Journal of Medicine in Scientific Research

Volume 5 | Issue 4 Article 6

Subject Area:

Could vitamin D3 be effective in prevention of risk of preeclampsia among pregnant women?

Adel G. Allam
Shibin El Kom Teaching Hospital

Ibrahim M. El-Maghraby
Shibin El Kom Teaching Hospital, ibrahim_mohie@yahoo.com

Recommended Citation

Allam, Adel G. and El-Maghraby, Ibrahim M. (2023) "Could vitamin D3 be effective in prevention of risk of preeclampsia among pregnant women?," *Journal of Medicine in Scientific Research*: Vol. 5: Iss. 4, Article 6.
DOI: https://doi.org/10.4103/jmisr.jmisr_79_21

Original Article

Could vitamin D3 be effective in prevention of risk of preeclampsia among pregnant women?

Ibrahim M. El-Maghraby, Adel G. Allam
Department of Obstetrics and Gynecology, Shibin El Kom Teaching Hospital, Shibin El Kom, Egypt

Abstract

Background
Preeclampsia, a pregnancy disease marked by high blood pressure and proteinuria, affects 2–8% of all pregnancies. Preeclampsia can be life-threatening for both the mother and the fetus and is still a significant cause of maternal and neonatal morbidity and mortality. The goal of this study was to assess if there was a link between maternal serum vitamin D3 levels and the severity of preeclampsia.

Patients and methods
A case–control study was conducted on 70 pregnant women at Shebin El Kom Teaching Hospital. All pregnant women were divided into two groups: group A included 30 apparently healthy pregnant women (control group) and group B included 40 pregnant patients with preeclampsia (patient group).

Results
The serum vitamin D levels of patients with preeclampsia were considerably lower than those of the control group. The serum level of vitamin D in patients with mild preeclampsia was substantially higher than in patients with severe preeclampsia.

Conclusion
Vitamin D deficiency in the mother is a significant risk factor for preeclampsia. Vitamin D deficiency was found to be associated with a higher risk of preeclampsia.

Keywords: Preeclampsia, pregnant women, severity, vitamin D

Introduction

Preeclampsia is a multisystem, progressive illness that affects 2–8% of pregnancies, depending on the location [1]. Preeclampsia can cause problems with the brain, liver, and kidneys, as well as clotting abnormalities; it also increases the risk of hypertension and related cerebrovascular and cardiovascular illness. Preeclampsia is one of the leading causes of prenatal and maternal illness and mortality worldwide, especially in low-income and middle-income countries [2].

Although the clinical presentation, diagnostic criteria, and management of preeclampsia are all well recognized, the underlying etiology of preeclampsia is not [3]. The hypothesis of aberrant placentation leading to severe maternal physiologic dysfunction is a commonly acknowledged cause of preeclampsia. Despite these challenges, it has been established that preeclampsia is caused by faulty placentation, which results in improper spiral artery remodeling, placental ischemia, hypoxia, and oxidative stress [3].

25-dihydroxyvitamin D3 [25(OH)D3] was first shown to play a role in bone metabolism, but recent studies have revealed that it can also affect the function of immune and nonimmune cells such as monocytes, dendritic cells, T and B lymphocytes, epithelial cells, and others. In addition, 25(OH)D3 receptors have been found in practically all immunocytes. By expressing

Access this article online

Quick Response Code:

Website: www.jmsr.eg.net

DOI: 10.4103/jmisr.jmisr_79_21

Correspondence to: Ibrahim M. El-Maghraby, MD, Department of Obstetrics and Gynecology, Shibin El Kom Teaching Hospital, Shibin El Kom, Egypt.
Postal/Zip Code: 048; Tel (Office): 0482327854; Fax: 0482327854;
E-mail: ibrahim_mohie@yahoo.com

Submitted: 12-Nov-2021 **Revised:** 15-Dec-2021 **Accepted:** 31-Dec-2021 **Published:** 11-Mar-2023

How to cite this article: El-Maghraby IM, Allam AG. Could vitamin D3 be effective in prevention of risk of preeclampsia among pregnant women? J Med Sci Res 2022;5:455-60.

25(OH)D3-activating enzymes, most immunocytes can convert vitamin D into 25(OH)D3 [4].

The effect of vitamin D insufficiency on female reproduction has broader ramifications; it predisposes to a number of disorders in both mothers and their kids. Vitamin D insufficiency in mothers is a worldwide issue. Despite the usage of prenatal vitamin supplements, a substantial percentage of infants and their mothers in New England (USA) were found to be vitamin D deficient [5]. As a result, taking prenatal vitamins on a regular basis may not be enough (i.e., the vitamins may not contain enough vitamin D) to ensure adequate vitamin D levels at the time of delivery [6].

