Fertil Gynecol Androl. 2022 December; 2(1):e128458. https://doi.org/10.5812/fga-128458.

Published online 2022 September 4. **Research Article**

Relationship Between Vitamin D Level and Preterm Labor in Pregnant Women in Zahedan, Iran

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Received 2022 May 27; **Revised** 2022 July 25; **Accepted** 2022 August 11.

Abstract

Background: Preterm labor (PL) is a leading cause of perinatal morbidity and mortality. Different factors can result in preterm labor, including maternal vitamin D.
Objectives: This study aimed to evaluate the level of vitamin D in pregnant women with PL.
Methods: This case-control study was conducted on 156 pregnant women (52 cases with PL and 104 controls without PL) in Ali Ibn Abitaleb Hospital, Zahedan, Iran, in 2018.
Results: The age was 30.92 ± 5.21 and 29.39 ± 4.86 years in the case and control groups, respectively. There were no significant (P-value > 0.05) differences between the two groups in baseline variables. Vitamin D supplement consumption (P-value = 0.128), sun exposure time (P-value = 0.304), history of admission in pregnancy (P-value = 0.608), and history of vaginal infection (P-value = 0.100) were not significantly different between the two groups. The mean vitamin D level was 30.88 and 31.93 ng/mL in pregnant women with and without PL, respectively, with no significant difference (P-value = 0.591). The mean babies' weight was significantly (P-value > 0.001) higher in the control group than in PL women (3338.75 ± 466.16 vs. 2655.76 ± 393.36 g).
Conclusions: Although this study showed no association between vitamin D levels and PL, abnormal vitamin D levels might be related to PL in pregnant women with other comorbidities or risk factors.

Keywords: Vitamin D, Obstetrics Labor, Prematurity, Birth Injuries, Obstetric Labor, Complications

1. Background

Preterm labor (PL) is defined as pregnancy termination before the end of the 37th week of gestational age (GA). It occurs in 8% to 10% of all pregnancies and 5% of the Iranian population (1). Preterm labor is one of the leading causes of perinatal morbidity and mortality worldwide (2-4). Acute and late complications, including the need for resuscitation, lower Apgar score, and visual problems, are noticeably higher in premature neonates (5).

Different factors can result in PL, including a history of PL, lower genital system infection, multiparty, low socioeconomic status, and smoking (6, 7). Since the insufficient level of vitamin D during pregnancy is related to a higher risk for some pregnancy complications, such as preeclampsia, gestational diabetes (GDM), and small for gestational age (SGA) (8-11), it is hypothesized that there may be an association between serum vitamin D and preterm labor.

There is no effective and safe treatment for PL, and it seems the best treatment for this complication is preventive strategies (12). On the other hand, there are inconsistent studies about the association between serum vitamin D concentration and preterm labor.

2. Objectives

This study was designed to compare the vitamin D level of pregnant women with PL and the control group.

3. Methods

This case-control study was conducted on 156 pregnant women (52 cases and 104 controls) in Ali Ibn Abitaleb Hospital, Zahedan, Iran, in 2018. A convenience sampling method was utilized. Using the proportion formula, we calculated the sample size based on the data reported in Baczynska-Strzecha and Kalinka study (10). The total sample size was 156, but the control group's sample size was twice that of the case group to compensate for the limited number of cases and improve study power.

Singleton pregnant women older than 18 years, whose gestational ages at delivery were lower than 37 weeks (according to first-trimester ultrasound), were included in the case group. Besides, singleton pregnant women older than 18 years with term delivery ($\geq$ 37 weeks' GA at delivery) were enrolled in the control group. The exclusion criteria for both case and control groups included pregnant women with underlying diseases such as hypertension, diabetes, cardiovascular diseases, cervical insufficiency, drug consumption affecting vitamin D absorption, smoking, alcohol drinking, and withdrawal from the study.

Blood samples were drawn at delivery without fasting to determine vitamin D. Vitamin D was measured by the enzyme immunoassay method. As we checked vitamin D levels at delivery, the treatment of vitamin D insufficiency and deficiency was initiated after pregnancy. Hence, the treatment of the patients did not compromise our data.

We gathered data including age, obstetrics history, body mass index (BMI), GA at delivery, and serum vitamin D level. The data were analyzed with SPSS version 24 software. Mean ± standard deviation and independent t test were applied for continuous variables, and percentages and the chi-square test were for categorical variables. The statistically significant level was considered less than 0.05.

4. Results

The age was 30.92 ± 5.21 and 29.39 ± 4.86 years in the case and control groups, respectively. The BMI was 26.55 ± 4.35 and 25.18 ± 4.55 kg/m^2 in the case and control groups, respectively. There were no significant (P-value > 0.05) differences between the two groups in baseline variables (Table 1).

Furthermore, vitamin D supplement consumption (P-value = 0.128), sun exposure time (P-value = 0.304), history of admission in pregnancy (P-value = 0.608), and history of vaginal infection (P-value = 0.100) were not significantly different between two groups.

