The Egyptian Journal of Hospital Medicine (October 2024) Vol. 97, Page 4485-4490

Relationship between Vitamin D Status in Normal Pregnancy and Preeclampsia

Yasmin Mohamed AboElazm*, Khaled S. Ismail, Nermin Y. Abo El-Kheir, Layla A. El-Boghdady
Department of Obstetrics and Gynecology, Faculty of Medicine, Mansoura University, Egypt
***Corresponding Author**: Yasmin Mohamed AboElazm, **Mobile**: (+20) 010 90462334, **Email**: asmin.m.aboelazm@gmail.com

ABSTRACT

Background: Preeclampsia (PE) is a hypertensive pregnancy disorder (HPD) that may happen after 20 weeks of pregnancy. Vitamin D is believed to be involved in PE development. The majority of studies on vitamin D and PE have been carried out in cases with small sample sizes, and hence, the results were not conclusive.
Objective: This study aimed to find the association between vitamin D status in normal pregnancy and PE.
Patients and methods: This cross-sectional observational study included 90 pregnant women who were divided into preeclamptic group and non-pre-eclamptic group (Control group), 45 cases in each group. Measurement of serum 25 hydroxyvitamin D [25(OH)D] level was conducted using an I^{125} radioimmunoassay (DiaSorin).
Results: The mean level of vitamin D in the cases with PE was statistically significantly lower compared to the control group. There were 22 cases with PE and 23 cases with severe preeclampsia (sPE). The mean level of vitamin D in the cases with severe PE was statistically significantly lower compared to the cases with PE. The best cutoff point of serum vitamin D value to detect the cases with severe PE (sPE) was < 26.05 ng/dl with 83.3% sensitivity, 78.9% specificity and 81.8% accuracy. **Conclusion**: We concluded that 25(OH)D has a significant association with PE as revealed by the fact that pregnant females with low 25(OH)D concentration were more susceptible to PE development.
Keywords: Preeclampsia, Severe PE, 25(OH)D.

INTRODUCTION

Preeclampsia (PE) is a fatal pregnancy condition characterized by gestational hypertension (HTN) and proteinuria [(1)]. It accounts for about 5 % of the pregnant females [(2)] and 12.5% of maternal deaths all over the world [(3)]. Its adverse events comprise eclampsia, consumptive coagulopathy and the HELLP syndrome [(2)]. Fetal consequences include IUGR and fetal death [(4)].

Several theories have been reported to contribute to PE pathogenesis; one of these theories is vitamin D deficiency (VDD). It has been demonstrated that vitamin D could modulate pro-inflammatory response, decrease the generation of free radicals in the context of PE state, promote VEGF-mediated angiogenesis, and decrease blood pressure (BP) [(5, 6)].

Furthermore, it is believed to have a considerable function in PE as an immune modulator. It could enhance the placental immune response with subsequent prevention of the production of anti-angiogenic factors that modulate the hypertension [(7)]. During normal pregnancy, RAS is activated with subsequent increased production of renin, angiotensinogen, and angiotensin II levels [(8)]. With regard to PE, serum angiotensin I and II, and aldosterone are diminished in comparison with pregnant females with normal BP, while autoantibodies towards the angiotensin II type I receptor and plasma active renin levels are elevated, stimulating receptor signaling to raise systemic BP [(9)].

This work aimed to find the relationship between vitamin D status in normal pregnancy and PE.

PATIENTS AND METHODS

This cross-sectional observational study was conducted at Obstetrics and Gynecology Department of Mansoura University Hospital, Dakahliya, Egypt, for 1 year (May 2022 – April 2023). This study included 90 pregnant females recruited at Mansoura University Hospital. They were divided into preeclamptic group and non-preeclamptic group (Control group), 45 cases in each group.

Inclusion criteria: Patients with parity up to previous 2 deliveries, with age between 18 to 35 years, with singleton pregnancy, in 3rd trimester, no past history of any medical disorder and no other medical complications during this pregnancy.

Exclusion criteria: Women with preexisting medical conditions such as rheumatologic diseases, thyroid diseases, hepatic or kidney dysfunction, diabetes, and nutritional deficiency, women less than 18 years old or more than 35 years old, with parity more than 2 previous deliveries, with multifetal pregnancy and with gestational age (GA) earlier than 3rd trimester.

