https://doi.org/10.46389/rjd-2023-1372
www.rjdnmd.org

Rom J Diabetes Nutr Metab Dis
2023; volume 30, issue 3, pages 292-297

Original Article

Vitamin D status: approaches to diagnosis and prevention in pregnant women at high risk of moderate preeclampsia

Ulyana Franchuk [1] *, Larysa Malanchuk [1], Iryna Malanchyn [1], Lyubov Lymar [1], Viktoriia Martyniuk [1], Maksym Franchuk [2]

[1] Department of Obstetrics and Gynecology, No 1, I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine, Ternopil, Ukraine

[2] Department of Internal Medicine, No 2, I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine, Ternopil, Ukraine

*Correspondence to: Ulyana Franchuk, Department of Obstetrics and Gynecology, No 1, I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine, Ternopil, 46001, Ukraine. E-mail: franchuk_uya@tdmu.edu.ua

Received: 13 June 2023 / Accepted: 19 September 2023

Abstract

Vitamin D deficiency is common, and there is a huge gap between the recommended dietary intake of vitamin D and low vitamin D stores in the general population. The aim of the study was to study the characteristics of vitamin D status and its effect on the course of pregnancy in patients at high risk of developing preeclampsia. In accordance with the set goal, 68 pregnant women were examined at a gestation period of 10–12 weeks. Group I included 30 pregnant women who had a high risk of developing preeclampsia and had vitamin D deficiency. Group II consisted of 18 pregnant women with a high risk of developing preeclampsia and vitamin D deficiency. Group III consisted of 20 somatically healthy pregnant women with normal levels of 25 – -hydroxycholecalciferol. The course of pregnancy in the studied groups was characterized by hemodynamic disturbances in the uterine arteries in 23.3% of pregnant women of the first group of the study and in 27.7% of the patients of the second group. In 3.33% of patients of the first group, pregnancy was complicated by premature detachment of the normally located placenta, and in 5.5% of the second group, respectively. The importance of determining the concentration of vitamin D during pregnancy for the timely prevention of obstetric and perinatal complications was investigated. It is recommended to use 2000 IU of vitamin D for pregnant women with a deficient level of this vitamin for a favorable course of pregnancy and childbirth for patients who are at high risk of developing moderate preeclampsia.

Keywords: preeclampsia, vitamin D, pregnancy, diagnostic, prevention.

Introduction

Preeclampsia is a common pregnancy complication associated with an increased risk of maternal and neonatal morbidity and mortality. Childbirth is currently the only cure for preeclampsia; therefore, effective options for preventing and treating this condition are urgently needed. Although vitamin D intake did not affect the risk of preeclampsia, decreased serum vitamin D levels were correlated with the risk of preeclampsia. Mirzahani and colleagues identified a number of gene pathways that are differentially regulated among women with low serum vitamin D who develop preeclampsia. These results indicate the need for further research into the role of vitamin D in developing preeclampsia [1–4].

Vitamin D deficiency and insufficiency is a global health problem affecting more than one billion children and adults worldwide. The consequences of vitamin D deficiency cannot be underestimated [5–8]. Vitamin D deficiency has been linked to a variety of acute and chronic diseases, including preeclampsia, childhood dental caries, periodontitis, autoimmune disorders, infectious diseases, cardiovascular disease, fatal cancers, type 2 diabetes, and neurological disorders [9, 10]. Low levels of vitamin D during pregnancy can be used as a risk factor for developing preeclampsia. The

researchers investigated that vitamin D supplementation starting at 10 to 18 weeks gestation did not reduce the incidence of preeclampsia in an intention-to-treat paradigm, but did reduce the occurrence of severe preeclampsia. Vitamin D levels of 30 ng/ml or higher at the start of the study and in late pregnancy were associated with a lower risk of preeclampsia [11–13].

There are correlations between an increased body mass index, the occurrence of preeclampsia, and vitamin D deficiency. Pregnant women who had a different prepregnancy BMI were found to have significantly different serum 25(OH)D concentrations. There was also a significant difference in the serum concentration of 25(OH)D in pregnant women of different ages. Serum 25(OH)D concentrations were significantly lower in pregnant women who subsequently developed severe preeclampsia compared with those who did not. Maternal vitamin D deficiency at 23–28 weeks gestation was strongly associated with an increased chance of severe preeclampsia. Further studies are needed to determine whether vitamin D supplementation will reduce the risk of severe preeclampsia and improve pregnancy outcomes [14–17].

