Tzu Chi Medical Journal 2024; 36 (2): 175-187

Original Article

Effectiveness of Vitamin D supplementation in combination with calcium on risk of maternal and neonatal outcomes: A quasi-experimental clinical trial

Deldar Morad Abdulah[a], Jinan Nori Hasan[b], Sheelan Bapir Hasan[c]*

[a]Department of Community and Maternity Health Nursing, College of Nursing, University of Duhok, Kurdistan, Duhok, Iraq, [b]Public Health Department, College of Health and Medical Technology/Shekhan, Duhok Polytechnic University, Duhok, Kurdistan Region, Iraq, [c]Duhok Maternity Hospital, Duhok General Directorate of Health, Kurdistan, Iraq

Submission : 25-Jul-2023
Revision : 21-Aug-2023
Acceptance : 05-Sep-2023
Web Publication : 31-Oct-2023

Abstract

Objectives: We examined the effectiveness of combining Vitamin D supplementation with calcium on maternal and neonatal outcomes, as opposed to using Vitamin D supplements alone. **Materials and Methods:** Pregnant women in their third trimester were divided into two groups. The control group received a daily dose of 1000 IU of Vitamin D, but, the experimental group received a combined daily dosage of 1000 IU of Vitamin D and 500 mg of calcium, until delivery. **Results:** The women in the Vitamin D + calcium group were less likely to develop gestational diabetes (2.78%; vs. 19.51%; $P = 0.0318$), preeclampsia (2.78% vs. 26.83%; $P = 0.004$), newly onset gestational hypertension (11.11% vs. 46.34%; $P = 0.001$), proteinuria (5.56% vs. 39.02%; $P = 0.0004$), and impaired glucose tolerance (2.78% vs. 21.95%; $P = 0.0163$) and had lower blood pressure at 20th and 39th weeks of gestation. The newborns in the Vitamin D + calcium group were less likely to experience low birth weight (5.71% vs. 31.58%; $P = 0.0066$), low birth length (5.71% vs. 44.74%; $P = 0.0007$), were less likely to be admitted to the neonatal intensive care unit (14.29% vs. 42.11%; $P = 0.0105$), have a larger head circumference (35.00 vs. 33.63; $P < 0.0001$), longer gestational age at birth (40.0 vs. 37.56 weeks; $P < 0.0001$), and higher APGAR scores (9.58 vs. 6.31; $P < 0.0001$.) compared to Vitamin D group, respectively. **Conclusions:** Taking Vitamin D and calcium by pregnant women in the third trimester is an effective treatment to decrease maternal, fetal, and neonatal outcomes.

Keywords: *Birth weight, Dietary supplements, Preeclampsia, Preterm birth, Preterm labor*

Introduction

Vitamin D, which belongs to the secosteroid hormone group, is primarily produced in the skin during exposure to sunlight. It is then converted into its active form, Vitamin D3, in the liver and kidneys. This fat-soluble hormone plays a crucial role in various physiological functions beyond its traditional role in regulating calcium and phosphorus levels [1]. In addition to maintaining calcium and phosphorus homeostasis, Vitamin D has been found to have nonclassical effects, such as acting as an antioxidant and modulating the immune system. These discoveries have expanded our understanding of the diverse functions of Vitamin D [2,3].

Vitamin D deficiency (VDD) is a common condition that affects individuals of all ages, with women of reproductive age being particularly susceptible [4]. A deficiency is indicated when the serum 25(OH)D level falls below 20 ng/mL. Extensive epidemiological studies have established a strong connection between VDD during pregnancy and an increased risk of various pregnancy complications, including preeclampsia, preterm labor, and abnormal blood pressure [5,6]. Randomized controlled trials (RCTs) have also demonstrated the significant role of Vitamin D supplementation in reducing the occurrence of complications such as preeclampsia and pregnancy-induced hypertension, emphasizing the importance of addressing VDD in pregnant women to optimize maternal and fetal health [7]. This highlights the importance of addressing and mitigating VDD in pregnant women to optimize maternal and fetal health outcomes.

Gestational VDD has been linked to adverse effects on neurobehavioral development in offspring and an increased risk of conditions like asthma and schizophrenia in adulthood [8]. In addition, studies have shown a correlation between gestational VDD and a higher likelihood of delivering

Access this article online

Quick Response Code:

Website: www.tcmjmed.com

DOI: 10.4103/tcmj.tcmj_184_23

**Address for correspondence:* Dr. Deldar Morad Abdulah, Department of Community and Maternity Health Nursing, College of Nursing, University of Duhok, Kurdistan, Duhok, Iraq.
E-mail: deldarmorad@gmail.com

How to cite this article: Abdulah DM, Hasan JN, Hasan SB. Effectiveness of Vitamin D supplementation in combination with calcium on risk of maternal and neonatal outcomes: A quasi-experimental clinical trial. Tzu Chi Med J 2024;36(2):175-87.

infants who are small for gestational age and have low birth weight (LBW). These findings underscore the critical need to address VDD during pregnancy to improve both maternal and neonatal health outcomes [9].

Preterm delivery, defined as birth occurring before the 37th week of gestation, is a significant contributor to neonatal mortality [10]. The relationship between gestational VDD and preterm delivery has been examined in various studies, but the findings have been inconclusive, leading to conflicting conclusions among researchers [11-13]. The World Health Organization (WHO) currently recommends Vitamin D supplementation for women with VDD, with a recommended daily intake of 200 IU (5 μg). However, specific recommendations for pregnant women regarding Vitamin D supplementation to improve maternal and perinatal outcomes have not been provided by the WHO [14]. In regions with a high prevalence of VDD, particularly in low- and middle-income countries, Vitamin D supplements are often given to women to address the widespread occurrence of VDD and improve women's overall health and well-being [4]. However, the WHO has expressed concerns about whether taking Vitamin D in combination with calcium increases the risk of preterm birth [14]. Therefore, our objective was to investigate the effectiveness of combining Vitamin D supplementation with calcium compared to using Vitamin D supplements alone in terms of maternal and neonatal outcomes. We hypothesized that women who received Vitamin D supplements along with calcium would have a lower likelihood of experiencing adverse maternal and neonatal outcomes compared to those who received Vitamin D supplements only.

Materials and methods

Study design and sampling

In this clinical trial, pregnant women in their third trimester underwent screening to determine their eligibility for inclusion in either the control or experimental groups. The control group received Vitamin D in addition to their regular pregnancy treatment until delivery. On the other hand, the experimental group received both Vitamin D and calcium in conjunction with their regular pregnancy treatment until delivery. The participants were monitored from the third trimester (28 weeks of gestation) until delivery (37 weeks of gestation). The newborns of the participants were followed up for 28 days after delivery. Both the control and experimental groups were observed for maternal and neonatal outcomes. The outcomes related to the mothers, fetuses, and newborns were documented using a predetermined questionnaire in both study groups.

To ensure allocation concealment and minimize potential biases, the second author (first physician) was responsible for recruiting and following up with the control group, while the third author (second physician) handled recruitment and follow-up for the experimental group. To eliminate any confounding effects, we collected data on the women's use of multivitamins and excluded its influence during analysis. In addition, we conducted screening to match participants based on age, education, parity, body mass index (BMI), and smoking, as these factors can pose risks to maternal and neonatal outcomes. Unfortunately, technical issues prevented us from measuring the Vitamin D and calcium levels in both study groups. Consequently, we relied solely on self-reported multivitamin use by pregnant women. The study clinicians confirmed that women did not take Vitamin D supplements before pregnancy, and their supplement situations were similar. Due to technical challenges, randomization was not feasible in this study.