The sun's ultraviolet B rays raise serum 25(OH)D levels; however, the relationship may differ depending on skin pigmentation among different racial/ethnic groups [7]. Many research studies have shown the role of vitamin D in fertilization, placental development, pregnancy outcomes, and offspring health [8]. Several pregnancy issues, including preeclampsia, preterm birth, and gestational diabetes, as well as complications showing in offspring later in life, such as asthma, psychomotor development, and cognitive abnormalities, are thought to be the result of vitamin D insufficiency [9].

Vitamin D3 administration reduces the expression of Toll-Like receptors (TLR4) on peripheral blood monocytes, which leads to a reduction in proinflammatory cytokine release in patients at risk of preeclampsia [10]. Low circulating 25(OH)D levels have been associated with a number of major health issues during pregnancy, including impaired bone mineralization in babies, low birth weight, and other negative pregnancy outcomes [11]. As a result, this study was carried out to see if there was a link between maternal serum vitamin D3 levels and the severity of preeclampsia.

Patients and methods

A case–control study was conducted on 70 pregnant women attending the outpatient obstetric clinic or admitted in Obstetrics Shebin Elk Om Teaching Hospital during February 2020 till August 2021. All of the women in this study were divided into two groups: group A, which included 30 seemingly healthy pregnant women, and group B, which included 40 pregnant women with preeclampsia. These individuals were categorized into mild and severe preeclampsia groups based on the severity of preeclampsia and the symptoms, as determined by the Canadian Hypertension Society [12].

Pregnant women aged 18–35 years old, primigravid, singleton pregnancy, gestational age 24–34 weeks, were included in the study.

We excluded pregnant women having a history of chronic hypertension; medical illnesses such as presentational diabetes mellitus, cardiovascular, thyroid, immunological, and chronic renal diseases; known thrombophilia; and multiple pregnancies. Pregnant women who were given vitamin D supplements were also helped.

All of the women in this study were given a complete medical and obstetric history, as well as a clinical evaluation that comprised general clinical tests, obstetric examinations, and vital sign measurements in a seated position twice 4 h apart. Transabdominal ultrasonography is used to determine fetal age and biometrics, as well as the placenta and amniotic fluid index (AFI). Total protein in urine analysis for 24 h and proteinuria assessment using the dipstick method were done. Estimation of maternal vitamin D levels in the blood was done: the maternal serum level of 25(OH)D3 was measured by enzyme-linked immunosorbent assay (ELISA) and reported in nanograms per milliliter from 5 ml of venous blood obtained from each woman. Vitamin D3 deficiency was defined as 25(OH)D less than 10 ng/ml. 25(OH)D total ELISA 90' (immunoenzymetric assay for the in-vitro quantitative determination of 25(OH) D2 and D3 in serum and plasma) purchased from DIA source Immuno Assays S.A, KAP1971/F1 and Belgium was used to screen all samples.

Statistical analysis

Statistical Package for the Social Sciences (SPSS), version 25 was used to gather, tabulate, and statistically analyze data (SPSS Inc., Chicago, Illinois, USA). Data were given in the form of mean, SD, and range in descriptive statistics, whereas qualitative data were presented in the form of numbers and percentages. The χ^2 test (2), analysis of variance (F) test, Kruskal–Wallis test, and Pearson's correlation test were among the analytical statistics used (r). P value of more than 0.05 was considered statistically nonsignificant.

Ethical consideration

The institutional committee's ethical criteria were followed during all proceedings. The Shebin Elkom Teaching Hospital's Local Medical Ethics Committee approved the study. Following an explanation of the purpose, procedures, and nature of the study to all participants, signed informed consent was obtained from each participant.

Results

This study comprised 70 pregnant patients. There were 40 individuals with preeclampsia and 30 healthy controls. In our investigation, no significant differences in demographic data were detected between the preeclampsia and normal groups. Vital indicators, on the contrary, showed a substantial difference between the groups studied ($P < 0.001$), as shown in Table 1.