Methods: All subjects participating in the study were subjected to history taking including demographic data (age, and sex), general medical history, history of present pregnancy and menstrual history (to be sure of her LMP and confirm the date). Thorough clinical examination included general examination with special emphasis on [BP, temperature, pulse, body weight, height, BMI]. Abdominal examination was conducted with a special focus on uterine assessment to determine the uterine level. Trans-abdominal sonography was conducted to report the viability of pregnancy and to ensure the gestational age. Laboratory analysis included complete blood count, liver and kidney functions tests to determine severity of PE and urine dipsticks to assess proteinuria.

Sample collection & preparation: Five millimeter of venous blood were withdrawn from all pregnant females. To allow the samples to coagulate and retract, they were left undisturbed for half an hour. These were then centrifuged for ten min at 3000×g, and the

Received: 18/07/2024
Accepted: 18/09/2024

supernatant (serum) was taken out and placed in another simple specimen bottle. Urinalysis with dipstick test. Proteinuria was graded from 0 to 4 (Absent: zero: 15–30 mg/dL, 1+: between 30 and 100 mg/dL, 2+: between 100 and 300mg/dL, 3+: between 300 and 1000 mg/dL and 4+: beyond 1000 mg/dL) [10].

Determination of severity of PE: Arterial BP was measured, and urine analysis was conducted every visit. All members underwent routine obstetric sonography. PE was detected by elevated BP (140/90 mmHg) that happened in a pregnant female after twenty weeks of gestation linked to proteinuria (more than 0.3 g/24h). In addition, sPE was diagnosed if at least one of the next was present: BP of 160/110 mmHg or more, excretion of five grams or more of protein in a 24 h urinary sample or urine dipstick revealing at least 3+ in a random urinary specimen, oliguria, pulmonary oedema, ocular affection, and stomach pain.

Measurement of serum vitamin D: It was measured using a chemiluminescent immunoassay (ELISAs Kits, Germany). (Using an ^{125}I radioimmunoassay (DiaSorin)).

Ethical consideration: The ethics committee of Faculty of Medicine, Mansoura University approved the current study design. The confidentiality was respected. Prior to their enrollment in the study, each participant provided written informed consent. Participants were free to leave the research at any time. No other purpose has been or will be used with the collected data. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

IBM SPSS version 22 was utilized to examine the data that was introduced into the computer. Number and percentage were utilized to describe the qualitative data. The Kolmogorov-Smirnov test was used to check for normality, and the median for non-parametric data and the mean ± SD for parametric data were used to summarize the quantitative data. For comparisons between two or more groups, the Chi-squared test was employed. The Monte Carlo test was used as a correction for the Chi-Square test. The significance of the result was set at ≤ 0.05.

RESULTS

The current study included 45 pregnant females with PE and 45 pregnant women with normal pregnancy (control group). Table **(1)** showed that the mean age of the pregnant females in the PE group was 29.06 ± 7.08 years with insignificant difference compared to the control group (28.84 ± 8.16 years) (p= 0.908). There were insignificant differences between both groups concerning the mean BMI (p= 0.110), the residence (p= 0.671), the occupation (p= 0.782) and the highest percentage of females in both groups were housewives. The mean age of menarche in both groups was 11.56 ± 1.14 years and 11.61 ± 1.09 years in the cases and control group respectively, with no significant difference between both groups (p= 0.852). The highest percentage of the cases in both groups had regular menstruation. Also, there was insignificant difference in the number of gravidity and parity between the cases and control group.