Study setting and sampling

The women for both the Vitamin D and Vitamin D + calcium groups were selected from the Duhok Maternity Hospital in Duhok, Iraqi Kurdistan, from January 2020 to November 2020. This hospital serves as the primary public health-care facility for providing counseling and treatment to pregnant women in the Duhok province. It offers comprehensive diagnostic, therapeutic, and surgical services, including cesarean sections and obstetric care, catering to women throughout all stages of pregnancy. To ensure a representative sample, we recruited patients over a suitable duration and made efforts to include individuals from various age groups. As the hospital attracts women from diverse geographic regions within the Duhok province seeking medical and therapeutic services, we are confident that our study encompasses participants with different sociodemographic characteristics.

Inclusion and exclusion criteria

The study aimed to recruit pregnant women in their third trimester, aged 18 years or older, from diverse sociodemographic backgrounds. However, certain exclusion criteria were established for both study groups. Participants who were unable to provide informed consent or had mental disorders were excluded. In addition, individuals with pregnancy complications such as pregnancy-induced hypertension, preeclampsia, and gestational diabetes were not included in the study. Furthermore, individuals with a history of chronic diseases, including diabetes, kidney stones, osteomalacia, active thyroid or parathyroid disorders, endocrine disorders, and hypertension, as well as those using diuretics or calcium-blockers, chronic hypertension, or documented allergy to the study supplements, were also excluded from the study.

To ensure the exclusion of specific medical conditions, the patients underwent thorough medical and clinical examinations, and their medical histories were carefully reviewed. A total of 256 women were assessed for eligibility by both gynecologists. Out of this initial pool, 157 women were excluded from the study for various reasons. After excluding these individuals, 99 women remained eligible for participation. Of 99 remaining women, the patients were assigned to the Vitamin D (n = 52) and Vitamin D + calcium groups (n = 47) by the second and third authors. During the study, two women from the Vitamin D group were lost to follow-up for unknown reasons. They did not attend the hospital for their scheduled follow-up visits and did not respond to the researcher's attempts to contact them. The remaining patients demonstrated homogeneity in terms of age, education, parity, and other medical and general

characteristics, except for BMI. To ensure BMI homogeneity between the two study groups, a manual assessment was conducted, resulting in the exclusion of nine patients from the Vitamin D group and eleven patients from the Vitamin D + calcium group [Figure 1].

Interventions

The patients assigned to the Vitamin D + calcium group were administered a daily dosage of 1000 IU of Vitamin D in addition to 500 mg of calcium in the form of calcium carbonate. In contrast, the patients in the Vitamin D group received a daily dosage of 1000 IU of Vitamin D only. These dosages were determined based on the opinions of the committee, which concluded that a daily intake of 1000–1200 international units of Vitamin D is considered safe, supported by clinical trials [15].

In this trial, the supplementation period for all participants began at 20 weeks of pregnancy, specifically during the 3rd month of pregnancy, corresponding to 20 weeks of gestation. The researchers were responsible for providing the necessary supplements to the patients. In the Vitamin D group, each patient received a box containing 100 soft gel dietary supplements, with each soft gel containing 1000 IU of Vitamin D. In the Vitamin D + calcium group, each patient received a box containing 100 soft gel dietary supplements, consisting of 1000 IU of Vitamin D, along with an additional box containing 100 soft gels of 500 mg calcium. Both the Vitamin D and calcium supplements were procured from the same company and received approval from the quality control Department of the Ministry of Health in the Kurdistan Region, ensuring their compliance with quality standards.

Outcome measurements

The study documented various maternal outcomes, including gestational diabetes, preeclampsia, eclampsia, new-onset gestational hypertension, proteinuria after 20 weeks of gestation, blood pressure measurements at the 20th and 39th week of gestation, pelvic muscle strength and control, delivery methods (such as normal vaginal delivery, elective or emergency cesarean section, episiotomy, and forceps delivery), preterm labor, hospital admissions, serum 25(OH) D concentration at baseline, impaired glucose tolerance (IGT), maternal death (occurring during pregnancy or within 42 days of pregnancy termination), and abortions. These outcomes were carefully recorded to assess their relationship with the interventions under study.

The study also conducted a comprehensive assessment of various neonatal outcomes to evaluate the effects of the interventions on the well-being and health of the newborns. These outcomes encompassed a wide range of parameters, including preterm birth (defined as delivery before 37 weeks' gestation), stillbirth, neonatal death, very preterm birth, birth weight (measured in grams), birth length (measured in centimeters), classification as small for gestational age, congenital malformations, admission to the neonatal intensive care unit (NICU), overall respiratory infections, upper

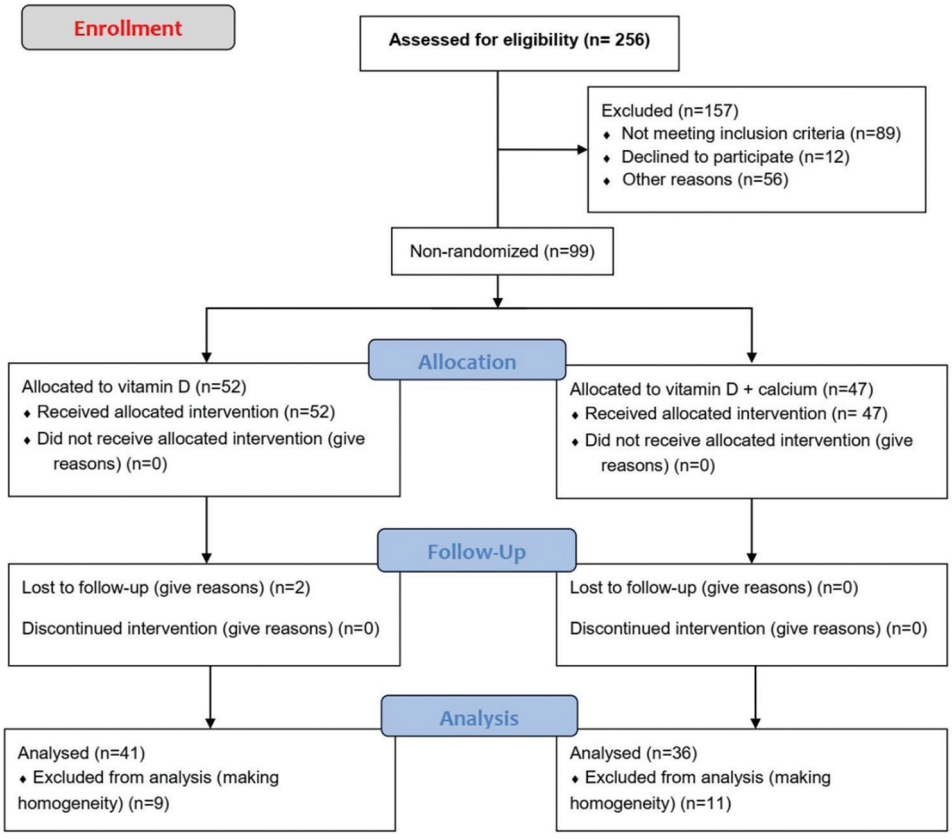

Figure 1: Flow chat of patient's recruitment

respiratory tract infections, lower respiratory tract infections, neonatal infections (such as respiratory infections within 28 days after delivery), head circumference at birth (measured in centimeters), gestational age at birth (measured in weeks), development of Type 1 diabetes mellitus, admission to special care (including intensive care) during the neonatal period, and APGAR score at 5 min.

