

Relationship between 25-Hydroxyvitamin D3 Levels with Pain Intensity and Duration of Labor Stages in Primiparous Women

Abstract

Background: Prolonged labor is associated with various maternal and neonatal complications. This study aims to investigate the relationship between 25-hydroxyvitamin D3 levels and pain intensity and duration of labor stages in primiparous women. **Materials and Methods:** This cross-sectional study was conducted in Iran from November 2021 to January 2022 and comprised primiparous women who were in active labor after a term pregnancy (37–42 weeks). Five milliliter of blood was taken from each subject and centrifuged for the measurement of vitamin D level using the enzyme-linked immunosorbent assay method. The High-Performance Liquid Chromatography (HPLC) method was used to measure 25-OH vitamin D. In addition, through history, examination, and investigations, the subjects were evaluated according to the pain intensity and duration of the first (active phase) and second stages of labor. **Results:** The results of the Pearson correlation test indicated a significant relationship between vitamin D and active phase duration ($r = 0.64, p = 0.012$), second stage duration ($r = 0.73, p = 0.001$), pain intensity of the active phase ($r = 0.61, p = 0.022$), and pain intensity of the second stage ($r = 0.65, p = 0.026$). According to the analysis of variance table, based on vitamin D, there were statistically significant differences between the groups in terms of the active phase duration, second stage duration, pain intensity of the active phase, and that of the second stage of labor ($p < 0.05$). **Conclusions:** Low levels of vitamin D may influence the progress of labor and increase the rate of prolonged labor.

Keywords: 25-Hydroxyvitamin D3, labor stage, labor pain, pregnancy

Introduction

Childbirth is one of the most unique moments in women's lives, but if its stages are prolonged, it becomes an unbearable phenomenon.^[1] According to studies conducted in Indonesia and Guatemala, the prevalence of prolonged labor was 2.8%.^[2] According to a study in public maternity centers in Kashan, Iran, the rate of cesarean section (CS) after prolonged delivery and lack of progress in labor was 7.4%^[3]; and in general, prolonged labor in Iran has been reported in 10% of pregnancies.^[4] Prolonged and difficult labor is a critical condition^[5] with maternal complications including the risk of uterine rupture, vesicovaginal or vesicocervical fistulas, severe rupture of the genital area, cystocele, rectocele, infertility, and fetal complications such as head compression, hypoxia, and a low Apgar score,^[1] which are associated with suffocation, seizures, cerebral palsy, and eventually fetal death.^[6] Recent reports suggest that poor

muscle function and contractile disorders may be signs of vitamin D deficiency.^[7] Nowadays, there is a possibility of a biological relationship between maternal vitamin D deficiency and the side effects of childbirth on muscle function.^[8]

Vitamin D deficiency can also affect the method of delivery in several ways. One of the possible cases is a decrease in the strength of the muscular structure of the uterus and the mother's ability to expel the fetus.^[9] Vitamin D, 1, and 25-dihydroxyvitamin D (25-OH-D) receptors are present in skeletal muscle and smooth muscle and naturally increase skeletal muscle function.^[10] For this reason, attention to the role of vitamin D in causing uterine contractions has led some researchers to conduct research in this field. Researchers concluded that vitamin D receptors are present in human muscle tissue and that the direct effect of vitamin D on muscle physiology is biologically acceptable.^[11]

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Another study showed that vitamin D regulates contractile proteins in myometrial cells.^[12] The results of some studies contradict the findings of previous studies; for example, a study conducted at Tehran Women's General Hospital showed that there was no relationship between vitamin D levels and the type of delivery or the length of labor phases.^[13]

The results of a review study indicate that serum levels of 25-OH-D were less than 25 ng/ml during pregnancy in 17% Caucasian pregnant women, 61% New Zealand pregnant women, 32–42% Indian pregnant women, 59–84% Kuwaiti pregnant women reported, 84% of Iranian pregnant women, and 75% of pregnant women in the United Arab Emirates (UAE).^[7] Due to the widespread deficiency of vitamin D in pregnant women, widespread and costly complications due to vitamin D deficiency, limited scientific research on labor pains and vitamin D, and considering the approach and policies of Iran to promote natural childbirth and increase the rate of primary CS with no medical symptoms or prolonged deliveries, it was decided to obtain effective factors in reducing the rate of CS and increasing natural childbirth.^[12] The aim of this study was to determine the relationship between 25-OH-D level and pain intensity and duration of labor in primiparous women, which is an important step to prevent the progression of these complications.