Table 2 shows that the systolic and diastolic blood pressures of patients with severe preeclampsia (160 ± 6.45 and 120 ± 5.65) were considerably higher than those of patients with mild preeclampsia (150 ± 9.3 and 90.3 ± 7.6) and the normal group (99.2 ± 5.2 and 70.4 ± 6.2 mmHg, respectively). Although there were significant differences between the analyzed groups in terms of vitamin D deficiency and sufficiency ($P = 0.05$), there were no significant differences in terms of vitamin D deficiency. In terms of vitamin D deficiency, however, there was no significant difference between the groups studied ($P > 0.05$), as shown in Table 2.

Moreover, as shown in Table 3, serum vitamin D levels were substantially higher in the normal group (15.54 ± 10.33 ng/ml) than in the mild preeclampsia group (14.12 ± 9.56 ng/ml) than in the severe preeclampsia group (10.13 ± 7.390 ng/ml) ($P < 0.05$), as shown in Table 3.

Aspartate aminotransferase, platelet, and hemoglobin levels were also substantially higher in the normal group (37.3 ± 9.35 IU/l, 300.1 ± 40.2 × 10^3/mm^3, and 11.66 ± 0.28 g/dl, respectively) than in the moderate preeclampsia group (37 ± 4.56 IU/l, 175 ± 40.67 × 10^3/mm^3, and 9.87 ± 0.76 g/dl, respectively) and the severe preeclampsia group (30.3 ± 6.55 IU/dl). However, alanine transaminase was substantially higher in the mild preeclampsia group (35 ± 2.32 IU/l) compared with the severe preeclampsia group (30.21 ± 7.3 IU/l) and the normal group (20.4 ± 0.43 IU/l) ($P = 0.05$). On the contrary, no significant differences were found between the studied groups regarding creatinine ($P > 0.05$), as shown in Table 4.

There was also no significant link between vitamin D level and age, gestational age, blood pressure, and laboratory examinations in the mild and severe preeclampsia groups, as shown in Table 5.

Table 1: Demographic and clinical characteristics of the studied groups

Studied variables	Normal group (*n*=30)	Preeclampsia (*n*=40)	Mann-Whitney test	*P*
Age (years)				
Range	18-37	18-35	0.742	0.321
Mean±SD	27.2±2.82	29±3.16		
Gestational age (weeks)				
Range	23-35	23-35	1.34	0.457
Mean±SD	32.4±3.0	33.2±2.11		
BMI (kg/m^2)				
Range	20-33	22.1-32	1.67	0.231
Mean±SD	27.4±2.43	26±2.87		
Systolic blood pressure				
Range (mmHg)	90-120	140-170	11.88	<0.001**
Mean±SD	97.4±9	170±10		
Diastolic blood pressure				
Range (mmHg)	60-80	80-120	7.21	<0.001**
Mean±SD	65.3±5.56	100.3±6.43		

**Significant.

Discussion

This study comprised 70 pregnant patients. There were 40 individuals with preeclampsia and 30 healthy controls. Testing for vitamin D in early pregnancy demonstrated poor predictability and was affected by individual variability in the current study, making it less effective for predicting the optimal vitamin D level during pregnancy. It also leads to overdiagnosis and treatment that is not essential [13]. In the current investigation, no significant differences in demographic data were detected between the preeclampsia and normal groups. However, there is a considerable difference in vital signs between the groups tested. These results were in accordance with Sahu *et al.* [14], Goel *et al.* [15], and Bakacak *et al.* [16], who observed no significant differences in age or BMI between the groups tested. Severe preeclampsia (160 ± 6.45 and

Table 2: The relation between vital signs and serum vitamin D3 among the studied groups

Studied variables	Normal group (*n*=30)	Preeclampsia		Kruskal-Wallis (*H*)	*P*
		Mild (*n*=23)	Severe (*n*=17)		
Systolic blood pressure (mmHg)					
Range	80-120	130-160	160-170	13.76	*P*<0.001*
Mean±SD	99.2±5.2	150±9.3	160±6.45		
Diastolic blood pressure (mmHg)					
Range	60-80	90-100	110-130	15.90	*P*<0.001*
Mean±SD	70.4±6.2	90.3±7.6	120±5.65		
Vitamin D (ng/ml) levels	*n* (%)	*n* (%)	*n* (%)	χ^2	*P*
Deficiency<10 ng/ml	7 (23.33)	7 (30.43)	11 (64.71)	2.16	0.076
Insufficiency 10-29 ng/ml	20 (66.67)	13 (56.52)	6 (35.29)	8.21	0.002*
Sufficiency 30 - 100 ng/ml	3 (10.00)	3 (13.04)	0	5.12	0.016*

*Significant.