Statistical methods

Descriptive statistical methods were used to present the frequency distribution and incidence of maternal and neonatal outcomes. The incidence rates of outcomes were calculated by dividing the number of affected patients or newborns by the total number of patients and multiplying by 100 in each study group. To assess the homogeneity of general and medical characteristics between the Vitamin D and Vitamin D + calcium groups, independent *t*-tests or Pearson's Chi-squared tests were conducted. Pearson's Chi-squared tests were also employed to examine differences in the occurrence of maternal and neonatal outcomes between the two study groups. The magnitude of these differences was determined by calculating the risk ratio, and the associated uncertainty was reported using a 95% confidence interval. Continuous outcomes between the study groups were compared using independent *t*-tests, with mean differences and confidence intervals indicating the level of uncertainty. The logistic regression model was used to identify controlling factors of preterm labor and birth weight. Statistical significance was determined by comparing *P* values to a predetermined threshold of <0.05. To ensure accuracy, reliability, and academic integrity, All Statistical Analyses were performed using JMP Pro 14.3.0, a Statistical Software Package (https://www.jmp.com/en_us/home.html) JMP®, Version 14.30. SAS Institute Inc., Cary, NC, 1989–2023.

Bias reduction techniques

In this study, allocation concealment bias was minimized as two independent gynecologists were responsible for recruiting women into either the Vitamin D group or the Vitamin D + calcium group. The second author recruited women into the Vitamin D group, while the third author recruited women into the Vitamin D + calcium group. This ensured that the allocation of patients was not influenced by a single individual. Furthermore, the patients were assessed by the same gynecologist who assigned them to their respective groups, reducing potential bias in the assessment process. By employing this approach, the study aimed to enhance the objectivity and integrity of the allocation process and minimize any potential biases that could have affected the results.

Ethical statement

The Ethical Approval of this study was received from the local health Ethics Committee in Duhok City. The committee responsible for health ethics consists of representatives from the Duhok General Directorate of Health and the University of Duhok. The study protocol was registered as 03122019-8 on December 3, 2019. Written informed consent was obtained from all patients before the inclusion of the patients in the study. Both the Vitamin D and Vitamin D + calcium groups received their regular treatment in accordance with the instructions provided by the ethics committee and the modified guidelines of the Helsinki Declaration. Throughout the study, strict measures were implemented to protect the confidentiality of patients' personal information, ensuring privacy and anonymity.

Results

The study observed comparable characteristics between the groups receiving D + calcium and Vitamin D alone, including age (29.31 vs. 29.46; $P = 0.8943$) and age groups ($P = 0.1324$), education ($P = 0.5177$), parity ($P = 0.1241$), smoking before pregnancy ($P = 0.1184$), smoking severity before pregnancy ($P = 0.1569$), current smoking ($P = 0.4956$), current smoking severity ($P = 0.4956$), BMI (28.42 vs. 29.38; $P = 0.0752$), BMI category ($P = 0.2167$), multivitamin use ($P = 0.0967$), physical activity (PA) during pregnancy ($P = 0.0864$), seasons of recruitment in the study ($P = 0.2431$), and ethnicity ($P = 0.4956$). However, a significant difference was noted between the two groups regarding the prevalence of preconception PA [$P = 0.0241$, Table 1].

The study findings demonstrated notable differences between the Vitamin D + calcium group and the Vitamin D group. Women in the Vitamin D + calcium group had significantly lower rates of gestational diabetes (2.78% vs. 19.51%; $P = 0.0318$), preeclampsia (2.78% vs. 26.83%; $P = 0.004$), newly onset gestational hypertension (11.11% vs. 46.34%; $P = 0.001$), and proteinuria (5.56% vs. 39.02%; $P = 0.0004$) compared to women in the Vitamin D group. In addition, the Vitamin D + calcium group exhibited a reduced likelihood of elective cesarean section (20.0% vs. 57.89%; $P = 0.0043$) and IGT (2.78% vs. 21.95%; $P = 0.0163$). Moreover, women in the Vitamin D + calcium group had lower blood pressure at the 20th and 39th weeks of gestation compared to women in the Vitamin D group. Notably, no cases of eclampsia or deaths occurred in either study group. There were no significant differences in the incidence of pelvic muscle issues (50.00% vs. 41.46%; $P = 0.4529$) or postdelivery hospital admissions (25.00% vs. 36.59%; $P = 0.2735$) between the Vitamin D + calcium and Vitamin D groups, respectively [Table 2 and Figure 2].

The study revealed that newborns in the Vitamin D + calcium group were less likely to experience LBW (5.71% vs. 31.58%; $P = 0.0066$), larger birth weight (3.25 vs. 2.78 kg; $P = 0.0004$), larger birth length (5.71% vs. 44.74%; $P = 0.0007$), and longer birth length (50.0 vs. 46.35 cm; $P < 0.0001$) compared to newborns in the Vitamin D group, respectively. In addition, newborns in the Vitamin D + calcium group were less likely to be admitted to the NICU (14.29% vs. 42.11%; $P = 0.0105$), have a larger head circumference (35.00 vs. 33.63; $P < 0.0001$), longer gestational age at birth (40.0 vs. 37.56 weeks; $P < 0.0001$), and higher APGAR scores [9.58 vs. 6.31; $P < 0.0001$; Table 3 and Figure 3].

We found that being obese, having a lower level of education, and no physical activity (PA) during and before

Table 1: Comparisons of general and medial characteristics between Vitamin D and Vitamin D + calcium groups

Characteristics	Study groups		*P* (two-sided)
	Vitamin D (*n*=41), *n* (%)	Vitamin D + calcium (*n*=36), *n* (%)	
Age (years), range	29.46 (4.27), 21–38	29.31 (6.06), 19–41	0.8943[a]
By age groups			
18–34	37 (90.24)	28 (77.78)	0.1324[b]
35 and older	4 (9.76)	8 (22.22)	
Education (years)			
<12	27 (65.85)	21 (58.33)	0.5177[b]
12	6 (14.63)	9 (25.00)	
>12	8 (19.51)	6 (16.67)	
Parity category			
No parity	3 (7.32)	1 (2.78)	0.1241[b]
Primi	14 (34.15)	22 (61.11)	
2–4	20 (48.78)	11 (30.56)	
≥5	4 (9.76)	2 (5.56)	
Smoking before pregnancy			
Nonsmoker	37 (90.24)	36 (100)	0.1184[b]
Smoker	4 (9.76)	0	
Smoking severity (before pregnancy)			
Nonsmoker	37 (90.24)	36 (100)	0.1569[b]
Light	3 (7.32)	0	
Moderate	1 (2.44)	0	
Current smoking			
Nonsmoker	39 (95.12)	36 (100)	0.4956[b]
Smoker	2 (4.88)	0	
Current smoking severity			
Nonsmoker	39 (95.12)	36 (100)	0.4956[b]
Light	2 (4.88)	0	
BMI category			
Normal weight	0	2 (5.56)	0.2167[b]
Overweight	28 (68.29)	20 (55.56)	
Obese	13 (31.71)	14 (38.89)	
BMI, range	28.42 (2.34), 24.97–34.29	29.38 (2.29), 24.13–33.46	0.0752[b]
Multivitamin use			
No	15 (36.59)	7 (19.44)	0.0967[b]
Yes	26 (63.41)	29 (80.56)	
Preconception PA			
None	2 (4.88)	0	**0.0241[b]**
Low intensity	11 (26.83)	20 (55.56)	
Medium intensity	17 (41.46)	13 (36.11)	
High intensity	11 (26.83)	3 (8.33)	
PA during pregnancy			
None	8 (19.51)	1 (2.78)	0.0864[b]
Low intensity	18 (43.90)	22 (61.11)	
Medium intensity	14 (34.15)	13 (36.11)	
High intensity	1 (2.44)	0	
Season			
Cold seasons	27 (65.85)	19 (52.78)	0.2431[b]
Hot seasons	14 (34.15)	17 (47.22)	
Race			
Kurdish	39 (95.12)	36 (100)	0.4956[b]
Arab	2 (4.88)	0	
Vitamin D (ng/mL)	21.61 (9.47)	25.75 (7.71)	**0.0405[a]**
Range	7–43	11–43	
Vitamin D			
Severe deficiency	1 (2.44)	0	
Deficient	15 (36.59)	6 (16.67)	0.1694[b]
Insufficient	17 (41.46)	21 (58.33)	
Sufficient	8 (19.51)	9 (25.00)	