Preeclampsia (PE) prevention remains one of the most important problems of perinatal medicine. In connection with the possible unpredictable course of hypertension in pregnant women, primarily PE, and the high level of complications for the mother, fetus and newborn, it is urgently necessary to offer pregnant women from risk groups effective methods of preventing the development of PE or delaying its onset. In addition, due to the association of PE with an increased risk of cardiovascular disease later in life, effective prevention of preeclampsia may also be important to reduce its incidence. The ideal prevention of PE should target the pathogenetic changes that lead to the development of PE, be safe for the mother and fetus, and be inexpensive and freely available [18].

Vitamin D deficiency is common, and there is a huge gap between the recommended dietary intake of vitamin D and low vitamin D stores in the general population. Although vitamin D is important for musculoskeletal health, accumulating evidence suggests that vitamin D may also be important for fertility, pregnancy outcomes, and lactation. Significant changes in vitamin D metabolism during pregnancy, such as increased production of the "active vitamin D hormone" calcitriol, support the important role of vitamin D in this situation [19–21].

Purpose of the study: Features of diagnosis and prevention of pregnant women, groups at high risk of developing preeclampsia and pregnancy occurring against the background of vitamin D deficiency.

Material and methods

Study design and patients

In accordance with the set goal, we examined 68 pregnant women in the period of 10–12 weeks of gestation. Group I included 30 pregnant women who were at high risk of developing preeclampsia and had vitamin D deficiency. Group II consisted of 18 pregnant women with a high risk of developing preeclampsia and vitamin D deficiency. Group III consisted of 20 somatically healthy pregnant women with normal levels of 25-hydroxycholecalciferol.

All women of the studied groups were selected by the method of random sampling and were observed about this pregnancy in women's consultations at their place of residence. To establish the relationship between the occurrence of obstetric complications, in particular preeclampsia, pregnant women of the studied groups had their blood taken to determine the concentration of vitamin D three times. In the first trimester, at 10–12 weeks of pregnancy, in connection with the end of the wave of trophoblast invasion. For women in the II trimester at 16–18 weeks of gestation and patients in the III trimester at 30–32 weeks, to detect late obstetric complications. The Immulite test system and analyzer (Siemens AG, Germany) were used to determine the level of 25-hydroxycholecalciferol.

Statistical analysis of the obtained results was carried out by calculating the average value of the value (M) and the standard error of the average value of the value (m). Qualitative indicators are presented in the form of %. Quantitative indicators were compared with normal distribution according to the Student's test ($p<0.05$). All calculations were carried out on a personal computer using the statistical software package Statistica 10.0 (StatSoft Inc., USA) and the package of statistical functions Microsoft Office Excel 2016 (Microsoft Corp., USA).

Results

Based on the goal and set tasks, 68 pregnant women were examined. According to the results of the study, depending on the received clinical and laboratory data, the diagnosis and the developed inclusion criteria, the

patients were divided into 3 groups: the 1st group included 30 pregnant women with vitamin D deficiency who received a prophylactic dose of 2000 IU of vitamin D in the term 16–18 weeks of pregnancy. Group II consisted of 18 pregnant women with a high risk of developing preeclampsia and vitamin D deficiency. Group III consisted of 20 somatically healthy pregnant women with normal levels of 25 – hydroxycholecalciferol. Randomization by the envelope method was used to assign pregnant women to the I and II groups. Women in the III group (control) were formed by the method of simple random selection in order to achieve representativeness. All groups were homogeneous in age. All patients met the set inclusion criteria; they were interviewed about this study, as a result of which they signed a voluntary consent to participate.

The analysis of the results of the clinical study shows that the average age of the patients included in this study was 24.08±2.18 in women of the I study group and 23.89±1.16 in the patients of the II group. The age qualification in women of the control group was 22.96± 2.48.