Table (1): Demographic data, menstrual and obstetric history of the study groups

Variables	PE group (N=45)	Control group (N=45)	Test of significance
Age (years)	29.06 ± 7.08	28.84 ± 8.16	t= 0.116 P = 0.908
BMI (kg/m^2)	27.90 ± 2.57	26.84 ± 2.60	t= 1.621 P = 0.110
Residence			
Urban	**26 (57.8%)**	**24 (53.3%)**	χ2= 0.180 P= 0.671
Rural	**19 (42.2%)**	**21 (46.7%)**	
Occupation			
Non-working (housewives)	**24 (53.3%)**	**26 (57.8%)**	MC= 1.080 P = 0.782
Heavy manual work	**9 (20%)**	**6 (13.3%)**	
Office work	**9 (20%)**	**11 (24.4%)**	
Trade/business	**3 (6.7%)**	**2 (4.4%)**	
Age of menarche (years)	11.56 ± 1.14	11.61 ± 1.09	t= 0.187 P = 0.852
Regularity of the menstrual cycles			
Regular	**35 (77.8%)**	**37 (82.2%)**	χ2= 1.831 P = 0.304
Irregular	**10 (22.2%)**	**8 (17.8%)**	
Gravidity	3 (1 – 5)	2 (1 – 7)	Z= - 1.239 P = 0.215
Parity	1 (0 – 2)	1 (0 – 2)	Z= - 0.490 P = 0.624

t= independent samples t-test, z: Mann Whitney U test, χ2: chi square test MC: Monte-Carlo test.

Table **(2)** showed that the GA at time of examination was 35.93 ± 2.25 weeks and 35.51 ± 1.12 weeks in the PE and control group correspondingly, with insignificant difference between both groups (p=0.903). SBP and DBP were significantly elevated in PE group compared to the controls (P<0.001).

Table (2): Analysis of the blood pressure and gestational age in the study groups

Variables	**PE group (N=45)**	**Control group (N=45)**	**Test of significance**
Gestational age at examination (Weeks)	35.93 ± 2.25	35.51 ± 1.12	t=0.059 P = 0.903
SBP (mmHg)	150.97 ± 14.91	114.84 ± 7.24	**t= 12.143** **P < 0.001****
DBP (mmHg)	97.74 ± 8.45	74.19 ± 6.20	**t= 12.507** **P < 0.001****

T: independent samples t-test.

Table **(3)** displayed that there was no significant difference in the standard laboratory investigations between the cases in the two study groups except for CRP and ESR that were significantly greater in the PE group compared to the controls. The mean level of vitamin d in the cases with PE was 29.02 ± 6.22 ng/ml that was statistically highly significantly decreased compared to the controls (39.54 ± 11.21 ng/ml) (**P < 0.001).** In the group with PE there were 4 females (8.9%) with vitamin d deficiency, 19 females (42.2%) with vitamin d insufficiency and 22 females (48.8%) with normal vitamin D levels. While in the controls, there were 13 females (28.9%) with vitamin d insufficiency and 32 females (71.1%) with normal vitamin d levels.

Table (3): Analysis of laboratory parameters and vitamin D (ng/ml) in the two study groups

Variables	**PE group (N=45)**	**Control group (N=45)**	**Test of significance**
Hemoglobin (g/dl)	11.05 ± 1.65	10.91 ± 0.54	t = 0.445 p= 0.658
WBCs (10^3/µl)	6.64±1.64	7.50±1.71	t = 0.445 p= 0.658
PLTs (10^3/µl)	283.52 ± 68.17	308.58 ± 47.30	t = - 1.774 p= 0.080
SGPT (ALT) (IU/L)	20 (15 - 295)	20 (16 - 28)	z = - 1.943 p= 0.052
SGOT (AST) (IU/L)	22 (16 - 34)	19 (15 - 29)	z = - 1.248 p= 0.138
CRP (mg/dl)	**8 (2 – 14)**	**7 (1-11)**	**z = -2.137** **P = 0.033***
ESR (mm/hr)	90 (6 -186)	10 (5 - 19)	**z = - 6.852** **p < 0.001***
Vitamin D (ng/ml)	29.02 ± 6.22	39.54 ± 7.32	**t= -5.508** **P < 0.001***
Vitamin D categories			
Vitamin d deficiency	**4 (8.9%)**	**0 (0%)**	**MC = 4.816** **P < 0.001***
Vitamin d insufficiency	**19 (42.2%)**	**13 (28.9%)**	
Normal vitamin d levels	**22 (48.8%)**	**32 (71.1%)**	

Median and range: Non parametric test. t= independent samples t-test, z: Mann Whitney U test, MC: Monte-Carlo test

Table **(4)** showed the grade of proteinuria, there were 13 cases (28.9%) with grade 1, 13 cases (28.9%) with grad 2, 12 cases (26.7%) with grade 3 and 7 cases (15.6%) with grade 4. Regarding the severity of PE, there were 22 cases (48.9%) with PE and 23 cases (51.1%) with severe PE.

