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The relationship between vitamin D deficiency and preeclampsia

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***Abstract*---Background:** Preeclampsia remains a leading cause of maternal and perinatal morbidity and mortality. Vitamin D deficiency has been associated with several adverse pregnancy outcomes. **Aim:** The current study aimed to determine the relationship between vitamin D deficiency and preeclampsia. **Research Design:** A case control design. **Setting:** The study was conducted at the antenatal clinic at Al zahraa hospital – Al-Azhar University, Cairo, Egypt. **Sample:** Purposive sample (120 pregnant women), was divided into study group (n=60) and control group (n=60). **Tools:** Two tools for data collection. **First tool:** A structured interviewing questionnaire which used to assess demographic data, obstetrical history, family history, physical examination to diagnose preeclampsia and laboratory investigation to confirm the diagnosis. **Second tool:** Serum vitamin D levels of both groups were measured by using an Enzyme Linked Immunosorbent Assay (ELISA) technique. **Result:** Significant lower mean vitamin D of study group compared to control group with highly statistical significant difference between both groups. In addition, there were 3-fold increased odds of developing preeclampsia in pregnant women who had vitamin D deficiency (<20 ng/ml). Also, observed that when vitamin D level decreases, the severity of preeclampsia increases. **Conclusion:** There is a relationship between vitamin D deficiency and Preeclampsia, suggesting that vitamin D deficiency may be a risk factor for Preeclampsia. **Recommendations:** Conducting awareness sessions on vitamin D importance and its deficiency effect on the pregnant women to improve pregnancy outcomes.

***Keywords*---Relationship, vitamin D deficiency, preeclampsia.**

Introduction

Preeclampsia (PE) is a multisystem disease during pregnancy, characterized by the new onset of gestational hypertension and proteinuria, complicating around 3–8% of pregnancies globally and is associated with increased maternal and fetal morbidity and mortality. PE can lead to eclampsia, which can put the mother and fetus at risk of death. Maternal PE is also associated with a higher incidence of cardiovascular and kidney disease later in the child's life. ***(Hu et al., 2022).***

Vitamin D (VD) plays a role in implantation and placental function potentially due to angiogenic, immune-modulatory and anti-inflammatory effects. VDD can affect the health of both mother and fetus by increasing the production of inflammatory cytokines and stimulating the activity of T-regulating cells which results in poor bone mineralization in infants, low birth weight, and other adverse pregnancy outcomes such as PE. ***(Ni et al., 2021).***

The role of vitamin D in PE is related to the effect of VD on renin-angiotensin system (RAS). VD is a negative endocrine regulator of RAS, which suppresses renin gene expression. Therefore, serum VD levels are inversely associated with blood pressure and renin activity. PE is thought to originate in early pregnancy when the maternal immune system limits placental invasion in mothers vulnerable to cardiovascular diseases. Calcitriol can be considered a pregnancy supporting factor that could work through several mechanisms to reduce PE risk including a direct influence of calcitriol on implantation, placental invasion and angiogenesis. ***(Karpa et al., 2022).***

Maternity nurse is a core stone for reproductive health services from primary to tertiary level of prevention. Nurses interact daily with the woman with PE to offer accurate information, counseling for healthy and unhealthy lifestyle through the time of pregnancy and positively decision-making to promote and participate in successful interventions that meet the objectives of reproductive health services which promote positive health behaviors and reduce health risks through multiple roles. ***(Ramadan et al., 2021).***

Significance of the study

Preeclampsia contributes to a very high percentage of maternal and fetal mortality and morbidity rates in Egypt and worldwide. As estimated by WHO, the occurrence of PE in developing countries is estimated to be seven times higher than the developed countries. The prevalence of PE ranges between 1.8 and 16.7% in developing countries. The global incidence of PE has been estimated at 5-14% of all pregnancies while the incidence in the United States is approximately 5%. ***(Mou et al., 2021).*** The prevalence of PE in Egypt is approximately 6% - 8% of all pregnancies and can be as high as 15% in referral centers such as university hospitals. ***(Ameen et al., 2022).***

Vitamin D deficiency is identified as a global health problem and has affected approximately 1 billion people globally, especially among pregnant women and around 50% of the global population has VD insufficiency. VDD and insufficiency prevalence during pregnancy ranges from 20 % to 90 % in the United States.