Table 1. Baseline Variables in the Study Groups

Variables	Study Group		P-Value
	Case	Control	
Age	30.92 ± 5.21	29.39 ± 4.86	0.073
Gravidity	1.78 ± 0.89	1.76 ± 0.81	0.893
Parous	0.57 ± 0.72	0.53 ± 0.62	0.730
Abortion	0.21 ± 0.45	0.24 ± 0.51	0.731
Body mass index	26.55 ± 4.35	25.18 ± 4.55	0.074

The average vitamin D levels in pregnant women with and without PL were 30.88 and 31.93 ng/mL, with no significant difference (P-value = 0.591). The babies' weight was significantly (P-value > 0.001) higher in the control group than in PL women (3338.75 ± 466.16 vs. 2655.76 ± 393.36 g).

5. Discussion

Vitamin D has different and important roles during pregnancy. Evidence (13) shows insufficient vitamin D is associated with gestational diabetes, preeclampsia, and low birth weight. However, the association between vitamin D level and incidence of PL has not been well understood. This study evaluated this possible association.

Our findings showed no significant difference in the frequency of vitamin D insufficiency subgroups between the two study groups. In line with our study, a former study (14) showed that mean vitamin D was not significantly different between women with PROM and the control group. However, Bodnar et al. (15) and Shibata et al. (16) showed that the deficient level of vitamin D (< 10 ng/mL) caused preterm labor. Bodnar et al.'s study (15) was conducted on twin pregnancies. Our study showed that both groups had a mean vitamin D level in normal ranges ($\geq$ 30 ng/mL). It might be due to an increase in pregnant women's knowledge about vitamin D's important role and daily consumption of vitamin D supplements.

Preterm labor is affected by different known or unknown factors (17, 18); for instance, women in the low and high range of reproductive ages are more susceptible to PL (19, 20). On the other hand, preventive strategies are more effective in decreasing PL incidence and its short- and long-term complications. Hence, vitamin D supplementation in pregnant women to counter vitamin D deficiency seems rational (21).

Despite the strengths of this study, such as having a control group and using the same laboratory for vitamin

D measurements, there were some limitations, including the low sample size, retrospective nature of the study, and broad inclusion criteria. Future research is suggested with more sample size of pregnant women with unknown PROM.

5.1. Conclusions

Although this study showed no significant association between vitamin D levels and PL, abnormal vitamin D levels may be related to PL in pregnant women with other comorbidities or risk factors such as preeclampsia and high BMI.

Footnotes

Authors' Contribution: Study concept and design: ATA and AA; drafting of the manuscript: MM and ZA; critical revision of the manuscript: AA and NM; statistical analysis: EA. All authors have given final approval for the version to be published.

Conflict of Interests: The authors declare no conflicts of interest.

Ethical Approval: This study was conducted in compliance with the Helsinki Declaration and approved by the Zahedan University of Medical Sciences Ethics committee (IR.ZAUMS.REC.1397.061). Link: ethics.research.ac.ir/EthicsProposalView.php?id=11406

Funding/Support: Zahedan University of Medical Sciences provided financial support.

Informed Consent: The participants signed written informed consent.