[a]An independent *t*-test and [b]Pearson's Chi-squared tests were performed for statistical analyses. The bold numbers show the significant differences.
BMI: Body mass index, PA: Physical activity

Table 2: Comparisons of maternal outcomes between Vitamin D and Vitamin D + calcium groups

Characteristics	Study groups		*P* (two-sided)	RR (95% CI)/mean difference (95% CI)
	Vitamin D (*n*=41), *n* (%)	Vitamin D + calcium (*n*=36), *n* (%)		
Gestational diabetes				
No	33 (80.49)	35 (97.22)	**0.0318**[b]	0.22 (0.03–1.39)
Yes	8 (19.51)	1 (2.78)		
Preeclampsia				
No	30 (73.17)	35 (97.22)	**0.004**[b]	0.15 (0.02–1.02)
Yes	11 (26.83)	1 (2.78)		
Eclampsia/no	41 (100)	36 (100)	NA	NA
New onset gestational hypertension				
No	22 (53.66)	32 (88.89)	**0.001**[b]	0.29 (0.12–0.73)
Yes	19 (46.34)	4 (11.11)		
Proteinuria				
No	25 (60.98)	34 (94.44)	**0.0004**[b]	0.19 (0.05–0.73)
Yes	16 (39.02)	2 (5.56)		
Pelvic muscle				
No	24 (58.54)	18 (50.00)	0.4529[b]	1.2 (0.75–1.93)
Yes	17 (41.46)	18 (50.00)		
Delivery			**0.0043**[b]	
NVD	9 (23.68)	17 (48.57)		Reference
Episiotomy	0	3 (8.57)		1.53 (1.16–2.02)
Elective C/S	22 (57.89)	7 (20.00)		0.37 (0.18–0.75)
Emergency C/S	7 (18.42)	8 (22.86)		0.82 (0.47–1.41)
Preterm labor				
No	28 (73.68)	34 (97.14)	**0.0071**[b]	0.17 (0.03–1.09)
Yes	10 (26.32)	1 (2.86)		
Admission to hospital				
No	26 (63.41)	27 (75.00)	0.2735[b]	0.74 (0.41–1.31)
Yes	15 (36.59)	9 (25.00)		
IGT				
No	32 (78.05)	35 (97.22)	**0.0163**[b]	0.19 (0.03–1.25)
Yes	9 (21.95)	1 (2.78)		
Maternal death/no	41 (100)	36 (100)	NA	NA
SBP (20th week)	109.51 (10.24)	100.27 (8.60)	**0.0006**[a]	−9.24 (−14.37–−4.11)
DBP (20th week)	70.12 (9.18)	60 (0.0)	**<0.0001**[a]	−10.12 (−14.75–−5.50)
SBP (39th week)	127.80 (16.01)	105.00 (7.60)	**<0.0001**[a]	−22.81 (−31.75–−13.86)
DBP (39th week)	82.56 (13.00)	74.75 (20.16)	0.0726[a]	−7.81 (−16.36–0.74)

[a]An independent *t*-test and, [b]Pearson's Chi-squared tests were performed for statistical analyses. The bold numbers show the significant differences. RR: Risk ratio, CI: Confidence interval, IGT: Impaired glucose tolerance, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, NVD: Normal vaginal delivery, NA: Not available

pregnancy, being a current smoker, and having pregnancy during cold seasons were predictors of having preterm labor among women who were included in the Vitamin D. In terms of neonatal and fetal outcomes, the study showed that not using multivitamin by women, smoking before pregnancy, being obese, and not having PA during pregnancy among Vitamin D group were the predictors of LBW of newborns [Table 4a].

The study showed that obese women were more likely to develop preterm labor compared to overweight women (53.85% vs. 12.00%; $P = 0.0161$). In addition, the patients with higher age groups, having more parity, being smokers, not having PA before and during pregnancy, and pregnancy in cold seasons were more likely to develop preterm labor compared to those women without these conditions, but the overall differences were not statistically significant. Furthermore, the newborns of these women were more likely to have LBW compared to the newborns of the women without these conditions, but the overall divergences were not statistically significant [Table 4b].

Discussion

This study provides evidence supporting the positive effects of daily co-supplementation of Vitamin D and calcium from 20 weeks of gestation until delivery in reducing maternal and neonatal outcomes. Importantly, numerous studies in the existing literature, including systematic reviews and meta-analyses, have extensively investigated the efficacy of Vitamin D and calcium in improving maternal and neonatal outcomes [16-18].

The literature provides evidence supporting the positive impacts of Vitamin D in decreasing maternal and neonatal outcomes. These effects include improvements in birth weight

Table 3: Comparisons of fetal and neonatal outcomes between Vitamin D and Vitamin D + calcium groups

Characteristics	Study groups		*P* (two-sided)	RR (95% CI)/mean difference (95% CI)
	Vitamin D (*n*=41), *n* (%)	Vitamin D + calcium (*n*=36), *n* (%)		
Fetal outcome				
Abortion	3 (7.32)	1 (2.78)	0.6135[b]	0.52 (0.09–2.89)
Alive	38 (92.68)	35 (97.22)		
Neonatal outcome			0.4193[b]	
Alive	37 (90.24)	35 (97.22)		Reference
Abortion	3 (7.32)	1 (2.78)		0.51 (0.09–2.85)
Dead	1 (2.44)	0		NA
Very preterm birth				
No	37 (97.37)	35 (100)	1.0000[b]	NA
Yes	1 (2.63)	0		
Birth weight (kg)	2.78 (0.54)	3.25 (0.52	**0.0004**[a]	0.47 (0.22–0.72)
Range	1.8–4.8	2.3–4.5		
Birth weight				
LBW	12 (31.58)	2 (5.71)	**0.0066**[b]	0.26 (0.07–0.94)
Normal weight	26 (68.42)	33 (94.29)		
Birth length (cm)	46.35 (2.51	50.00 (0)	**<0.0001**[a]	3.65 (2.1–5.18)
Birth length				
Normal birth length	20 (52.63)	32 (91.43)		Reference
Low birth length	17 (44.74)	2 (5.71)	**0.0007**[b]	0.17 (0.05–0.65)
Long birth length	1 (2.63)	1 (2.86)		0.81 (0.20–3.30)
SGA				
No	31 (81.58)	31 (88.57)	0.5192[b]	0.73 (0.32–1.65)
Yes	7 (18.42)	4 (11.43)		
Congenital malformations				
No	41 (100)	35 (97.22)	0.4675[b]	2.17 (1.70–2.77)
Yes	0	1 (2.78)		
Admission to NICU				
No	22 (57.89)	30 (85.71)	**0.0105**[b]	0.41 (0.19–0.92)
Yes	16 (42.11)	5 (14.29)		
Respiratory infections				
No	31 (81.58)	34 (97.14)	0.0573[b]	0.24 (0.04–1.52)
Yes	7 (18.42)	1 (2.86)		
URTI				
No	36 (94.74)	34 (97.14)	1.0000[b]	0.69 (0.14–3.46)
Yes	2 (5.26)	1 (2.86)		
LRTI				
No	38 (100)	34 (97.14)	0.4795[b]	2.12 (1.66–2.70)
Yes	0	1 (2.86)		
Neonatal infection				
No	35 (92.11)	35 (100)	0.2409[b]	NA
Yes	3 (7.89)	0		
T1DM				
No	38 (100)	35 (100)	NA	NA
Admission to special care				
No	36 (94.74)	34 (97.14)	1.0000[b]	0.69 (0.14–3.46)
Yes	2 (5.26)	1 (2.86)		
Head circumference (cm)	33.63 (0.88)	35.00 (0)	**<0.0001**[a]	1.37 (1.05–1.69)
Gestational age at birth	37.56 (1.83)	40 (0.0)	**<0.0001**[a]	2.44 (1.81–3.08)
Apgar score	6.31 (0.94)	9.58 (0.66)	**<0.0001**[a]	3.27 (2.87–3.67)
Apgar				
Low Apgar score	22 (57.89)	1 (2.86)	**<0.0001**[b]	0.06 (0.01–0.44)
Normal Apgar score	16 (42.11)	34 (97.14)		