During the analysis of extragenital pathology, it was established the presence of disorders of the endocrine system in the form of thyroid gland diseases (I group n=1, 3.33%, II group n=2, 11.1%). Among the diseases of the cardiovascular system, arterial hypertension (I group n=2, 6.66%, II group n=2, 11.1%) and sinus tachycardia (I group n=1, 3.33%, II group n=1, 5.55%). Diseases of the organs of vision were represented by impaired visual acuity (I group n=4, 13.3%, II group n=6, 33.3%). The urinary system was characterized by chronic pyelonephritis in the anamnesis (I group n=4, 13.3%, n=2, 11.1%). No accompanying extragenital pathology was found in the patients of the III study group.

Studying the structure of gynecological diseases, it is worth noting the presence of chronic adnexitis (I group n=2, 6.66%, II group n=2, 11.1%), and uterine leiomyoma (I group n=1, 3.33%, II group n=1, 5.55%). In the control group, genital herpes was present in one patient (n=1.5%). By analyzing the data on surgical interventions on the organs of the small pelvis (tubectomy, myomectomy, polypectomy), there were no effective changes in any group.

By analyzing the course of pregnancy in the high-risk group for the development of preeclampsia, it was found that in the first group – in 21 women (70%), pregnancy was complicated by moderate preeclampsia with a diastolic pressure level of 90–99 mm Hg, and in 9 patients (30%) – preeclampsia of a moderate degree with a diastolic pressure level of 99–109 mm Hg. In the II group, 10 women (55.5%) had moderate preeclampsia with a diastolic pressure level of 90–99 mm Hg, and 8 women (44.4%) had moderate preeclampsia with a diastolic pressure level of 99–109 mmHg Art. In the second research group, preeclampsia of a moderate degree with a diastolic pressure level of 99–109 mm Hg. was 1.5 times more frequent. It is important to note that the studied group of patients had pregnancies without severe preeclampsia (Figure 1).

Obstetric anamnesis, which included the number of pregnancies, deliveries, and spontaneous abortions, did not reveal significant differences between the studied groups. It was established that the women of the I group mostly had only one pregnancy in their history, unlike the II group (Table 1).

Swelling was observed in almost half of the women of the II research group. The level of proteinuria also increased depending on the degree of preeclampsia.

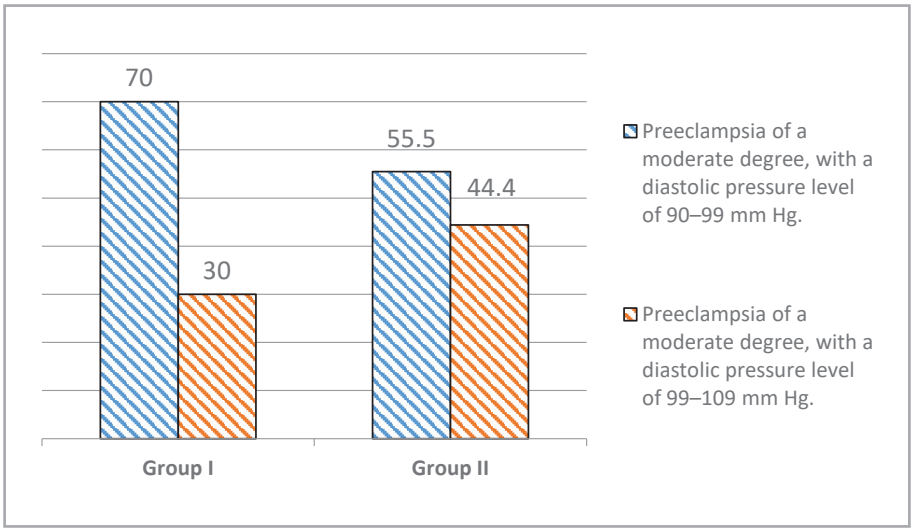

Figure 1: Distribution of patients according to the severity of the course of preeclampsia.

https://doi.org/10.46389/rjd-2023-1372

Table 1: Obstetric history of patients included in the study.