References

1. Seifi M, Farshbaf-Khalili A, Aghaee H, Pourzeinali S. [The Relationship of Iron Deficiency Anemia with Preterm delivery in Pregnant Women Referred to Health Centers of Tabriz: A Case-Control Study]. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2015;**18**(159):8-17. Persian.
2. van Schalkwyk J, Yudin MH, Yudin MH, Allen V, Bouchard C, Boucher M, et al. Vulvovaginitis: Screening for and Management of Trichomoniasis, Vulvovaginal Candidiasis, and Bacterial Vaginosis. *J Obstet Gynaecol Can*. 2015;**37**(3):266–74. https://doi.org/10.1016/s1701-2163(15)30316-9.
3. Vouga M, Greub G, Prod'hom G, Durussel C, Roth-Kleiner M, Vasilevsky S, et al. Treatment of genital mycoplasma in colonized pregnant women in late pregnancy is associated with a lower rate of premature labour and neonatal complications. *Clin Microbiol Infect*. 2014;**20**(10):1074–9. [PubMed ID: 24849820]. https://doi.org/10.1111/1469-0691.12686.
4. Fairlie T, Zell ER, Schrag S. Effectiveness of intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal disease. *Obstet Gynecol*. 2013;**121**(3):570–7. [PubMed ID: 23635620]. https://doi.org/10.1097/AOG.0b013e318280d4f6.
5. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Voladan M, Razzaghi S, Ghorbani MH, translators. *[Williams Obstetrics 2014, vol 1]*. Tehran: Arjmand Press; 2014. Persian.
6. Ratzon R, Sheiner E, Shoham-Vardi I. The role of prenatal care in recurrent preterm birth. *Eur J Obstet Gynecol Reprod Biol*. 2011;**154**(1):40–4. [PubMed ID: 20869804]. https://doi.org/10.1016/j.ejogrb.2010.08.011.
7. Gervasi MT, Romero R, Bracalente G, Erez O, Dong Z, Hassan SS, et al. Midtrimester amniotic fluid concentrations of interleukin-6 and interferon-gamma-inducible protein-10: evidence for heterogeneity of intra-amniotic inflammation and associations with spontaneous early (<32 weeks) and late (>32 weeks) preterm delivery. *J Perinat Med*. 2012;**40**(4):329–43. [PubMed ID: 22752762]. [PubMed Central ID: PMC3498502]. https://doi.org/10.1515/jpm-2012-0034.
8. Dabbaghmanesh MH, Forouhari S, Ghaemi SZ, Khakshour A, Kiani Rad S. Comparison of 25-hydroxyvitamin D and Calcium Levels between Preeclampsia and Normal Pregnant Women and Birth Outcomes. *Int J Pediatr*. 2015;**3**(6.1):1047–55.
9. Abedi P, Mohaghegh Z, Afshary P, Latifi M. The relationship of serum vitamin D with pre-eclampsia in the Iranian women. *Matern Child Nutr*. 2014;**10**(2):206–12. [PubMed ID: 23782626]. [PubMed Central ID: PMC6860245]. https://doi.org/10.1111/mcn.12058.
10. Baczynska-Strzecha M, Kalinka J. Assessment of correlation between vitamin D level and prevalence of preterm births in the population of pregnant women in Poland. *Int J Occup Med Environ Health*. 2017;**30**(6):933–41. [PubMed ID: 28832028]. https://doi.org/10.13075/ijomeh.1896.01146.
11. Khalessi N, Kalani M, Araghi M, Farahani Z. The Relationship between Maternal Vitamin D Deficiency and Low Birth Weight Neonates. *J Family Reprod Health*. 2015;**9**(3):113–7. [PubMed ID: 26622309]. [PubMed Central ID: PMC4662754].
12. Dodd JM, Crowther CA, Middleton P. Oral betamimetics for maintenance therapy after threatened preterm labour. *Cochrane Database Syst Rev*. 2012;(12). CD003927. https://doi.org/10.1002/14651858.CD003927.pub3.
13. Ciebiera M, Wojtyla C, Lukaszuk K, Zgliczynska M, Zareba K, Rawski W, et al. The role of vitamin D in perinatology. An up-to-date review. *Arch Med Sci*. 2021;**17**(4):992–1005. [PubMed ID: 34336027]. [PubMed Central ID: PMC8314414]. https://doi.org/10.5114/aoms.2019.81747.
14. Lian RH, Qi PA, Yuan T, Yan PJ, Qiu WW, Wei Y, et al. Systematic review and meta-analysis of vitamin D deficiency in different pregnancy on preterm birth: Deficiency in middle pregnancy might be at risk. *Medicine (Baltimore)*. 2021;**100**(24). e26303. [PubMed ID: 34128867]. [PubMed Central ID: PMC8213249]. https://doi.org/10.1097/MD.0000000000026303.
15. Bodnar LM, Rouse DJ, Momirova V, Peaceman AM, Sciscione A, Spong CY, et al. Maternal 25-hydroxyvitamin d and preterm birth in twin gestations. *Obstet Gynecol*. 2013;**122**(1):91–8. [PubMed ID: 23743453]. [PubMed Central ID: PMC3706065]. https://doi.org/10.1097/AOG.0b013e3182941d9a.
16. Shibata M, Suzuki A, Sekiya T, Sekiguchi S, Asano S, Udagawa Y, et al. High prevalence of hypovitaminosis D in pregnant Japanese women with threatened premature delivery. *J Bone Miner Metab*. 2011;**29**(5):615–20. [PubMed ID: 21384110]. https://doi.org/10.1007/s00774-011-0264-x.
17. Chapman E, Reveiz L, Illanes E, Bonfill Cosp X, Reveiz L. Antibiotic regimens for management of intra-amniotic infection. *Cochrane Database Syst Rev*. 2014;(12). CD010976. [PubMed ID: 25526426]. https://doi.org/10.1002/14651858.cd010976.

18. Changaee F, Akbari S, Janani F. [The effect of clindamycin vaginal cream on prevention of preterm labor]. *Yafteh*. 2016;**18**(2):23–8. Persian.
19. Heaman M, Kingston D, Chalmers B, Sauve R, Lee L, Young D. Risk factors for preterm birth and small-for-gestational-age births among Canadian women. *Paediatr Perinat Epidemiol*. 2013;**27**(1):54–61. [PubMed ID: 23215712]. https://doi.org/10.1111/ppe.12016.
20. Alizadeh Y, Zarkesh M, Moghadam RS, Esfandiarpour B, Behboudi H, Karambin MM, et al. Incidence and Risk Factors for Retinopathy of Prematurity in North of Iran. *J Ophthalmic Vis Res*. 2015;**10**(4):424–8. [PubMed ID: 27051487]. [PubMed Central ID: PMC4795392]. https://doi.org/10.4103/2008-322X.176907.
21. Li H, Ma J, Huang R, Wen Y, Liu G, Xuan M, et al. Prevalence of vitamin D deficiency in the pregnant women: an observational study in Shanghai, China. *Arch Public Health*. 2020;**78**:31. [PubMed ID: 32518650]. [PubMed Central ID: PMC7271532]. https://doi.org/10.1186/s13690-020-00414-1.