[a]An independent *t*-test and [b]Pearson's Chi-squared tests were performed for statistical analyses. The bold numbers show the significant differences. NICU: Neonatal intensive care unit, URTI: Upper respiratory tract infection, LRTI: Lower respiratory tract infection, T1DM: Type 1 diabetes mellitus, SGA: Small for gestational age, LBW: Low birth weight, RR: Risk ratio, CI: Confidence interval, NA: Not available

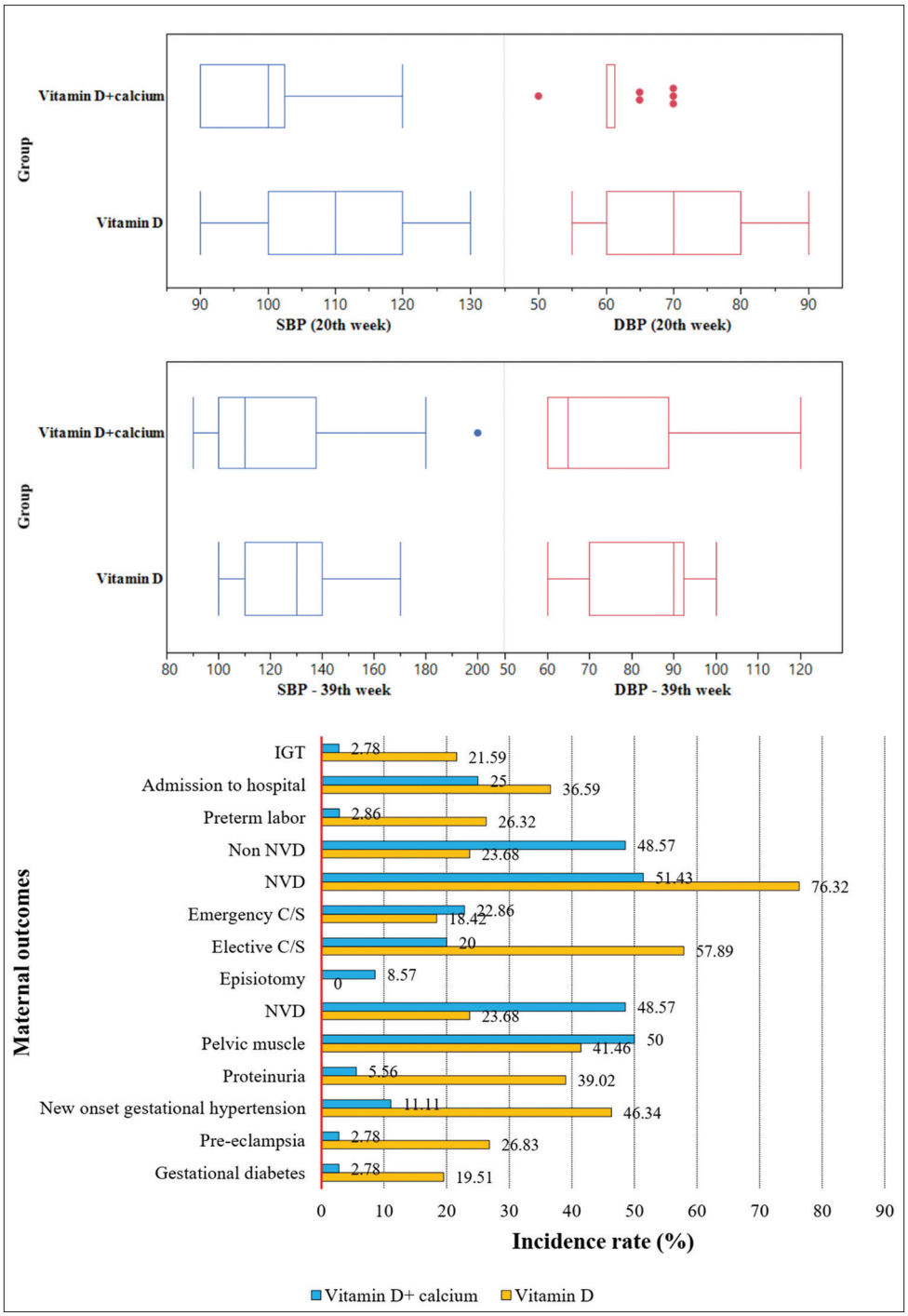

Figure 2: Maternal outcomes of Vitamin D and Vitamin D + calcium study groups. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, IGT: Impaired glucose tolerance, NVD: Normal vaginal delivery

and a reduction in the incidence of small for gestational age among infants [19] and preeclampsia [17], and effects of calcium on preeclampsia [16]. In addition, there are some studies on the effects of Vitamin D + calcium versus no treatment/placebo on some maternal outcomes for instance preeclampsia [20]. Even some of these studies have not reported the positive effects of Vitamin D + calcium on maternal outcomes [21,22]. The effects of the combination of vitamin and calcium have been evaluated for gestational diabetes and reported no effects [22] and preterm birth [20,22], gestational hypertension [23], and neonatal death [20]. The placebo group received no minerals or vitamins. However, the effectiveness of vitamin + calcium versus Vitamin D has not been investigated in the literature yet.