Table (4): Grades of proteinuria and severity of PE in the cases group

Variables	PE group (N=45)
Proteinuria Grades	
I	13 (28.9 %)
II	13 (28.9 %)
III	12 (26.7 %)
IV0	7 (15.6 %)
Severity of PE	
PE	22 (48.9 %)
Severe PE	23 (51.1 %)

Table **(5)** displayed that the best cutoff point of serum vitamin d level to identify the cases with PE was < 29.85 ng/dl with 75.6% sensitivity, 66.5% specificity and 70.4% accuracy (p <0.001).

Table (5): Diagnostic performance and test characteristics of serum vitamin D (ng/ml) in detection of PE (Cases group)

Test characteristics	Serum vitamin d (ng/ml)
Best cutoff value	< 29.85
AUC	0.768
P-value	**< 0.001 ***
Sensitivity %	75.6 %
Specificity %	66.5 %
Positive predictive value %	68.2 %
Negative predictive value %	74.4 %
Accuracy %	70.4 %

Table **(6)** displayed that the mean level of vitamin D in the cases with severe PE was 25.52 ± 3.84 ng/ml that was significantly lower compared to the cases with PE (32.50 ± 6.42 ng/ml) (P < 0.001).

Table (6): Analysis of serum vitamin D (ng/ml) in the cases with PE and severe PE

Variables	PE (N=22)	Severe PE (N=23)	Test of significance
Serum vitamin d (ng/ml)	32.50 ± 6.42	25.52 ± 3.84	t = 6.841 p < 0.001*

T= independent samples t-test.

Table (7) demonstrated that the best cutoff point of serum vitamin D level to identify the cases with severe PE was < 26.05 ng/dl with 83.3% sensitivity, 78.9% specificity and 81.8% accuracy (p <0.001).

Table (7): Diagnostic performance and test characteristics of serum vitamin D (ng/ml) in detection of severe PE

Test characteristics	Serum vitamin d (ng/ml)
Best cutoff value	< 26.05
Area under the curve	0.789
P-value	**< 0.001 ***
Sensitivity %	83.3 %
Specificity %	78.9 %
Positive predictive value %	76.3 %
Negative predictive value %	80.4 %
Accuracy %	81.8 %

DISCUSSION

Preeclampsia (PE) is still a primary etiology of maternal and fetal death; hence early prediction of PE is crucial [11, 12]. Till now, the actual mechanism of PE is still not well-identified. Interestingly, VDD has been reported to be accompanied by a greater risk for PE [13].

The mean age of the pregnant females in the PE group was 29.06 ± 7.08 years with insignificant difference compared to the control group (28.84 ± 8.16 years) (p= 0.908). The lower incidence of PE indicated that, in contrast to western nations, marriage and pregnancy occur at a younger age in our nation, which is the same result of our studies. This agrees with the concept of **Nirmala *et al.*** [14] who displayed that most of patients were between 21-30 years of age for two groups. Likewise, **Abd El-Aal *et al.*** [15] found that there was insignificant difference between the PE and normal pregnancy groups concerning age (P > 0.05).

This result also contradicts that of **Hassan *et al.*** [16] who demonstrated that females over 40 years of age had the highest incidence of PE. Also, the results disagree with **Gabal *et al.*** [17] who displayed that the age of hypertensive cases was significantly increased compared to normotensives ones (29.1 ± 3.6 versus 25.4±4.6) (Odds ratio=1.3). The variation may be clarified by alteration in sample sizes between these studies, including our current study.

In this study, there was insignificant difference between the PE and normal pregnancy groups concerning the mean BMI (p= 0.110). Similarly, **Abd El-Aal *et al.*** [15] revealed insignificant difference between both groups concerning BMI (P>0.05).

However, **Aabidha *et al.*** [18] displayed that the incidence of PE increases with increase in BMI. The difference could be explained due to the characteristics of the included females, as the Egyptian females are generally characterized by high BMI compared to other countries. This was confirmed in an Egyptian study based on data from the Ministry of Health and Population for the year 2014. According to this study report, about 50% of females (50.3%) and 33.3% of males (26.4%) complained of being overweight [19].