Characteristics	Group I (n=30)	Group II (n=18)	Group III (n=20)
Average number of pregnancies	1.41±0.70	2.51±1.37	1.22±0.86
	p_1 0.243	p_2 0.262	p_3
The average number of births	0.38±0.28	0.94±0.90	0.56±0.52
	p_1 0.039	p_2 0.106	p_3 0.216
The average number of spontaneous terminations of pregnancy up to 12 weeks in the anamnesis	0.35±0.47	0.53±0.49	0.44±0.32
	p_1 0.199	p_2 0.184	p_3 0.254
The average number of late miscarriages	0.09±0.29	0.07±0.26	0.01±0.02
	p_1 0.152	p_2 0.099	p_3 0.126

Note: The reliability of differences between I and II groups is p_1; the reliability of differences between I and III groups – p_2; the reliability of differences between II and III groups – p_3.

It is worth noting that the main target organ in PE is the kidneys. An increase in systolic and diastolic blood pressure is also characteristic, depending on the degree of preeclampsia.

Discussion

A low content of 25-hydroxycholecalciferol in the blood was found in patients who are in the group of high risk of developing preeclampsia. In particular, it was established that the concentration of vitamin D decreases more in the second trimester of pregnancy, which leads to an increase in the deficiency and insufficiency of vitamin D. That is why it was decided to prescribe 2000 IU in the period of 16–18 weeks, according to literary sources, to prevent the occurrence of severe preeclampsia.

The level of vitamin D in patients was studied by trimester of pregnancy. It was found that in a larger number of pregnant women, the concentration of vitamin D in the I trimester of pregnancy is 28±1.19 ng/ml, a sharp decrease in the concentration of vitamin D in the II trimester of pregnancy, which is 23.18±2.12 ng/ml, and in III trimester 22.41±1.16 ng/ml., which indicates vitamin D insufficiency in blood serum. In patients of the control group, the vitamin D level was 34± 3.18 ng/ml (Figure 2).

The course of pregnancy in the studied groups was characterized by hemodynamic disturbances in the uterine arteries in 23.3% of pregnant women of the first group of the study and in 27.7% of the patients of the

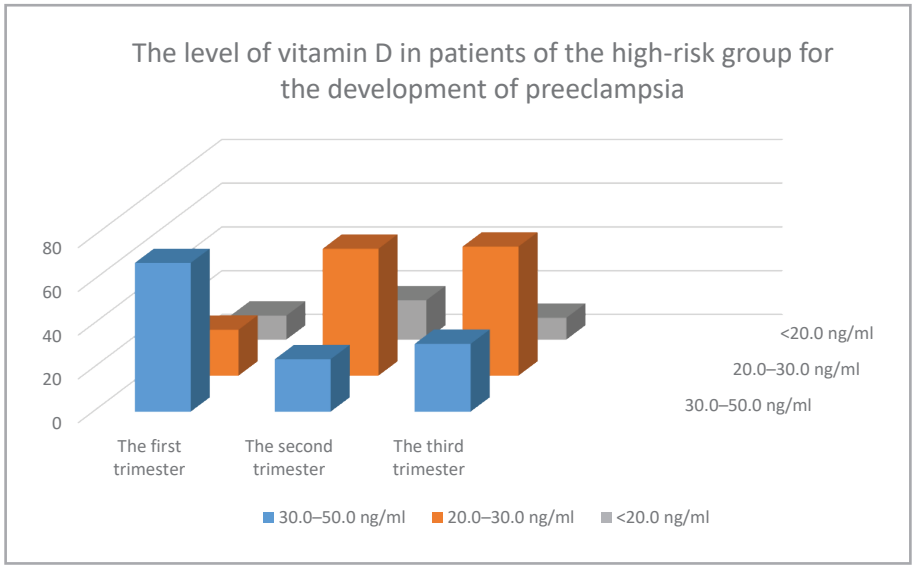

Figure 2: Concentration of vitamin D in patients of the high-risk group of preeclampsia by trimester.

Table 2: Outcomes of pregnancy in patients with moderate preeclampsia.