(Siddiqee et al., 2021). In Egypt, the prevalence of VDD ranges between 21.3% and 60.9% while accounting for 54% among pregnant women. ***(Sherief et al., 2021).***

Aim of the study

The aim of this study was to determine the relationship between vitamin D deficiency and preeclampsia.

Research question

What is the relationship between vitamin D deficiency and preeclampsia?

Subjects and Methods

Technical Design

The technical design includes research design, setting, subjects and tools for data collection.

Research design

A case control design was utilized to conduct this study.

Setting

The study was conducted at the antenatal clinic at Al zahraa hospital which is affiliated to Al-Azhar University Hospitals.

Sampling

A purposive sample included 120 pregnant women who attended the antenatal clinic. The subjects for the study were calculated according to the equation based on ***(Lewis., 1999).***

$$n = \frac{(Z_\alpha + Z_\beta)^2 \ 2SD^2}{MD^2}$$

The subjects were divided into a study group (= 60 Preeclamptic women) and a control group (= 60 Normotensive pregnant women), which met the inclusion and exclusion criteria and agreed to participate in this study as the following:

Inclusion criteria included

1. Age range from 20 to 35 years.
2. Women with singleton, viable pregnancy morphologically normal by ultrasound.
3. Pregnant women with gestational age > 20 weeks and confirmed diagnosis of preeclampsia (study group).

4. Normotensive pregnant women at the same gestational age > 20 weeks (control group).

Exclusion criteria included

1. Women with known medical disorders, including chronic hypertension, diabetes mellitus, kidney disease, gestational diabetes, cardiovascular disorders, thyroid problems and microbial infections.
2. Pregnant women taking vitamin D supplement.
3. Free from medications that influence on bone, vitamin D or calcium metabolism e.g. Antiepileptic/theophylline drugs in the last 6 months.

Tools of data collection

Two tools were used as the following:
Tool (I): A structured interviewing questionnaire was developed by the researcher and was adapted from ***(Osman et al., 2020)*** to collect data about the subjects and was divided into 3 parts as the following:
Part one: - Consisted of five questions in Arabic language used to assess the demographic data of the pregnant women such as age, residence, level of education, occupation and economical status.
Part two: - Consisted of ten questions (most of them were open ended questions) in Arabic language used to assess the health history of the pregnant women which included data such as menstrual cycle history, obstetrical history and family history.
Part three: - Consisted of sixteen questions (most of them were open ended questions) in Arabic language used to assess the physical examination and laboratory investigation of the pregnant women which included blood pressure measurement, calculation of pre-pregnancy body mass index (BMI), signs of edema, urine analysis, complete blood count, liver and kidney function tests.
Tool (II): Measurement of serum 25(OH) vitamin D level by using an Enzyme Linked-Immunosorbent Assay (ELISA) for the quantitative measurement of serum 25-OH vitamin D and adopted from ***(Raia-Barjat et al., 2021).***

Tool Validity

The data collection tools were reviewed by a panel of three professors experienced in maternal and newborn health nursing department, two professors at Helwan University and one professor at Ain-Shams University to measure the content validity of the tools to ensure applicability, comprehensiveness, understanding and ease of implementation of the tools. Necessary modifications were made according to the panel judgments, comments and recommendations; minor modifications had been made such as rephrasing and rearrangements of some sentences to ensure the sentence clarity and content appropriateness.

Tool Reliability

The Cronbach's alpha test through SPSS computer package was used to assess the reliability of the first tool "structured interviewing questionnaire sheet" which was 0.76 and the second tool's reliability was 0.87.

Ethical consideration

An official permission to conduct the proposed study was obtained from the scientific research ethics committee in the Faculty of Nursing, Helwan University. Participation in the study was voluntary and subjects were given complete full information about the study and their role before signing the informed consent. The ethical considerations included explaining the purpose and nature of the study, stating the possibility to withdraw at any time and confidentiality of the information where it wasn't accessed by any other party without taking permission of the participants. Ethics, values, culture and beliefs were respected.