According to the current results, the mean SBP and DBP were significantly elevated in PE group compared to the controls (P<0.001). Also, **Eser *et al.* [20]**, **Orabona *et al.* [21]** and **El-Maghraby *et al.* [22]** included 70 pregnant patients. There were 40 individuals with PE and 30 healthy controls. In their investigation, blood pressure displayed a significant difference between the studied groups (P<0.001), with significant increase in the BP in the PE group.

With regard to the grade of proteinuria in this study, there were 13 cases (28.9%) with grade 1, 13 cases (28.9%) with grade 2, 12 cases (26.7%) with grade 3 and 7 cases (15.6%) with grade 4. This is in agreement with **Rao *et al.* [23]** who displayed that 74 (75.5%) were demonstrated to be positive (+3) by urinary dipstick grading.

According to the current results, the vitamin D value in the cases with PE was 29.02 ± 6.22 ng/ml that was significantly reduced as compared to the controls (39.54 ± 11.21 ng/ml)**.** In the group with PE there were 4 females (8.9%) with vitamin D deficiency, 19 females (42.2%) with vitamin D insufficiency and 22 females (48.8%) with normal vitamin D levels.

Similarly; **Abedi *et al.* [24]** included 59 pregnant females with PE and 59 healthy pregnant females in their study. PE revealed a significant relationship with VDD. Additionally, **Singla *et al.* [25]** measured 25(OH)D levels in PE cases and health controls (normal BP) and displayed that serum 25(OH)D level was significantly reduced among PE cases (9.7±4.95 ng/ml) compared to health controls (normal BP) (14.8 ± 6.68 ng/ml) (p<0.001). Within the same context, **Richard *et al.* [26]** illustrated that vitamin D value in cases with PE was significantly decreased compared to the controls. In agreement, **AlSubai *et al.* [27]**. revealed in their study that vitamin D intake was significantly accompanied by a minimal risk of PE (p = 0.001), whereas VDD was significantly accompanied by increased risk of PE (p = 0.001). Also, opposite to the current results, **Youssef *et al.* [28]** illustrated that there was no significant difference between healthy pregnant females (normal BP) and PE groups regarding vitamin D level (22.21 ± 9.35 versus 18.49 ± 8.43) (P>0.05). The role of VDD in severe inflammatory disorders is believed to be due to its effect in the disturbance of endothelial stability with a consequent increase in the liability for vascular leaking. Experimental studies of PE obviously demonstrated that such disturbance in endothelial functions causes placental ischemia [29].

Our study illustrated that the mean value of 25(OH)D in the cases with sPE was 25.52 ± 3.84 ng/ml that was significantly lower compared to PE cases (32.50 ± 6.42 ng/ml). Likewise, **Zhao *et al.* [30]** displayed that serum 25(OH)D value was significantly reduced in pregnant females who afterwards acquired sPE compared to those who didn't. They revealed that maternal VDD had a strong association with elevated odds for sPE. **Jindal *et al.* [31]** revealed a relationship between VDI and the degree of PE, with significant differences in 25(OH)D serum levels between the normal and severe PE groups, as well as between mild and sPE groups. In addition, **El-Maghraby *et al.* [22]** recorded that vitamin D levels were substantially greater in the normal group (15.54 ± 10.33 ng/ml) than in the mild PE group (14.12 ± 9.56 ng/ml) than in the sPE group (10.13 ± 7.390 ng/ml) (P < 0.05). While, **Hashemipour *et al.* [32]** conducted their study on a total of seventy five healthy pregnant females and seventy four pregnant females with PE (forty six mild PE and twenty eight sPE). They displayed that there were insignificant differences between the normal, mild PE, and sPE groups with regard to serum 25(OH)D level (27.7±15.3 versus 22.9±15.9 versus 27.6±16.6) (P >0.05), which disagree with our study.