One major flaw in the aforementioned studies is that the observed effectiveness of the combination of vitamins and calcium compared to a placebo might be attributed primarily to the presence of Vitamin D rather than the combination of

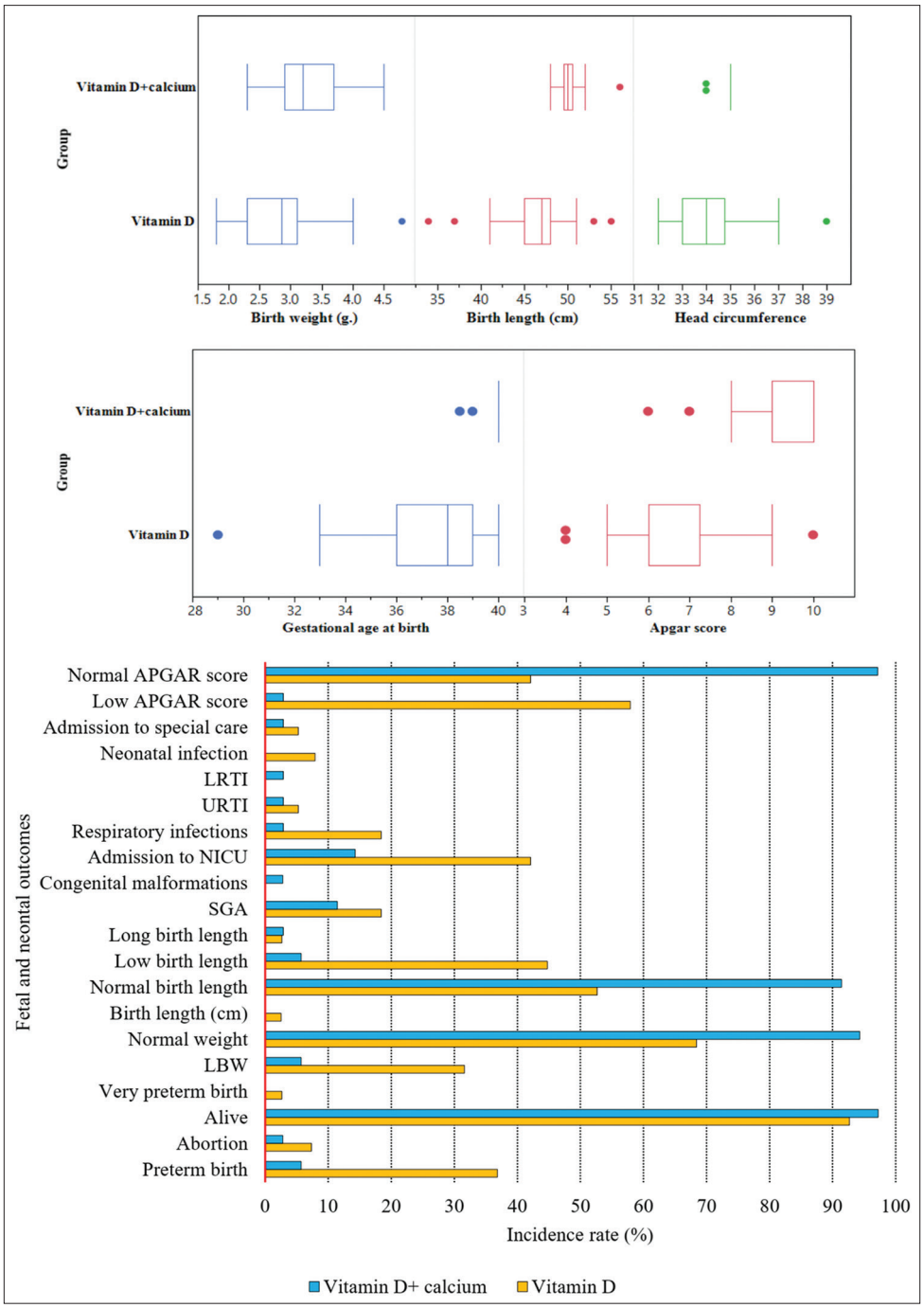

Figure 3: Neonatal and fetal outcomes of Vitamin D and Vitamin D + calcium groups. NICU: Neonatal intensive care unit, LBW: Low birth weight, URTI: Upper respiratory tract infection, LRTI: Lower respiratory tract infection, SGA: Small for gestational age

Vitamin D and calcium. This knowledge gap in the existing literature prompted us to design the present study. It is important to note that only one RCT, conducted in 2015, has previously investigated the effects of Vitamin D and calcium–Vitamin D supplementation on pregnancy and birth outcomes. The study primarily focused on evaluating the pregnancy duration, delivery type, and infant anthropometric indicators. However, the study suffered from significant shortcomings in terms of research methodology and outcome measurement. Consequently, the reliability of the study's findings is questionable and cannot be considered definitive evidence within the existing body of literature [24]. Taking 50,000 IU/week Vitamin D + 1000 mg/day calcium co-supplementation results in decreased serum insulin levels and Homeostatic Model Assessment for Insulin Resistance score, and a substantial increase in quantitative insulin-sensitivity check index (QUICKI) score in persons with insufficient Vitamin D with Type 2 diabetes mellitus for 8 weeks [25].

Limited information is currently available regarding the potential advantages of co-supplementing with Vitamin D

Table 4a: Predictors of preterm labor among women in the Vitamin D study group

Controlling factors	Outcome: Preterm labor	*P*
BMI category		<0.0001
Maternal education		<0.0001
During pregnancy PA		<0.0001
Preconception PA		<0.0001
Current smoking		<0.0001
Season		0.00466
Parity category		0.05575
Multivitamin use		0.30632
Smoking before pregnancy		0.98087
Age groups		0.99997
Controlling factors	**Outcome: Preterm weight (LBW)**	***P***
Multivitamin use		0.00053
Smoking before pregnancy		0.01375
BMI category		0.03041
During pregnancy PA		0.03072
Season		0.06215
Parity category		0.16221
Current smoking		0.37428
Preconception PA		0.53937
Maternal education		0.73166
Age groups		0.77468

Nominal logistic regression was performed for statistical analyses. LBW: Low birth weight, BMI: Body mass index, PA: Physical activity

and calcium in relation to glucose homeostasis. Specifically, existing studies have indicated that 3 months of Vitamin D and calcium supplementation does not appear to have a substantial impact on insulin metabolism in overweight women with polycystic ovary syndrome who are also deficient in Vitamin D. This finding emphasizes the necessity for additional research to deepen our understanding of the potential influences of Vitamin D-calcium co-supplementation on glucose regulation and other interconnected metabolic parameters. By conducting further investigations in this field, we can gain valuable insights into the effects of this co-supplementation approach [26].

The precise mechanisms through which co-supplementation with Vitamin D and calcium impacts maternal and neonatal outcomes have yet to be fully comprehended. However, it is hypothesized that their effectiveness might be attributed to their influence on blood pressure. One potential mechanism involves their impact on the renin-angiotensin system, which plays a vital role in blood pressure regulation. Moreover, Vitamin D and calcium may affect vascular endothelial function and intracellular calcium concentrations within vascular smooth muscle, potentially contributing to their effects on blood pressure control. To gain a deeper understanding of the observed benefits of Vitamin D and calcium co-supplementation on maternal and neonatal outcomes, further research is necessary to investigate and elucidate the specific mechanisms involved [27,28]. In a recent study, researchers aimed to assess the efficacy of calcium carbonate–Vitamin D3 supplementation in preventing hypertensive disorders during pregnancy. To investigate this, they randomly divided pregnant women into two groups: one receiving standard pregnancy care (observation group) and the other receiving standard pregnancy care along with calcium carbonate–Vitamin D3 supplementation (experimental group). The study findings indicated that the experimental group exhibited significantly lower systolic blood pressure and diastolic blood pressure compared to the observation group. Furthermore, the administration of Vitamin D3 and calcium was associated with a reduced incidence rate of hypertensive disorders and adverse outcomes when compared to standard pregnancy care alone [29]. These results suggest that calcium carbonate–Vitamin D3 supplementation may have a beneficial effect in mitigating hypertensive disorders during pregnancy.