Patient data	Group I n=30 (%)	Group II n=18 (%)
Violation of hemodynamics in the uterine arteries	7 (23.3%)	5 (27.7%)
Premature rupture of the membranes	3 (10%)	1 (5.5%)
Premature detachment of a normally located placenta	1 (3.33%)	1 (5.55%)
Pelvic presentation	4 (13.3%)	2 (11.1%)

second group. Premature rupture of the membranes occurred in 10% of pregnant women in the first group and 5.5% of the second group. In 3.33% of patients of the first group, pregnancy was complicated by premature detachment of the normally located placenta, and in 5.5% of the second group, respectively. Pelvic presentation was observed in 13.3% of pregnant women in the first studied group and 11.1% of pregnant women in the II group (Table 2).

Conclusion

The importance of determining the concentration of vitamin D during pregnancy for the timely prevention of obstetric and perinatal complications was investigated. It is recommended to use 2000 IU of vitamin D for pregnant women with a deficient level of this vitamin for a favorable course of pregnancy and childbirth for patients at high risk of developing moderate preeclampsia. In patients with a high risk of developing PE, a low content of 25-hydroxycholecalciferol in the blood was found. When prescribing a dose of vitamin D 2000 IU at 16–18 weeks of pregnancy, there was no pronounced early onset of PE, as well as a severe course. Taking vitamin D in a dose of 2000 IU allows you to reach the lower limit of its normal level. Addressing hypovitaminosis D during pregnancy clearly has long-term benefits for both the mother and unborn child.

Implications for practice

Maternal vitamin D deficiency <30 ng/ml in the early stages of pregnancy may be an independent risk factor for PE. The relevance of vitamin D supplementation for women of childbearing age should be explored as a strategy to reduce PE and promote healthier pregnancies.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Ternopil National Medical University, Ternopil, Ukraine (approval ID: protocol No. 65, dated September 1, 2021).

Consent to participate

Written informed consent was obtained from the participants.

References

1. Brown, D. (2020). Preeclampsia, hypertension, and a possible treatment for preeclampsia. Med. Hypotheses., 140, 109669. DOI: 10.1016/j.mehy.2020.109669.
2. Grotegut C. A. (2016). Prevention of preeclampsia. The Journal of clinical investigation, 126(12), 4396–4398. https://doi.org/10.1172/JCI91300.
3. Li, X. (2016). Similarities and differences between the risk factors for gestational hypertension and preeclampsia: A population based cohort study in south China. Pregnancy Hypertens. 6(1):66–71.
4. Pilz, S., Zittermann, A., Obeid, R., Hahn, A., Pludowski, P., Trummer, C., Lerchbaum, E., Pérez-López, F. R., Karras, S. N., & März, W. (2018). The Role of Vitamin D in Fertility and during Pregnancy and Lactation: A Review of Clinical Data. International journal of environmental research and public health, 15(10), 2241. https://doi.org/10.3390/ijerph15102241.
5. Achkar, M., Dodds, L., Giguère, Y., Forest, J. C., Armson, B. A., Woolcott, C., Agellon, S., Spencer, A., & Weiler, H. A. (2015). Vitamin D status in early pregnancy and risk of preeclampsia. American journal of obstetrics and gynecology, 212(4), 511.e1–511.e5117. https://doi.org/10.1016/j.ajog.2014.11.009.