Table 3: Serum level of vitamin D among cases and control groups

Studied variables	Normal group (*n*=30)	Preeclampsia		Kruskal-Wallis test	*P*
		Mild (*n*=23)	Sever (*n*=17)		
Serum vitamin D (ng/ml)					
Range	5-52.0	4-46	4-28	9.430	*P*<0.001*
Mean±SD	15.54±10.33	14.12±9.56	10.13±7.90		

*Significant.

Table 4: Laboratory investigations among the studied groups

Studied variables	Normal ($n=30$)	Preeclampsia		Kruskal-Wallis	*P*
		Mild ($n=23$)	Sever ($n=17$)		
Creatinine level					
Range (mg/ml)	0.5-1.35	0.5-1.145	0.5-1.00	1.32	0.087
Mean±SD	0.89±0.26	0.92±0.18	0.82±0.27		
ALT (IU/l)					
Range	12-30	18-36	18-48	6.11	*P*<0.001*
Mean±SD	20.4±0.43	35±2.32	30.21±7.3		
AST (IU/l)					
Range	18-27	19-32	20-55	7.80	*P*<0.001*
Mean±SD	37.3±9.35	37±4.56	30.3±6.55		
Platelet (10^3/mm^3)					
Range	125-460	85-248	86-910	5.76	*P*<0.001*
Mean±SD	300.1±40.2	175±40.67	150.11±50.45		
Hemoglobin (g/dl)					
Range	10.43-12.6	9-11	9-11	4.98	*P*<0.001*
Mean±SD	11.66±0.28	9.87±0.76	9.3±0.38		

ALT, alanine transaminase; AST, aspartate aminotransferase.*Significant.

Table 5: Pearson correlation between serum vitamin D and other parameters among patients with preeclampsia

Studied variables	Vitamin D	
	r	*P*
Age (years)	−0.044	0.67
Gestational age (weeks)	−0.011	0.832
Systolic blood pressure	−0.032	0.932
Diastolic blood pressure	−0.012	0.843
Creatinine (mg/ml)	0.190	0.721
ALT (IU/l)	0.209	0.634
AST (IU/l)	0.155	0.866
Platelet (10^3/mm^3)	−0.200	0.059
HB (g/dl)	−0.013	0.730

ALT, alanine transaminase; AST, Aspartate aminotransferase; HB, hemoglobin; *r*, Pearson correlation.

120 ± 5.65 mmHg), mild preeclampsia (150 ± 9.3 and 90.3 ± 7.6 mmHg), and normal group (99.2 ± 5.2 and 70.4 ± 6.2 mmHg) had significantly higher systolic and diastolic blood pressures, respectively. Although there were significant differences between the study groups in terms of vitamin D deficiency and sufficiency, there were no significant differences in terms of vitamin D deficiency. In terms of vitamin D deficiency, however, there was no significant difference between the groups studied. This is in terms of the Canadian Hypertension Society's consensus on mild and severe preeclampsia [12].

There was a significant difference between cases in the normal group and cases in the severe group, as well as between cases with mild and cases with severe preeclampsia, in the current study. This is in line with the findings of Yuan *et al*. [17], who found that vitamin D insufficiency is more common in severe preeclampsia than in mild preeclampsia.

Serum vitamin D levels were substantially higher in the normal group than in the mild preeclampsia group and the severe preeclampsia group, according to our findings. These findings also agree with Jindal *et al*. [18], Yuan *et al*. [17], and Mehmood and Karim [19], who found that when compared with 68% of controls, 80% of study group patients (preeclampsia group) were substantially more vitamin D deficient, demonstrating that higher vitamin D insufficiency was associated with increased preeclampsia severity. Jindal *et al*. [18] discovered a link between vitamin D insufficiency and the severity of preeclampsia, with statistically significant differences in vitamin D serum levels between the normal and severe preeclampsia groups, as well as between mild and severe preeclampsia groups. The study by Srinivas *et al*. [20] showed that preeclampsia has been linked to a lack of vitamin D. Although the mechanism by which vitamin D insufficiency affects preeclampsia is unknown, numerous possibilities have been proposed. These ideas include modulating proinflammatory responses and reducing oxidative stress in preeclampsia, boosting angiogenesis through vascular endothelial growth factor (VEGF) and gene regulation, and lowering blood pressure through the renin–angiotensin system [21,22].