Materials and Methods

A cross-sectional analytical study was conducted in Isfahan City from November 2021 to January 2022. In the present study, primiparous women with cephalic presentation, dilatation of the cervix of 4 cm, spontaneous uterine contractions for at least 40–60 s, and three contractions in 10 minutes were included in the study. Primiparous women aged 18–35 years in active labor (4 cm cervical dilatation with uterine contractions) with gestational age between 37–42 completed weeks (calculated from reliable last menstrual periods and the first or early second trimester ultrasound), with the single viable fetus, longitudinal lie, and cephalic presentation were included and enrolled from the labor room. In cases of problems such as preeclampsia, active bleeding, or evidence of fetal distress in heart rate monitoring, multiple pregnancies, fetal congenital malformations like anencephaly and hydrocephaly, macrosomic fetuses weighing 4 kg or more, abnormalities of amniotic fluid, cephalopelvic disproportion, or any indication for emergency CS during labor like fetal distress, intrauterine fetal death, or intrauterine growth restriction, samples were excluded from the study.

The study was carried out in Zahraye Marzieh Hospital (due to the high statistics of natural vaginal delivery). Before the collection of data, the aim of this study was explained, and informed consent was obtained from all participants. Data were gathered by the researcher in the delivery room using demographic questionnaires (age, Body Mass Index (BMI), economic status, level of education, occupation, and place

of residence) and reproductive questionnaires (gestational age, number of abortions, and number of pregnancies) and a delivery progress registration form (partograph). The visual analog scale was a 5-cc syringe and an ELISA kit. The visual pain scale in this study included a straight horizontal ruler that was graded from zero to 10. Number zero indicates the absence of pain, and number 10 indicates the maximum pain intensity. This scale is an effective tool with sensitivity and validity, and its validity and reliability in measuring pain have been evaluated in various studies.^[14-16] An examination was performed for all pregnant women, which included measuring height and weight, calculating BMI (using height and weight before or in the first 12 weeks of pregnancy available in the medical record), measuring vital signs, and fetal heart rate (every 30 minutes in the first stage and every 15 minutes in the second stage).

The required sample size was calculated by dividing the correlation coefficient from the pilot study by 0.35, alpha 0.05, and beta 0.085 according to the formula, which equals 91 samples.

After teaching the visual scale to measure pain intensity to the participating women, the amount of pain in the active phase and the second stage of labor was measured by a standard instrument of the visual scale (a ruler).

A partograph diagram was used to record the length of labor stages from the beginning of the active phase to the end of the second stage of labor. The reason for recording dilatation and presentation at the beginning of the active phase of maternal mating at admission was to ensure that all specimens were admitted under the same conditions. After the initial measures, an amniotomy was performed with a 5-cm dilatation to strengthen the labor and check if the amniotic sac is healthy and the fetal head is fixed. Moreover, oxytocin injections were used for patients with dysfunctional uterine contractions. It was started at 2 mIU per minute, and gradually its flow rate and dose could be increased (until three uterine contractions occurred in 10 minutes).

The BMI was categorized as normal when it was $<25 \text{ kg/m}^2$, overweight when it was $25.1\text{--}29.9 \text{ kg/m}^2$, and obese when it was $\leq 30 \text{ kg/m}^2$.^[17]

For measuring vitamin 25-OH-D level, at the time of admission, 5 mL of venous blood was drawn from each participant and placed in sterile tubes with the patient's name. The separated sera were kept at -30°C until all samples were completed, and then, while being kept in a cold box, they were transferred to a reference laboratory (Abu Reyhan) for measuring 25-OH vitamin D. The enzyme-linked immunosorbent assay (ELISA) method from Immunodiagnostic Systems Limited, validated against the HPLC method, was used to measure 25-OH vitamin D (Monobind Company, USA), and all measurements were reported by nanogram. Participants were classified into the following groups based on the amount of vitamin D:

25-OH-D <20 ng/ml and 20/1–29 ng/ml were considered severe deficiency and moderate insufficiency, respectively, and ≥ 30 ng/ml was considered normal.

The level of vitamin D (25 OH D) has a biological half-life of three weeks, making the measurement of this element the most reliable indicator of vitamin D. All methods were performed in accordance with the relevant guidelines and regulations.