 https://doi.org/10.46389/rjd-2023-1372

6. Dhariwal, N.K., & Lynde, G.C. (2017). Update in the management of patients with preeclampsia. Anesthesiol. Clin.,35 (1), 95-106. DOI: 10.1016/j.anclin.2016.09.009.
7. Gryshchenko, O. V. (2017). Vplyv traducijnogo likuvannja na pokaznyky gemodinamiky y ginok z preeclampsijejy. Zbirnyk naukovych prac asociacii akusheriv-ginekologiv Ukrainu 1(39):31–36.
8. Holick M. F. (2017). The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Reviews in endocrine & metabolic disorders, 18(2), 153–165. https://doi.org/10.1007/s11154-017-9424-1].
9. Curtis, E. M., Moon, R. J., Harvey, N. C., & Cooper, C. (2018). Maternal vitamin D supplementation during pregnancy. British medical bulletin, 126(1), 57–77. https://doi.org/10.1093/bmb/ldy010.
10. Fogacci, S., Fogacci, F., Banach, M., Michos, E. D., Hernandez, A. V., Lip, G. Y. H., Blaha, M. J., Toth, P. P., Borghi, C., Cicero, A. F. G., & Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group (2020). Vitamin D supplementation and incident preeclampsia: A systematic review and meta-analysis of randomized clinical trials. Clinical nutrition (Edinburgh, Scotland), 39(6), 1742–1752. https://doi.org/10.1016/j.clnu.2019.08.015.
11. Farhat, S., Zafar, M.U., Sheikh, M.A., Qasim, C.M., Urooj, F., & Fatima, S.S. (2020). Association of resolvin level in pregnant women with preeclampsia and metabolic syndrome. Taiwan J. Obstet. Gynecol, 59 (1), 105-108. DOI: 10.1016/j.tjog.2019.11.016.
12. Mirzakhani, H., Litonjua, A. A., McElrath, T. F., O'Connor, G., Lee-Parritz, A., Iverson, R., Macones, G., Strunk, R. C., Bacharier, L. B., Zeiger, R., Hollis, B. W., Handy, D. E., Sharma, A., Laranjo, N., Carey, V., Qiu, W., Santolini, M., Liu, S., Chhabra, D., Enquobahrie, D. A., … Weiss, S. T. (2016). Early pregnancy vitamin D status and risk of preeclampsia. The Journal of clinical investigation, 126(12), 4702–4715. https://doi.org/10.1172/JCI89031.
13. Poon, L., Shennan, A., Hyett, J., Kapur, A., Hadar, E., Divakar, H. …, & Hod, M. (2019). The International Federation of Gynecology and Obstetrics (FIGO) initiative on preeclampsia: a pragmatic guide for first-trimester screening and prevention. Int. J. Gynecol. Obstet., 145(S1), 1-33. DOI: 10.1002/ijgo.12802.
14. Mitchenko, O. Y., Romanov, V. Yu., Yavorska, K. O. (2012) Vysokiy kardiovaskularnuy ryzyk y xvoryx z arterialnou hypertenziey ta ogurinniam. Zdorovya Ukrainy, 3/4 (23-24), 24-25. [in Ukrainian].
15. Poniedziałek-Czajkowska, E., & Mierzyński, R. (2021). Could Vitamin D Be Effective in Prevention of Preeclampsia?. Nutrients, 13(11), 3854. https://doi.org/10.3390/nu13113854.
16. Ukah, U.V., De Silva, D.A., Payne, B., Magee, L.A., Hutcheon, J.A., Brown, H., …, & von Dadelszen, P. (2018). Prediction of adverse maternal outcomes from preeclampsia and other hypertensive disorders of pregnancy: a systematic review.Pregnancy Hypertens.,11, 115-123. DOI: 10.1016/j.preghy.2017.11.00.
17. Zhao, X., Fang, R., Yu, R., Chen, D., Zhao, J., & Xiao, J. (2017). Maternal Vitamin D Status in the Late Second Trimester and the Risk of Severe Preeclampsia in Southeastern China. Nutrients, 9(2), 138. https://doi.org/10.3390/nu9020138.
18. Franchuk, U., Khmil, S., & Malanchuk, L. (2023). Metabolic syndrome as a risk factor for the development of preeclampsia in pregnant women. Romanian Journal of Diabetes Nutrition and Metabolic Diseases, 30(2), 254-258.
19. Serrano-Díaz, N. C., Gamboa-Delgado, E. M., Domínguez-Urrego, C. L., Vesga-Varela, A. L., Serrano-Gómez, S. E., & Quintero-Lesmes, D. C. (2018). Vitamin D and risk of preeclampsia: A systematic review and meta-analysis. Biomedica: revista del Instituto Nacional de Salud, 38 Suppl 1, 43–53. https://doi.org/10.7705/biomedica.v38i0.3683.
20. Spradley, F.T. (2017). Metabolic abnormalities and obesity's impact on the risk for developing preeclampsia. Am. J. Physiol. Regul. Integr. Comp. Physiol., 312 (1), R5-R12. DOI: 10.1152/ajpregu.00440.2016.
21. Yuliani, D., Hadisaputro, S., & Nugraheni, S. (2019). Distribution of preeclampsia risk factors in pregnant woman with mild preeclampsia in banyumas district. J. Kebid, 9, 135. DOI: 10.31983/jkb.v9i2.5162.