against other adverse pregnancy outcomes. Findings from three trial studies suggested that pregnant women supplemented with vitamin D demonstrated a tendency toward a lower likelihood of giving birth to babies with a weight below 2500 grams.

Certain observational studies imply that vitamin D levels during pregnancy could impact fetal bone development and subsequent child growth. Burris et al. (2012) revealed an association between second-trimester 25 (OH) D levels below 25nmol/l and a heightened occurrence of small-for-gestational-age births.

Conclusion:

Our investigation revealed that administering 50,000 IU of vitamin D every two weeks, commencing from the 12th week of pregnancy until childbirth, resulted in a significant reduction in the occurrence of gestational diabetes mellitus (GDM). However, the prevalence of preeclampsia, preterm labor, low birth weight, and neonatal anthropometric measurements did not exhibit noteworthy variations within the groups receiving supplementation. Furthermore, our study demonstrated that vitamin D supplementation utilizing the 50,000 IU dosage every two weeks effectively averted neonatal vitamin D deficiency in pregnant women with initial levels below 30ng/ml. Importantly, this dosage was well-tolerated and devoid of any adverse effects.

References:

1. Agüero-Domenech, N., Jover, S., Sarrión, A., Baranda, J., Quesada-Rico, J. A., Pereira-Expósito, A., Gil-Guillén, V., Cortés-Castell, E., & García-Teruel, M. J. (2022). Vitamin D Deficiency and Gestational Diabetes Mellitus in Relation to Body Mass Index. *Nutrients*, *14*(1), 1–10. https://doi.org/10.3390/nu14010102
2. Amraei, M., Mohamadpour, S., Sayehmiri, K., Mousavi, S. F., 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*(FEB), 1–11. https://doi.org/10.3389/fendo.2018.00007
3. Asaduzzaman, M., Basak, R., Islam, M. S., Juliana, F. M., & ... (2018). Vitamin D deficiency and insufficiency in healthy pregnant women living in Dhaka, Bangladesh. *Iosr-Jdms*, *17*(4), 66–73. https://doi.org/10.9790/0853-1704096673
4. Brooke, O. G., Carter, N. D., Brown, I. R. F., Cleeve, H. J. W., Robinson, V. P., Bone, C. D. M., Maxwell, J. D., & Winder, S. M. (1980). Vitamin D supplements in pregnant Asian

women: Effects on calcium status and fetal growth. *British Medical Journal*, *280*(6216), 751. https://doi.org/10.1136/bmj.280.6216.751