All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 23 (IBM Corp., Armonk, NY, USA). Quantitative variables were described by the mean and standard deviation (SD), and categorical variables were also provided by frequency (percentage). Descriptive statistics were used to provide frequency tables, mean indices, and SD, and the Pearson correlation coefficient and analysis of variance were used to measure the correlation. The significance level was less than 5% ($p < 0.05$).

Ethical considerations

In order to conduct this research, after obtaining the permission of the ethics committee (IR.AJUMS.REC.1400.140), all participants were granted their permission by signing the informed consent form before entering into the study. All participants were allowed to be excluded at any time during the study if they did not wish to continue the research.

Results

Among 200 women referring to the Zahraye Marzieh Hospital in Isfahan, 91 women were included according to the inclusion criteria [Figure 1]. Variance analysis and multiple comparisons were used for comparison in different groups. According to the results, there was a significant difference between the average duration and pain intensity of the active phase and the second stage of labor at three levels of vitamin D ($p = 0$).

Discussion

The purpose of the present study was to evaluate the relationship between 25-hydroxy vitamin D3 levels and pain intensity and duration of labor stages in primiparous women. Vitamin D deficiency is more prevalent in Iranian women.^[18]

According to Table 1, the mean and SD of maternal age in the group were 18–35 years (27.07 ± 4.312). Lean considers the elderly age of the mother as a factor in the inefficiency of the uterus as a result of prolonged labor.^[19] In this study, the highest economic status was in the moderate group (50.5%), and weak economic status (21.1%) was less common than other conditions. Studies have shown that long and difficult deliveries are more common in women with poor economic status.^[20]

Our findings indicated that 87.4% of the participants were homemakers. In this study, the highest level of maternal

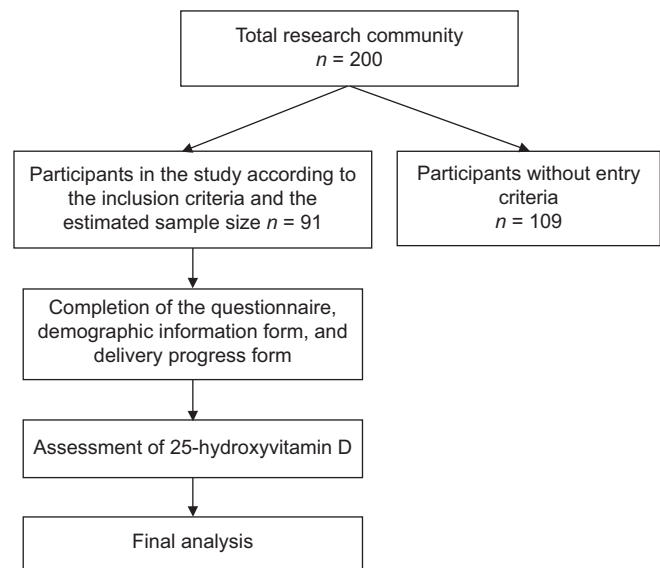


Figure 1: Flowchart of the cross-sectional study

education was in the high school group (77.9%). One of the most effective factors in health care is the mother's education. Having a minimum basic education allows the mother to use educational books to better understand the educational tips and content; therefore, considering the observance of nutritional principles and other health care during pregnancy, education can have a role in overshadowing the results of pregnancy.^[21] In this study and according to the mentioned materials, the subjects were at the appropriate level to read, write, and understand educational concepts. Our findings indicated that 76.8% of the participants had a normal BMI. In various studies, the effect of maternal overweight and obesity has been proven by pregnancy results, so that the average length of the second and third stages of labor in the group of overweight women was higher than that of underweight women.^[22] In the present study, the highest status of women was in the city group (86.3%), who experience a longer delivery^[23] according to studies of city women.

According to Table 2, the highest number of pregnancies occurred in primigravid women (86.3%). Increasing the number of pregnancies is one of the factors associated with prolonging the third stage of labor.^[24] Ahmari *et al.*^[25] concluded that long and difficult deliveries were observed in women with 0 or 1 more pregnancies. In the present study, all women participating in the study underwent amniotomies (95.8%). A study by Tafazli *et al.*^[26] evaluated the performance of midwives showed that one of the reasons for their undergoing amniotomy was to reduce the duration of labor.