Clinical investigations show that vitamin D-mediated hypertension reduction requires enhanced activation of the renin–angiotensin–aldosterone pathway, which is the major regulator of electrolyte and volume homeostasis and contributes to arterial hypertension development [23]. Benachi *et al*. [24], in contrast to our findings, observed no link between vitamin D insufficiency and the risk of preeclampsia in the first trimester. Nonetheless, women who had adequate vitamin D levels in both the first and third trimesters had a lower risk of preeclampsia. They explained that maternal features and the season of testing caused a change in 25(OH)D serum levels in the first trimester. Wetta *et al*. [25] conducted a study on midtrimester vitamin D level and found no significant link to the onset of preeclampsia. However, the limitations of

this study were that it was retrospective and had a limited sample size.

In addition, our findings revealed that in both moderate and severe preeclampsia groups, there was no significant association between vitamin D levels and age, gestational age, blood pressure, or laboratory examinations. These findings were in agreement with Yuan *et al*. [17] and Hamedanian *et al*. [26]. We used ELISA to measure 25(OH)D concentrations in this investigation because it was readily available, sensitive, quick, and accurate compared with other tests that required radioisotopes or a costly radiation counter. Singla *et al*. [27] compared serum vitamin D concentrations in two groups using the ELISA technique (74 nulliparous preeclamptic women with singleton pregnancy and without any known medical disorder and 100 healthy nulliparous controls of same age). They found that mean serum 25(OH)D levels were substantially lower in cases compared with controls; hence, they postulated that patients with preeclampsia had much lower vitamin D levels than healthy women. Wei *et al*. [28] used chemiluminescence immunoassay to measure maternal serum 25(OH)D concentrations at 12–18 and 24–26 weeks of pregnancy and discovered a clear positive connection between the two gestational ages. For maternal 25(OH)D levels at 12–18 weeks of pregnancy, the link was not statistically significant. Wetta *et al*. [25] investigated vitamin D insufficiency and preeclampsia using liquid chromatography-tandem mass spectrometry and found no link. Using radioimmunoassay in vitamin D assay, Halhali *et al*. [29] found a substantial link between vitamin D insufficiency and preeclampsia. Because radioimmunoassay works best in an aqueous environment, yet vitamin D is poorly soluble in water, it is difficult to employ.

It is difficult to generalize across studies with any degree of precision owing to variances in ethnicity, geographic location, and gestational age at vitamin D measurement and different tests.