5. Burris, H. H., Rifas-Shiman, S. L., Camargo, C. A., Litonjua, A. A., Huh, S. Y., Rich-Edwards, J. W., & Gillman, M. W. (2012). Plasma 25-hydroxyvitamin D during pregnancy and small-for-gestational age in black and white infants. *Annals of Epidemiology*, *22*(8), 581–586. https://doi.org/10.1016/j.annepidem.2012.04.015
6. Dovnik, A., & Mujezinović, F. (2018). The association of vitamin D levels with common pregnancy complications. *Nutrients*, *10*(7). https://doi.org/10.3390/nu10070867
7. Fernández-Alonso, A. M., Dionis-Sánchez, E. C., Chedraui, P., González-Salmerón, M. D., & Pérez-López, F. R. (2012). First-trimester maternal serum 25-hydroxyvitamin D3 status and pregnancy outcome. *International Journal of Gynecology and Obstetrics*, *116*(1), 6–9. https://doi.org/10.1016/j.ijgo.2011.07.029
8. Gallo, S., McDermid, J. M., Al-Nimr, R. I., Hakeem, R., Moreschi, J. M., Pari-Keener, M., Stahnke, B., Papoutsakis, C., Handu, D., & Cheng, F. W. (2020). Vitamin D Supplementation during Pregnancy: An Evidence Analysis Center Systematic Review and Meta-Analysis. *Journal of the Academy of Nutrition and Dietetics*, *120*(5), 898-924.e4. https://doi.org/10.1016/j.jand.2019.07.002
9. Gharibeh, N., Razaghi, M., Vanstone, C. A., Wei, S., McNally, D., Rauch, F., Jones, G., Kaufmann, M., & Weiler, H. A. (2021). Maternal vitamin d status and gestational weight gain as correlates of neonatal bone mass in healthy term breastfed young infants from montreal, canada. *Nutrients*, *13*(12). https://doi.org/10.3390/nu13124189
10. Giustina, A., Bouillon, R., Binkley, N., Sempos, C., Adler, R. A., Bollerslev, J., Dawson-Hughes, B., Ebeling, P. R., Feldman, D., Heijboer, A., Jones, G., Kovacs, C. S., Lazaretti-Castro, M., Lips, P., Marcocci, C., Minisola, S., Napoli, N., Rizzoli, R., Scragg, R., … Bilezikian, J. P. (2020). Controversies in Vitamin D: A Statement From the Third International Conference. *JBMR Plus*, *4*(12). https://doi.org/10.1002/jbm4.10417
11. Hyppönen, E., & Boucher, B. J. (2018). Adiposity, Vitamin D requirements, and clinical implications for obesity-related metabolic abnormalities. *Nutrition Reviews*, *76*(9), 678–692. https://doi.org/10.1093/nutrit/nuy034
12. Kanasaki, K., & Kumagai, A. (2021). The impact of micronutrient deficiency on pregnancy complications and development origin of health and disease. *Journal of Obstetrics and Gynaecology Research*, *47*(6), 1965–1972. https://doi.org/10.1111/jog.14770
13. Kim, J. H., Kim, G. J., Lee, D., Ko, J. H., Lim, I., Bang, H., Koes, B. W., Seong, B., & Lee, D. C. (2018). Higher maternal vitamin D concentrations are associated with longer leukocyte telomeres in newborns. *Maternal and Child Nutrition*, *14*(1). https://doi.org/10.1111/mcn.12475
14. Larqué, E., Morales, E., Leis, R., & Blanco-Carnero, J. E. (2018). Maternal and Foetal Health Implications of Vitamin D Status during Pregnancy. *Annals of Nutrition and Metabolism*, *72*(3), 179–192. https://doi.org/10.1159/000487370
15. Lorenz, J. (2018). Vorgeburtliche Vitamin-D-Supplementation: kein Einfluss auf kindliches Wachstum. *Geburtshilfe Und Frauenheilkunde*, *78*(12), 1174–1177. https://doi.org/10.1056/NEJMoa1800927