During pregnancy, the metabolic needs of women increase significantly to support the growth and development of the fetus. Adequate calcium intake is crucial during this period, as a deficiency in calcium predisposes pregnant women to developing hypertensive disorders [30]. Calcium plays a vital role in maintaining normal contraction of vascular smooth muscles. Insufficient calcium levels can lead to abnormal smooth muscle contractions, resulting in elevated blood pressure levels and an increased risk of hypertensive disorders [31]. Calcium carbonate–Vitamin D3 tablets, commonly used in clinical practice, provide a calcium supplement. These tablets contain calcium carbonate along with Vitamin D3. Vitamin D3 helps improve the absorption and utilization of calcium in pregnant women. It also reduces the kidney's metabolism of calcium elements and assists in maintaining the proper concentration of calcium in the bloodstream [32]. By combining calcium and Vitamin D3 supplementation, pregnant women can optimize their calcium levels, supporting maternal and fetal health during pregnancy.

When considering the intake of Vitamin D alongside calcium, it is important to note that maintaining a proper balance necessitates sufficient calcium intake. Calcium absorption occurs within the small intestines, facilitated by Vitamin D [33]. The primary route of calcium excretion is through the kidneys, with only minor fecal loss. The major function of Vitamin D is to optimize intestinal calcium and phosphorus absorption for the proper formation of the bone mineral matrix. Calcium is transported across the intestine by a paracellular or transcellular pathway. The paracellular pathway is predominately a passive process, whereas the transcellular process is highly regulated by 1,25-dihydroxyvitamin D (1,25(OH)2D). Several Vitamin D-dependent calcium transport proteins regulate intestinal calcium absorption. Transient receptor potential cation channel, subfamily V, member 6 (TRPV6), denotes a calcium channel sited on the

Table 4b: Incidence of preterm labor and birth weight among Vitamin D women with different characteristics

	Preterm labor		*P*	Birth weight		*P*
	No, *n* (%)	Yes, *n* (%)		LBW, *n* (%)	Normal weight, *n* (%)	
Age groups						
18–34	26 (74.29)	9 (25.71)	1.000	12 (34.29)	23 (65.71)	0.5377
35 and older	2 (66.67)	1 (33.33)		0	3 (100)	
Maternal education (years)						
<12	18 (72.00)	7 (28.00)	0.5202	8 (32.00)	17 (68.00)	0.8017
12	3 (60.00)	2 (40.00)		1 (20.00)	4 (80.00)	
>12	7 (87.50)	1 (12.50)		3 (37.50)	5 (62.50)	
BMI category						
Overweight	22 (88.00)	3 (12.00)	0.0161	9 (36.00)	16 (64.00)	0.4859
Obese	6 (46.15)	7 (53.85)		3 (23.08)	10 (76.92)	
Parity category						
No parity	3 (100.00)	0	0.0770	2 (66.67)	1 (33.33)	0.3752
Primi	11 (78.57)	3 (21.43)		5 (35.71)	9 (64.29)	
2–4	14 (73.68)	5 (26.32)		4 (21.05)	15 (78.95)	
≥5	0	2 (100)		1 (50.00)	1 (50.00)	
Smoking before pregnancy						
Nonsmoker	26 (74.29)	9 (25.71)	1.000	11 (31.43)	24 (68.57)	1.000
Smoker	2 (66.67)	1 (33.33)		1 (33.33)	2 (66.67)	
Smoking severity						
Nonsmoker	26 (74.29)	9 (25.71)	0.6243	11 (31.43)	24 (68.57)	0.6784
Light	1 (50.00)	1 (50.00)		1 (50.00)	1 (50.00)	
Moderate	1 (100.00)	0		0	1 (100.00)	
Current smoking						
Nonsmoker	27 (75.00)	9 (25.00)	0.4623	11 (30.56)	25 (69.44)	0.5377
Smoker	1 (50.00)	1 (50.00)		1 (50.00)	1 (50.00)	
Current smoking severity						
Nonsmoker	27 (75.00)	9 (25.00)	0.4623	11 (30.56)	25 (69.44)	0.5377
Light	1 (50.00)	1 (50.00)		1 (50.00)	1 (50.00)	
Multivitamin use						
No	10 (71.43)	4 (28.57)	1.000	7 (50.00)	7 (50.00)	0.0812
Yes	18 (75.00)	6 (25.00)		5 (20.83)	19 (79.17)	
Preconception PA						
None	2 (100.00)	0	0.0746	0	2 (100.00)	0.1226
Low intensity	5 (45.45)	6 (54.55)		6 (54.55)	5 (45.45)	
Medium intensity	12 (80.00)	3 (20.00)		5 (33.33)	10 (66.67)	
High intensity	9 (90.00)	1 (10.00)		1 (10.00)	9 (90.00)	
During pregnancy PA						
None	5 (62.50)	3 (37.50)	0.1736	3 (37.50)	5 (62.50)	0.0516
Low intensity	9 (60.00)	6 (40.00)		7 (46.67)	8 (53.33)	
Medium intensity	13 (92.86)	1 (7.14)		1 (7.14)	13 (92.86)	
High intensity	1 (100.00)	0		1 (100.00)	0	
Season						
Cold seasons	16 (66.67)	8 (33.33)	0.2685	9 (37.50)	15 (62.50)	0.4722
Hot seasons	12 (85.71)	2 (14.29)		3 (21.43)	11 (78.57)	

Pearson's Chi-squared tests were performed for statistical analyses. LBW: Low birth weight, BMI: Body mass index, PA: Physical activity

inner lining of enterocytes. Its primary function involves enabling the passage of calcium into these enterocytes. Notably, the regulation of TRPV6 heavily relies on 1,25(OH) 2D, and its expression is particularly prominent in the duodenum when compared to the jejunum and ileum [34]. In women, the levels of TRPV6 experience a decline as they age, which contributes in part to the observed reduction in calcium absorption linked to aging [35]. A significant player in the calcium transport process is Calbindin 9k, a protein dedicated to transporting calcium from the inner surface of enterocytes to their basal surface. Concluding the intricate calcium regulatory system are two additional Vitamin D-modulated cation exchange proteins, PMCA1b and NCX1. These proteins are positioned on the basal surface of enterocytes and function to expel calcium into the bloodstream [36].

Limitations of the study

The weak point of this study must be found in the nonapplication of the randomization process on the patients owing to the technical issues. In addition, we had not an

independent researcher for the assessment of the outcomes, but the researchers were not aware of the women's outcomes of another group. The daily doses of Vitamin D supplements are different for women which makes a difficult to compare the findings between studies. Also, the study subjects to the alpha error due to possible issues in the recruitment of the patients. We call for more randomized clinical trials on the effectiveness of taking Vitamin D and calcium in pregnant women. We measured the Vitamin D levels for patients in both the Vitamin D and Vitamin D + calcium groups before the intervention to ensure homogeneity. We were unable to measure it at delivery due to insufficient funds.