Operational Design
Preparatory phase

The Preparatory phase included reviewing of related literature and theoretical knowledge of various aspects of the study using books, articles, papers, periodicals and magazines to develop tools for data collection.

A Pilot study

A pilot study was conducted on 10% (12 pregnant women) of the entire sample to test the feasibility of the study sample, the applicability of the study tools and to estimate the required time to fill the questionnaire sheet and evaluate the suitability of setting to perform the interview. All the necessary modifications were done and pregnant women who participated in the pilot study were excluded from the main study.

Field work

- This study was carried out in Al Zahraa hospital. The process of data collection was carried out over the period of four months from the beginning of December 2021 to the end of March 2022.
- The researcher attended the antenatal clinic in Al Zahraa hospital two days per week from 9.00 am to 2.00 pm to collect data till the sample size reached the pre-determined number.
- The researcher met the physician and the nurse in the antenatal clinic and explained the aim of the study to gain cooperation. A permission was obtained from the clinic's nurse to withdraw blood samples from the pregnant women who were selected by the researcher according to pre-mentioned inclusion and exclusion criteria.
- The researcher met the pregnant women in the antenatal clinic whether before or after the obstetrician's examination. Also, the researcher kept in mind the protective measures during collecting data because of coronavirus pandemic.
- At the beginning of interview, the researcher introduced herself to the pregnant women and briefly explained the nature and purpose of the study to each pregnant woman before participation. Women were informed that the collected data would be confidential and will be only used for the

research purposes. After that, the pregnant women's oral consent was obtained.

- The researcher interviewed each woman individually in the antenatal clinic to fill tool (I) which consisted of three parts. 1st part includes questions related to the pregnant women's demographic data, 2nd part includes questions used to assess menstrual, obstetrical and family history.
- Also, the 3rd part includes questions related to the pregnant women's current pregnancy history, which contains a general and abdominal examination. Blood pressure was measured, oedema was assessed and pre-pregnancy body mass index (BMI) (kg/m^2) was calculated by the maternal self-reported weight and height. If the pre-pregnancy weight wasn't known, the weight at the first visit in the first trimester was used as a proxy. Leopold's maneuver was done to determine the gestational age. Laboratory investigation were checked such as urine analysis, complete blood count, liver and kidney function tests according to the physician's order as the routine lab tests. The pregnant women were assessed regarding the signs and symptoms of preeclampsia.
- Then, the researcher used tool (II), their questions used to assess if the pregnant women previously performed VD blood tests and the signs and symptoms of VDD, the researcher asked the nurse to withdraw three ml of a venous blood sample.
- The time taken by the researcher to complete the data in the questionnaire sheet was 20-25 minutes.
- The researcher took 2 cases: 2 controls pregnant women per day till the sample size reached pre-determined number over the period of 4 months.
- After confirming these data, the researcher divided the selected pregnant women into 2 groups:
  - Control group (n=60): This group included 60 normal pregnant women who attended the antenatal clinic.
  - Study group (n=60): This group included 60 pregnant women who meet the criteria of preeclampsia and their diagnosis was confirmed by high blood pressure and proteinuria. In Al Zahraa hospital, the physician must do boiling of urine sample to detect protein and not only depend on urine analysis.
- Regarding the signs and symptoms of preeclampsia which were assessed by the researcher, the study group were subdivided into 2 subgroups:
  - Subgroup (A) (n=40): Cases with mild preeclampsia.
  - Subgroup (B) (n=20): Cases with severe preeclampsia.
- The three ml of venous blood sample which was withdrawn by venipuncture was put in a plain vacutainer immediately at the time of admission to ensure collecting the woman's blood sample before giving any medication to women.
- The collected samples were allowed to clot for 30 minutes then, centrifuged at 3500 rpm for 10 minutes for getting the serum and putting it in an epindorf container.
- The researcher stored a container of serum in the refrigerator at 2- 8 ^{o}C could be stored for up to 48 hours without any problem then, the

researcher completed the next day of collecting data and blood samples and did the same way for the separation of serum.