The best cutoff point of serum vitamin D value to detect cases with PE was < 29.85 ng/dl with 75.6% sensitivity, 66.5% specificity and 70.4% accuracy. Also, the best cutoff point of serum vitamin D value to detect cases with sPE was <26.05 ng/dl with 83.3% sensitivity, 78.9% specificity and 81.8% accuracy. Of note, no preceding research has determined the best cutoff point of vitamin D to predict the development of PE or sPE. Much research is needed to prove or disprove this point.

The small numbers of cases and carrying the study out in a single center have been considered the main limitations that may affect the power of the obtained results.

CONCLUSION

We concluded that 25(OH)D had a significant association with PE as revealed by the fact that pregnant females with low 25(OH)D concentration were more susceptible to PE development.

Financial support and sponsorship: Nil.
Disclosure statement: Nil.
Conflict of interest: Nil.

REFERENCES

1. **Roberts J, Cooper D (2001):** Pathogenesis and genetics of pre-eclampsia. The Lancet, 357 (9249): 53-6.
2. **Duley L (2009):** The Global Impact of Pre-eclampsia and Eclampsia. Seminars in Perinatology, 33 (3): 130-7.
3. **Belay Tolu L, Yigezu E, Urgie T *et al.* (2020):** Maternal and perinatal outcome of preeclampsia without severe feature among pregnant women managed at a tertiary referral hospital in urban Ethiopia. Plos One, 15 (4): e0230638. doi: 10.1371/journal.pone.0230638.
4. **Srinivas S, Edlow A, Neff P *et al.* (2009):** Rethinking IUGR in preeclampsia: dependent or independent of maternal hypertension? Journal of Perinatology, 29 (10): 680-4.
5. **Tarcin O, Yavuz D, Ozben B *et al.* (2009):** Effect of vitamin D deficiency and replacement on endothelial function in asymptomatic subjects. The Journal of Clinical Endocrinology & Metabolism, 94 (10): 4023-30.