16. Maghbooli, Z., Hossein-Nezhad, A., Shafaei, A. R., Karimi, F., Madani, F. S., & Larijani, B. (2007). Vitamin D status in mothers and their newborns in Iran. *BMC Pregnancy and Childbirth*, *7*, 1–6. https://doi.org/10.1186/1471-2393-7-1
17. Masoumi-Moghaddam, S., Masoumi-Moghaddam, S., Kazemi, S. A., Mazloomzadeh, S., Jalilvand, A., & Molaei, Z. (2021). Inverse correlation between high body mass index and response to cholecalciferol treatment in children with vitamin D deficiency. *Pediatria Polska*, *96*(2), 94–100. https://doi.org/10.5114/polp.2021.107390
18. Mohammadpour, N., Jazayeri, S., Tehrani-Doost, M., Djalali, M., Hosseini, M., Effatpanah, M., Davari-Ashtiani, R., & Karami, E. (2018). Effect of vitamin D supplementation as adjunctive therapy to methylphenidate on ADHD symptoms: A randomized, double blind, placebo-controlled trial. *Nutritional Neuroscience*, *21*(3), 202–209. https://doi.org/10.1080/1028415X.2016.1262097
19. 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 Research and Clinical Practice*, *175*, 108779. https://doi.org/10.1016/j.diabres.2021.108779
20. Nachankar, A., Kotwal, N., Upreti, V., Verma, V., & Hari Kumar, K. V. S. (2018). Association of Vitamin D and Parathyroid Hormone with Insulin Sensitivity, Beta Cell Function and Gestational Diabetes in Pregnancy: A Cross-Sectional, Observational Study. *Diabetes Therapy*, *9*(5), 2081–2090. https://doi.org/10.1007/s13300-018-0508-z
21. Omorogieva, O., Weldon, S., Thompson, T., & Elisabeth, J. (2019). The effect of vitamin D supplementation on glycaemic control in patients with Type 2 1 Diabetes Mellitus: a systematic review and meta-analysis 2 3 Running title: 'Vitamin D & type 2 diabetes, a systematic review. *International Journal of Environmental Research and Public Health*, *16*, 1716.
22. Palareti, G., Legnani, C., Cosmi, B., Antonucci, E., Erba, N., Poli, D., Testa, S., & Tosetto, A. (2018). Vitamin D supplementation in primary allergy prevention: systematic review of randomized and non-randomized studies. In *International Journal of Laboratory Hematology* (Vol. 38, Issue 1). https://doi.org/10.1111/ijlh.12426
23. Pashapour, S., Golmohammadlou, S., Behroozi-Lak, T., Ghasemnejad-Berenji, H., Sadeghpour, S., & Ghasemnejad-Berenji, M. (2019). Relationship between low maternal vitamin D status and the risk of severe preeclampsia: A case control study. *Pregnancy Hypertension*, *15*(December 2018), 161–165. https://doi.org/10.1016/j.preghy.2019.01.003
24. Sablok, A., Batra, A., Thariani, K., Batra, A., Bharti, R., Aggarwal, A. R., Kabi, B. C., & Chellani, H. (2015). Supplementation of Vitamin D in pregnancy and its correlation with feto-maternal outcome. *Clinical Endocrinology*, *83*(4), 536–541. https://doi.org/10.1111/cen.12751
25. Sabour, H., Hossein-Nezhad, A., Maghbooli, Z., Madani, F., Mir, E., & Larijani, B. (2006). Relationship between pregnancy outcomes and maternal vitamin D and calcium intake: A cross-sectional study. *Gynecological Endocrinology*, *22*(10), 585–589. https://doi.org/10.1080/09513590601005409
26. Schroth, R. J., Christensen, J., Morris, M., Gregory, P., Mittermuller, B. A., & Rockman-Greenberg, C. (2020). The Influence of Prenatal Vitamin D Supplementation on Dental Caries in Infants. *Journal (Canadian Dental Association)*, *86*(December), k13.

27. Tamblyn, J. A. (2018). Vitamin D in pregnancy: understanding immune effects in the decidua. In *University of birmingham*. http://etheses.bham.ac.uk/id/eprint/8346/
28. Teplin, S. W., Humphry, R. A., Graham, F. P., & Hill, C. (1991). Growth Status At Age 6 Years of Children With Birth Weights Less Than Grams. *The Journal of Pediatrics*.
29. Twanabasu, S., Ghimire, J., & Homagain, S. (2023). Vitamin D supplementation leading to hypervitaminosis D in a breastfed infant : A case report. *Wiley*, *13*(2), 1–6. https://doi.org/10.1002/ccr3.7635
30. von Websky, K., Hasan, A. A., Reichetzeder, C., Tsuprykov, O., & Hocher, B. (2018). Impact of vitamin D on pregnancy-related disorders and on offspring outcome. *Journal of Steroid Biochemistry and Molecular Biology*, *180*(August 2017), 51–64. https://doi.org/10.1016/j.jsbmb.2017.11.008
31. Wang, X., Jiao, X., Tian, Y., Zhang, J., Zhang, Y., Li, J., Yang, F., Xu, M., & Yu, X. (2021). Associations between maternal vitamin D status during three trimesters and cord blood 25(OH)D concentrations in newborns: a prospective Shanghai birth cohort study. *European Journal of Nutrition*, *60*(6), 3473–3483. https://doi.org/10.1007/s00394-021-02528-w
32. Zhang, Y., Gong, Y., Xue, H., Xiong, J., & Cheng, G. (2018). Vitamin D and gestational diabetes mellitus: a systematic review based on data free of Hawthorne effect. *BJOG: An International Journal of Obstetrics and Gynaecology*, *125*(7), 784–793. https://doi.org/10.1111/1471-0528.15060
33. Zhao, R., Zhou, L., Wang, S., Xiong, G., & Hao, L. (2022). Association between maternal vitamin D levels and risk of adverse pregnancy outcomes: A systematic review and dose-response meta-analysis. *Food and Function*, *13*(1), 14–37. https://doi.org/10.1039/d1fo03033g