- Serum samples with special codes were shipped in a dry ice box to external lab and stored at –80°C till the day of analysis.
- The serum 25(OH) D concentration was measured using an Enzyme Linked-Immunosorbent Assay (ELISA) and the results were reported as ng/ml. The IDS 25(OH) D EIA kit is an enzyme immunoassay for quantitation of 25(OH) D. The participants were classified according to vitamin D levels as the following: deficiency <20 ng/ml, insufficiency 20 and 29 ng/ml and normal ≥30 ng/ml.

Administrative Design

To carry out this study, a written approval letter was obtained from the dean of Faculty of Nursing Helwan University to Al zahraa Hospital _ Al-Azhar University for conducting the study and ensure cooperation. The approval letter was included the aim of the study and the expected outcomes. It ensured the confidentiality of the information obtained.

Statistical Design

The data was entered and analyzed by using SPSS (Statistical Package for Social Science) statistical package version 25. Graphics were done using Excel program. Quantitative data were presented by mean (X) and standard deviation (SD). It was analyzed using Independent T-test for comparison between two means and ANOVA (F) for comparison between more than two means. Qualitative data were presented in the form of frequency distribution tables, number and percentage (%). It was analyzed by Chi-square (X2) test. For the pair-wise comparison of outcomes, the Odds ratio was computed with 95 % confidence interval. The correlation between preeclampsia and serum vitamin D level was evaluated using Pearson's correlation (r). All statistical tests were evaluated as P-value (≤ 0.05) for significant result and P-value (< 0.01) for high significant result while P-value (> 0.05) for non-significant result.

Results

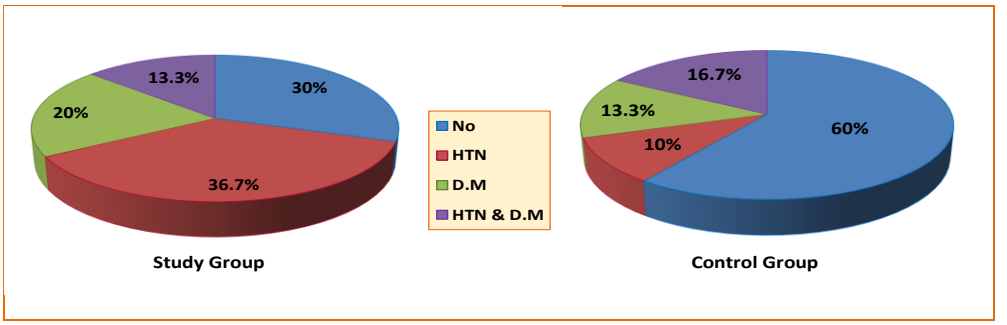
Table (1): Distribution of the studied women regarding their demographic characteristics (Study Group n = 60 & Control Group n = 60)

Demographic Characteristics	Study Group No. (60)		Control Group No. (60)		X^2	P-value
	No.	%	No.	%		
Age (years)						
• 20-25	10	16.7	14	23.3		
• 26-30	18	30.0	24	40.0	3.376	0.185
• 31-35	32	53.3	22	36.7		
Mean ± SD	30.5 ± 4.69		29 ± 3.91		T=1.900	0.060
Residence						
• Rural	40	66.7	48	80.0	2.727	0.099
• Urban	20	33.3	12	20.0		

Level of Education						
• Illiterate	34	56.7	24	40.0		
• Write and read	10	16.7	8	13.3	6.015	0.111
• Secondary school	8	13.3	10	16.7		
• University	8	13.3	18	30.0		
Occupation						
• worker	8	13.3	12	20.0	0.960	0.327
• House Wife	52	86.7	48	80.0		
Economical Status						
• Enough	24	40.0	32	53.3	2.143	0.143
• Not Enough	36	60.0	28	46.7		