6. **Robinson C, Alanis M, Wagner C *et al.* (2010):** Plasma 25-hydroxyvitamin D levels in early-onset severe preeclampsia. American Journal of Obstetrics and Gynecology, 203 (4): 366-67.
7. **Pérez-López F, Pasupuleti V, Mezones-Holguin E *et al.* (2015):** Effect of vitamin D supplementation during pregnancy on maternal and neonatal outcomes: a systematic review and meta-analysis of randomized controlled trials. Fertility and Sterility, 103 (5): 1278-88.
8. **Irani R, Xia Y (2008):** The functional role of the renin–angiotensin system in pregnancy and preeclampsia. Placenta, 29 (9): 763-71.
9. **Faulkner J, Amaral L, Cornelius D *et al.* (2017):** Vitamin D supplementation reduces some AT1-AA-induced downstream targets implicated in preeclampsia including hypertension. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 312 (1): 125-31.
10. **Amin S, Illipilla S, Hebbar S *et al.* (2014):** Quantifying proteinuria in hypertensive disorders of pregnancy. International Journal of Hypertension, 14: 941408. doi: 10.1155/2014/941408
11. **Tabatabaeian M, Kordi M, Dadgar S *et al.* (2018):** Evaluation of the role of serum markers and Doppler ultrasonography of uterine artery in predicting preeclampsia at the second trimester of pregnancy: A systematic review. The Iranian Journal of Obstetrics, Gynecology and Infertility, 21: 76-85.
12. **Başbuğ D, Başbuğ A, Gülerman C (2017):** Is unexplained elevated maternal serum alpha-fetoprotein still important predictor for adverse pregnancy outcome? Ginekologia Polska, 88 (6): 325-30.
13. **Samimi M, Kashi M, Foroozanfard F *et al.* (2016):** Expression of Concern: The effects of vitamin D plus calcium supplementation on metabolic profiles, biomarkers of inflammation, oxidative stress and pregnancy outcomes in pregnant women at risk for pre-eclampsia. Journal of Human Nutrition and Dietetics, 29 (4): 505-15.
14. **Nirmala T, Kumar Pradeep L, Vani B *et al.* (2015):** Study of coagulation profile in pregnancy induced hypertension. Indian Journal Of Pathology and Oncology, 2 (1): 1-6.
15. **Abd El-Aal N, El-Halaby A, Taie A (2019):** Combined second trimester maternal serum a-fetoprotein and uterine artery Doppler in the prediction of pre-eclampsia. Menoufia Medical Journal, 32 (2): 430-35.
16. **Hassan S, Gouda A, El-Monshed A *et al.* (2020):** Effect of Cognitive Behavioral Therapy on Anxiety, Stress, Depression, and Coping Pattern among Pregnant Women with Preeclampsia. American Journal of Nursing Research, 8 (2): 269-277.
17. **Gabal M, Abousaif H, Salah-Eldin W *et al.* (2017):** Frequency of hypertension associated with pregnancy among the pregnant women attending maternal and child care centers in Belbeis City. The Egyptian Journal of Community Medicine, 35 (3): 83. doi.10.21608/EJCM.2017.4101
18. **Aabidha P, Cherian A, Paul E *et al.* (2015):** Maternal and fetal outcome in pre-eclampsia in a secondary care hospital in South India. Journal of Family Medicine and Primary Care, 4 (2): 257-60.
19. **Radwan G, Adawy A (2019):** The Egyptian health map: a guide for evidence-based decision-making. Eastern Mediterranean Health Journal, 25 (5): 350-61.
20. **Eser A, Zulfıkaroglu E, Eserdag S *et al.* (2011):** Predictive value of middle cerebral artery to uterine artery pulsatility index ratio in preeclampsia. Archives of Gynecology and Obstetrics, 284: 307-11.
21. **Orabona R, Gerosa V, Gregorini M *et al.* (2015):** The prognostic role of various indices and ratios of Doppler velocimetry in patients with pre-eclampsia. Clinical and Experimental Hypertension, 37 (1): 57-62.
22. **El-Maghraby I, Allam A (2022):** Could vitamin D3 be effective in prevention of risk of preeclampsia among pregnant women? Journal of Medicine in Scientific Research, 5 (4): 455-60.
23. **Rao S, Somalwar S, Bhalerao A *et al.* (2023):** Accuracy of Spot Urine Albumin Creatinine Ratio With Respect to 24-Hour Urine Albumin for the Detection of Proteinuria in Antenatal Women With Preeclampsia: A Descriptive Study. Cureus, 15 (6): e39961. doi: 10.7759/cureus.39961.
24. **Abedi A, Shahidi H, Chataigner C *et al.* (2014):** Excavations at Kul Tepe (Hadishahr), north-western Iran, 2010: first preliminary report. Ancient Near Eastern Studies, 51: 33-165.
25. **Singla R, Gurung P, Aggarwal N *et al.* (2015):** Relationship between preeclampsia and vitamin D deficiency: a case control study. Archives of Gynecology and Obstetrics, 291: 1247-51.
26. **Richard K, Marcelline B, Jean-Pierre E *et al.* (2020):** Vitamin D Status and the Determinants of Preeclampsia in Pregnant Women in Goma (Democratic Republic of the Congo). Open Journal of Obstetrics and Gynecology, 10 (6): 820-35.
27. **AlSubai A, Baqai M, Agha H *et al.* (2023):** Vitamin D and preeclampsia: A systematic review and meta-analysis. Sage Open Medicine, 11: 20503121231212093. doi: 10.1177/20503121231212093.
28. **Youssef A, Salem H, El-Dahshan T (2022):** Maternal Serum Level of Vitamin D and the Incidence of Preeclampsia. Al-Azhar International Medical Journal, 3 (8): 88-93.
29. **Hollis B, Wagner C (2017):** New insights into the vitamin D requirements during pregnancy. Bone Research, 5 (1): 1-16.
30. **Zhao X, Fang R, Yu R *et al.* (2017):** Maternal vitamin D status in the late second trimester and the risk of severe preeclampsia in Southeastern China. Nutrients, 9 (2): 138. doi: 10.3390/nu9020138
31. **Jindal S, Sharma J, Sharma M (2019):** Association of deficiency of maternal vitamin D levels with severity of preeclampsia. Epidemiology International, 4 (3): 10-6.
32. **Hashemipour S, Esmailzadehha N, Ziaee A *et al.* (2017):** The relationship of vitamin D and calcium level with preeclampsia severity: a case-control study. Int J Pediatr., 5 (6): 5203-10.