Conclusion

This study showed that taking vitamins and calcium by pregnant women in the third trimester is an effective treatment to decrease maternal, fetal, and neonatal outcomes.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

We would like to present our deep thanks to the administration of the Duhok Maternity Hospital and the patients who participated in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Del Valle HB, Yaktine AL, Taylor CL, Ross AC. Dietary reference intakes for calcium and Vitamin D. Washington (DC): Institute of Medicine; 2011.
2. Suaini NH, Zhang Y, Vuillermin PJ, Allen KJ, Harrison LC. Immune modulation by Vitamin D and its relevance to food allergy. Nutrients 2015;7:6088-108.
3. Xu S, Chen YH, Tan ZX, Xie DD, Zhang C, Xia MZ, et al. Vitamin D3 pretreatment alleviates renal oxidative stress in lipopolysaccharide-induced acute kidney injury. J Steroid Biochem Mol Biol 2015;152:133-41.
4. Roth DE, Abrams SA, Aloia J, Bergeron G, Bourassa MW, Brown KH, et al. Global prevalence and disease burden of Vitamin D deficiency: A roadmap for action in low- and middle-income countries. Ann N Y Acad Sci 2018;1430:44-79.
5. Amegah AK, Klevor MK, Wagner CL. Maternal Vitamin D insufficiency and risk of adverse pregnancy and birth outcomes: A systematic review and meta-analysis of longitudinal studies. PLoS One 2017;12:e0173605.
6. Vivanti AJ, Monier I, Salakos E, Elie C, Tsatsaris V, Senat MV, et al. Vitamin D and pregnancy outcomes: Overall results of the FEPED study. J Gynecol Obstet Hum Reprod 2020;49:101883.
7. Hollis BW, Wagner CL. Vitamin D and pregnancy: Skeletal effects, nonskeletal effects, and birth outcomes. Calcif Tissue Int 2013;92:128-39.
8. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, et al. Serum Vitamin D levels and markers of severity of childhood asthma in Costa Rica. Am J Respir Crit Care Med 2009;179:765-71.
9. Chen YH, Fu L, Hao JH, Yu Z, Zhu P, Wang H, et al. Maternal Vitamin D deficiency during pregnancy elevates the risks of small for gestational age and low birth weight infants in Chinese population. J Clin Endocrinol Metab 2015;100:1912-9.
10. Bond DM, Middleton P, Levett KM, van der Ham DP, Crowther CA, Buchanan SL, et al. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. Cochrane Database Syst Rev 2017;3:CD004735.
11. Thorp JM, Camargo CA, McGee PL, Harper M, Klebanoff MA, Sorokin Y, et al. Vitamin D status and recurrent preterm birth: A nested case-control study in high-risk women. BJOG 2012;119:1617-23.
12. Boyle VT, Thorstensen EB, Mourath D, Jones MB, McCowan LM, Kenny LC, et al. The relationship between 25-hydroxyvitamin D concentration in early pregnancy and pregnancy outcomes in a large, prospective cohort. Br J Nutr 2016;116:1409-15.
13. Miliku K, Vinkhuyzen A, Blanken LM, McGrath JJ, Eyles DW, Burne TH, et al. Maternal Vitamin D concentrations during pregnancy, fetal growth patterns, and risks of adverse birth outcomes. Am J Clin Nutr 2016;103:1514-22.
14. World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: World Health Organization; 2016.
15. Mohamed SA, Al-Hendy A, Schulkin J, Power ML. Opinions and practice of US-based obstetrician-gynecologists regarding Vitamin D screening and supplementation of pregnant women. J Pregnancy 2016;2016:1454707.
16. Patrelli TS, Dall'asta A, Gizzo S, Pedrazzi G, Piantelli G, Jasonni VM, et al. Calcium supplementation and prevention of preeclampsia: A meta-analysis. J Matern Fetal Neonatal Med 2012;25:2570-4.
17. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal Vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab 2007;92:3517-22.
18. Tabesh M, Salehi-Abargouei A, Tabesh M, Esmaillzadeh A. Maternal Vitamin D status and risk of pre-eclampsia: A systematic review and meta-analysis. J Clin Endocrinol Metab 2013;98:3165-73.
19. Roth DE, Leung M, Mesfin E, Qamar H, Watterworth J, Papp E. Vitamin D supplementation during pregnancy: State of the evidence from a systematic review of randomised trials. BMJ 2017;359:j5237.
20. Taherian AA, Taherian A, Shirvani A. Prevention of preeclampsia with low-dose aspirin or calcium supplementation. Arch Iran Med 2002;5:151-6.
21. Marya RK, Rathee S, Lata V, Mudgil S. Effects of Vitamin D supplementation in pregnancy. Gynecol Obstet Invest 1981;12:155-61.
22. Asemi Z, Tabassi Z, Heidarzadeh Z, Khorammian H, Sabihi SS, Samimi M. Effect of calcium-Vitamin D supplementation on metabolic profiles in pregnant women at risk for pre-eclampsia: A randomized placebo-controlled trial. Pak J Biol Sci 2012;15:316-24.
23. Li X, Gou W. Study on prevention of pregnancy induced hypertension and effect of platelet intracellular free ca (2+) by calcium supplementation. J Xian Med Univ 2000;21:46-8.
24. Mohammad-Alizadeh-Charandabi S, Mirghafourvand M, Mansouri A, Najafi M, Khodabande F. The effect of Vitamin D and calcium plus Vitamin D during pregnancy on pregnancy and birth outcomes: A randomized controlled trial. J Caring Sci 2015;4:35-4425.
25. Tabesh M, Azadbakht L, Faghihimani E, Tabesh M, Esmaillzadeh A. Effects of calcium-Vitamin D co-supplementation on metabolic profiles in Vitamin D insufficient people with type 2 diabetes: A randomised controlled clinical trial. Diabetologia 2014;57:2038-47.
26. Pal L, Berry A, Coraluzzi L, Kustan E, Danton C, Shaw J, et al. Therapeutic implications of Vitamin D and calcium in overweight women with polycystic ovary syndrome. Gynecol Endocrinol 2012;28:965-8.
27. Nasri H, Behradmanesh S, Ahmadi A, Rafieian-Kopaei M. Impact of oral Vitamin D (cholecalciferol) replacement therapy on blood pressure in type 2 diabetes patients; a randomized, double-blind, placebo controlled clinical trial. J Nephropathol 2014;3:29-33.

28. Wilson C. Nutrition: Vitamin D improves blood pressure in type 2 diabetes. Nat Rev Endocrinol 2010;6:533.
29. Chen Z, Chen J. The efficacy of calcium carbonate-Vitamin D3 in pregnant women for the prevention of hypertensive disorders in pregnancy. Evid Based Complement Alternat Med 2022;2022:7971976.
30. Rajaie H, Rabiee MR, Bellissimo N, Faghih S. Independent and combined effects of calcium and Vitamin D supplementation on blood lipids in overweight or obese premenopausal women: A triple-blind randomized controlled clinical trial. Int J Prev Med 2021;12:52.
31. Wang SZ, Wang ZK, Gong JS, Qin J, Dong TT, Xu ZH, et al. Improving the biocatalytic performance of co-immobilized cells harboring nitrilase via addition of silica and calcium carbonate. Bioprocess Biosyst Eng 2020;43:2201-7.
32. Janoušek J, Pilařová V, Macáková K, Nomura A, Veiga-Matos J, Silva DD, et al. Vitamin D: Sources, physiological role, biokinetics, deficiency, therapeutic use, toxicity, and overview of analytical methods for detection of Vitamin D and its metabolites. Crit Rev Clin Lab Sci 2022;59:517-54.
33. Anderson D. Harrison's principles of internal medicine. USA: AAN Enterprises; 2005.
34. Walters JR, Balesaria S, Chavele KM, Taylor V, Berry JL, Khair U, et al. Calcium channel TRPV6 expression in human duodenum: Different relationships to the Vitamin D system and aging in men and women. J Bone Miner Res 2006;21:1770-7.
35. Pattanaungkul S, Riggs BL, Yergey AL, Vieira NE, O'Fallon WM, Khosla S. Relationship of intestinal calcium absorption to 1,25-dihydroxyvitamin D [1,25(OH)2D] levels in young versus elderly women: Evidence for age-related intestinal resistance to 1,25(OH)2D action. J Clin Endocrinol Metab 2000;85:4023-7.
36. Walters JR, Balesaria S, Khair U, Sangha S, Banks L, Berry JL. The effects of Vitamin D metabolites on expression of genes for calcium transporters in human duodenum. J Steroid Biochem Mol Biol 2007;103:509-12.