(T): Independent sample t test
P-value: level of significance
P> 0.05 (Non-significant)
***P ≤ 0.05 (significant)**
****P < 0.01(Highly significant)**

Table (1): Reveals that there was no statistical significant difference between both groups' demographic characteristics (P> 0.05) where more than half (53.3%) of the study group aged between (31-35) years compared to more than one-third (36.7%) of the control group with slightly higher mean age (30.5 ± 4.69) of the study group in comparison to (29 ± 3.91) of the control group. In addition, two-thirds (66.7%) and the majority (80%) of both the study and control group respectively, live in rural area. Also, more than half (56.7%) of the study group and less than half (40%) of the control group were illiterate. Meanwhile, the majority (86.7% and 80%) of the study and control group respectively, were housewives. Also, less than two-thirds (60%) of the study group hadn't enough income compared to nearly half (46.7%) of the control group.



HTN: Hypertension **D.M: Diabetes Mellitus**

Figure (1): Distribution of the studied women according to their family history of chronic diseases (Study Group n = 60 & Control Group n = 60).

Figure (1): Shows that more than one-third (36.7%) of the study group had family history of HTN compared to one-tenth (10%) of the control group.

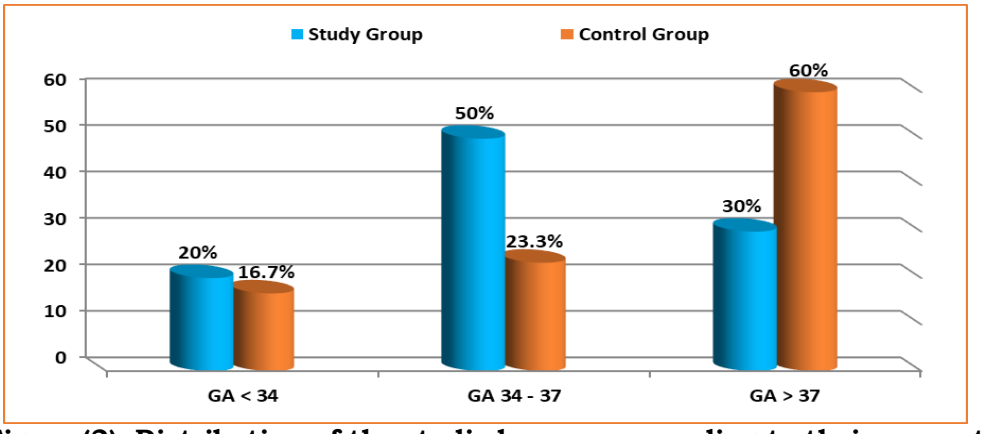


Figure (2): Distribution of the studied women according to their current gestational age (weeks) (Study Group n = 60 & Control Group n = 60).

Figure (2): Shows that half (50%) of the study group had gestational age between 34 to 37 weeks compared to less than quarter (23.3%) of the control group conversely, less than two-thirds (60%) of the control group had gestational age more than 37weeks compared to almost one-third (30%) of the study group.

Table (2): Distribution of the studied women regarding their measurement of serum 25(OH) vitamin D level (Study Group n = 60 & Control Group n = 60)

Serum vitamin D (ng/ml) in current pregnancy	Study Group No. (60)		Control Group No. (60)		X^2	P-value	Odds ratio (95 % CI)
	No.	%	No.	%			
• Deficient < 20 ng/ml	28	46.7	12	20.0			
• Insufficient 20-29 ng/ml	20	33.3	24	40.0	10.764	0.005**	
• Normal ≥ 30 ng/ml	12	20.0	24	40.0			3(1.18 – 6.03)
Mean ± SD	19.85 ± 11.07		28.72 ± 7.59		**T= -5.12**	<0.001**	

CI: confidence interval
N.B: All of the studied women hadn't performed vitamin D blood test before.
N.B: Odds ratio is done between low level vitamin D < 30 ng/ml & Normal vitamin D ≥ 30 ng/ml
N.B: Low level vitamin D < 30 ng/ml include {1- Deficient < 20 ng/ml, 2- Insufficient 20-29 ng/ml}

Table (2): Reveals that nearly half (46.7%) of the study group had deficient vitamin D less than 20 ng/ml in current pregnancy compared to less than quarter (20%) of the control group with significantly lower mean vitamin D (19.85 ± 11.07) of the study group in comparison to (28.72 ± 7.59) of the control group with highly statistical significant difference between the two groups (p <0.01). In addition, there were 3-fold increased odds of developing preeclampsia in pregnant women who had vitamin D deficiency (<20 ng/ml).