Our findings showed that oxytocin was administered to 95.8% of participants. Ebrahimzadeh *et al.*^[27] found that oxytocin did not change the shape of contractions or prolong labor. Our results showed that as vitamin D increases, the active phase and second stage duration decrease.

In line with the results of the present study, in a cross-sectional study, Humadi *et al.*^[12] showed that in women with long stage 1, the mean level of vitamin D (32.7 ± 16.7) nmol/L was lower than in those without long stage 1 (43.9 ± 22.2) nmol/L, which showed a significant relationship between the two variables ($p < 0.05$). Furthermore, in women with

long stage 2, the level of vitamin D (28.1 ± 14.1) nanomoles per liter was lower than in those without long stage 2 (44.3 ± 22.2) nanomoles per liter ($p < 0.05$). In a study, Gernand *et al.*^[11] also found that without adjusting BMI before pregnancy, race, or study location, the association between 25-OH-D and the prolonged first and second stages of labor was observed, which is in line with the results of the present study. Contrary to the results of the present study, after adjusting for BMI, race, and prenatal study site, Gernand *et al.* showed that a concentration of 25-OH vitamin D was not associated with a risk of prolonging stages 1 and 2 of labor.^[11]

According to Table 3, our results showed that as vitamin D increases, the pain intensity of the active phase and second stage of labor also increases. In line with the results of the present study, in a study, Ahrari *et al.*^[28] showed that the average of 25-OH-D in the plasma of women with labor pain was 59.78 ± 08.2 more than that of those without labor pain, $66.51 (4.2)$ ($p = 0.007$).

The number of studies that have addressed the relationship between 25-OH-D3 levels and pain intensity and duration of labor stages is very low, and to the best of our knowledge, no study has ever been conducted among Iranian women.

In this study, blood samples and the completion of the demographic questionnaire and delivery progress form were done simultaneously, whereas in other studies, questionnaires were completed with a time interval between sampling or patient records were used. On the other hand, the serum level of vitamin D in all samples was assessed by one person, which adds to the accuracy of the research.

Conclusion

A low 25-OH-D3 level during labor was an important predictor of prolonged labor. It means that there was a significant association between 25-OH-D3 deficiency and prolonged stages of labor and poor pain intensity.

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Table 1: Frequency distribution of demographic characteristics of the studied units

Variables	Mean (SD)/n (%)
Age (y*)	
18–35 y*	27.07 (4.31)
Economic situation	
Good	23 (24.21)
Moderate	48 (50.53)
Weak	20 (21.11)
Job	
Homemaker	83 (84.74)
Employee	7 (7.45)
Education	
Primary	8 (8.45)
High school	74 (77.94)
University education	9 (9.57)
Body mass index (kg/m ²)	
Underweight	12 (12.62)
Normal	73 (76.81)
Overweight	6 (6.32)
Lodging	
City	82 (86.33)
Town	9 (9.53)
Number of pregnancies	
Primigravida	82 (86.33)
Multigravida	9 (9.53)
Amniotomy	
Yes	91 (100)
No	0
Oxytocin	
Yes	91 (100)
No	0
Mode of delivery	
Normal vaginal delivery	91 (100)
Cesarean section	0

SD=standard deviation

Table 2: Comparison of the mean and standard deviation of active phase and second stage duration by three levels of vitamin D

Variables	Vitamin D level (ng/mL)			p
	≥30	20–29	<20	
	Mean (SD)			
Active phase duration (Min/hr*) n=91	248.85 (34.09)	282.03 (15.12)	337.88 (55.80)	0.012
Second-stage duration (Min/hr*) n=91	34.62 (8.59)	46.25 (5.38)	61.56 (12.92)	0.001

SD=standard deviation

Table 3: Comparison of the mean and standard deviation of pain intensity in the active phase and second stage of labor by three levels of vitamin D

Variables	Vitamin D level (ng/mL)			p
	≥30	20–29	<20	
Active phase intensity (Based on the McGill ruler) (n=91)	7.77 (0.71)	7.22 (0.42)	6.88 (0.70)	0.022
Second-stage intensity (Based on the McGill ruler) (n=91)	9.31 (0.67)	8.50 (0.50)	8.27 (0.58)	0.02

SD=standard deviation

Conflicts of interest

Nothing to declare.

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