The differences in outcomes between countries are most likely explained by differences in latitude, skin color, and multivitamin use. Null results and potential differences in study findings may be explained by differences in study size and population characteristics, and there is currently no consensus on a cutoff for vitamin D deficiency in the pregnant population, as most studies extrapolate cutoffs from the nonpregnant population.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Abbas RA, Ghulmiyyah L, Hobeika E, Usta IM, Mirza F, Nassar AH. Preeclampsia: a review of early predictors. maternal-fetal. Medicine 2021; 3:197–202.
2. Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, *et al*. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. Int J Gynecol Obstetr 2019; 145:1–33.
3. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. Nat Rev Nephrol 2019; 15:275–289.
4. Zhang L, Ni H, Zhou Z, Yuan X, Xia J, Jiang B, Li Y. 1α, 25-dihydroxyvitamin D3 supplementation during pregnancy is associated with allergic rhinitis in the offspring by modulating immunity. J Immunol Res 2021; 2021:6638119.
5. Merewood A, Mehta SD, Grossman X, Chen TC, Mathieu JS, Holick MF, Bauchner H. Widespread vitamin D deficiency in urban Massachusetts newborns and their mothers. Pediatrics 2010; 125:640–647.
6. Heyden EL, Wimalawansa SJ. Vitamin D: effects on human reproduction, pregnancy, and fetal well-being. J Steroid Biochem Mol Biol 2018; 180:41–50.
7. Sawicki CM, Van Rompay MI, Au LE, Gordon CM, Sacheck JM. Sun-exposed skin color is associated with changes in serum 25-hydroxyvitamin D in racially/ethnically diverse children. J Nutr 2015; 146:751–757.
8. Karras SN, Wagner CL, Castracane VD. Understanding vitamin D metabolism in pregnancy: From physiology to pathophysiology and clinical outcomes. Metabolism 2018; 86:112–123.
9. Poniedziałek-Czajkowska E, Mierzyński R. Could vitamin D be effective in prevention of preeclampsia?. Nutrients 2021; 13:3854.
10. Qian L, Wang H, Wu F, Li M, Chen W, Lv L. Vitamin D3 alters Toll-like receptor 4 signaling in monocytes of pregnant women at risk for preeclampsia. Int J Clin Exp Med 2015; 8:18041.
11. Wei SQ, Audibert F, Hidiroglou N, Sarafin K, Julien P, Wu Y, *et al*. Longitudinal vitamin D status in pregnancy and the risk of pre-eclampsia. BJOG 2012; 119:832–839.
12. Helewa ME, Burrows RF, Smith J, Williams K, Brain P, Rabkin SW. Report of the Canadian Hypertension Society Consensus Conference: 1. Definitions, evaluation and classification of hypertensive disorders in pregnancy. CMAJ 1997; 157:715–725.
13. Yu CK, Ertl R, Skyfta E, Akolekar R, Nicolaides KH. Maternal serum vitamin D levels at 11-13 weeks of gestation in preeclampsia. J Hum Hypertens 2013; 27:115–118.
14. Sahu M, Bhatia V, Aggarwal A, Rawat V, Saxena P, Pandey A, Das V. Vitamin D deficiency in rural girls and pregnant women despite abundant sunshine in northern India. Clin Endocrinol (Oxf) 2009; 70:680–684.
15. Goel P, Garg G, Kaur J, Mehra R, Tandon R, Huria A. Association of vitamin D deficiency during pregnancy with preeclampsia and eclampsia. Int J Reprod Contracept Obstet Gynecol 2016; 5:9.
16. Bakacak M, Serin S, Ercan O, Köstü B, Avci F, Kılınç M, *et al*. Comparison of vitamin D levels in cases with preeclampsia, eclampsia and healthy pregnant women. Int J Clin Exp Med 2015; 8:9.
17. Yuan Y, Tai W, Xu P, Fu Z, Wang X, Long W, *et al*. Association of maternal serum 25-hydroxyvitamin D concentrations with risk of preeclampsia: a nested case-control study and meta-analysis. J Mater Fetal Neonat Med 2021; 34:10.
18. Jindal S, Sharma JC, Sharma M. Association of deficiency of maternal vitamin D levels with severity of preeclampsia. Epidem Int 2019; 4:3.
19. Mehmood S, Karim SA. Vitamin D deficiency during pregnancy and its relationship with pre-eclampsia, eclampsia and gestational hypertension. Austin J Nutr Metab 2016; 3:2.
20. Srinivas SK, Edlow AG, Neff PM, Sammel MD, Andrela CM, Elovitz MA. Rethinking IUGR in preeclampsia: dependent or independent of maternal hypertension?. J Perinatol 2009; 29:10.
21. Kaufmann P, Black S, Huppertz B. Endovascular trophoblast invasion:

implications for the pathogenesis of intrauterine growth retardation and preeclampsia. Biol Reprod 2003; 69:1.
22. Ganguly A, Tamblyn JA, Finn-Sell S, Chan SY, WestwoodM, Gupta J, *et al*. Vitamin D, the placenta and early pregnancy: effects on trophoblast function. J Endocrinol 2018; 236:R93–R103.
23. Ke L, Mason RS, Kariuki M, Mpofu E, Brock KE. Vitamin D status and hypertension: a review. Integr Blood Press Control 2015; 8:13–35.
24. Benachi A, Baptiste A, Taieb J, Tsatsaris V, Guibourdenche J, Senat MV, *et al*. Relationship between vitamin D status in pregnancy and the risk for preeclampsia: A nested case-control study. Clinical nutrition 2020;39:440-6.
25. Wetta LA, Biggio JR, Cliver S, Abramovici A, Barnes S, Tita AT. Is midtrimester vitamin D status associated with spontaneous preterm birth and preeclampsia?. Am J Perinatol 2014; 31:6.
26. Hamedanian L, Badehnoosh B, Razavi-Khorasani N, Mohammadpour Z, Mozaffari-Khosravi H. Evaluation of vitamin D status, parathyroid hormone, and calcium among Iranian pregnant women with preeclampsia: a case-control study. Int J Reprod Biomed 2019; 17:831–840.
27. Singla R, Gurung P, Aggarwal N, Dutta U, Kochhar R. Relationship between preeclampsia and vitamin D deficiency. Arch Gynecol Obstet 2014; 291:1247–1251.
28. Wei S, Audibert F, Hidiroglou N. Longitudinal vitamin D status in pregnancy and the risk of pre-eclampsia. BJOG 2012; 119:832–839.
29. Halhali A, Dıaz L, Avila E. Decreased fractional urinary calcium excretion and serum1, 25-dihydroxyvitamin D and IGF-I levels in preeclampsia. J Steroid Biochem Mol Biol 2007; 103:803–806.