Table (3): Comparison of serum of 25(OH) vitamin D between normal pregnancy and the severity of preeclampsia

serum vitamin D level	Control No. (60)	Mild No. (40)	Severe No. (20)	Test of significance	P-value	Sig.
Mean ± SD	28.72 ±7.59	24.09 ±10.74	11.37 ±5.49	**F=** 31.206	**P_1=** <0.001**	HS
• Deficient < 20 ng/ml	12 (20%)	12 (30%)	16 (80%)			
• Insufficient 20-29 ng/ml	24 (40%)	16 (40%)	4 (20%)	**X^2=** 14.743	**P_2=** 0.001**	HS
• Normal ≥ 30 ng/ml	24 (40%)	12 (30%)	0 (0%)			

F= ANOVA Test analysis of variance
X^2 = Chi-Square Test
P_1= for comparison between control, mild, severe groups
P_2= for comparison between mild and severe groups

Table (3): Highlights that there was a high statistically significant difference in serum level of vitamin D between mild, severe preeclampsia and control groups (P <0.01). Serum vitamin D level was significantly lower in cases of severe preeclampsia than mild preeclampsia and control groups. In addition, there was a high statistically significant relation between serum vitamin D and both degree of preeclampsia (P <0.01) where the majority of severe preeclampsia cases (80%) had vitamin D deficient less than 20 ng/ml compared to less than one third (30%) of mild preeclampsia cases. On the other hand, no one case of severe preeclampsia had normal vitamin D ≥ 30 ng/ml compared to less than one-third (30%) of mild preeclampsia cases.

Table (4): Correlation between serum vitamin D and preeclampsia of the study group (N = 60)

Preeclampsia	Serum Vitamin D	
	Pearson Correlation	P-value
SBP	-0.40	0.005**
DBP	-0.50	0.<001**
Oedema	-0.20	0.118
Proteinuria	-0.54	0.<001**

Table (4): shows that there were a highly significant strong negative correlation between serum vitamin D and (systolic blood pressure, diastolic blood pressure and proteinuria) as when the vitamin D level decreases, the severity of preeclampsia increases (P <0.01).

Discussion

According to the women's demographic characteristics, in relation to age categories of the studied women, the present study finding revealed that women with preeclampsia were slightly elder than normotensive pregnant women (30.5 ± 4.69 vs. 29 ± 3.91 years old) but with no statistical significant difference between the two groups. This finding was in agreement with **(Benachi et al., 2020)** who studied the relationship between vitamin D status in pregnancy and the risk for

preeclampsia: A nested case-control study in France and reported that the difference in maternal age between cases and control groups wasn't statistically significant (32.2 ± 5.9 vs. 31.7 ± 5.0 years old). This finding was disagree with **(Tammo and Yildiz., 2022)** who studied the vitamin D deficiency and its clinical results in preeclamptic mothers and their babies in Turkey and reported that maternal age was statistically significant higher in preeclamptic mothers compared to healthy mothers (27.7±5.4 vs. 25.2±4.9 years old).

Concerning residence of the studied women, the current study revealed that two-thirds and the majority of both the study and control group respectively, live in a rural area with no statistically significant difference between both groups. This result was supported by **(Karpa et al., 2022)** who compared serum vitamin D status in preeclamptic and non-preeclamptic pregnant women in labour: A tertiary care centre study of Northern India and reported that the majority of both preeclampsia group and healthy normotensive group belonged to a rural area and the difference remained non-significant. This result was contradicted with **(Sharma et al., 2020)** who studied the prevalence of vitamin D deficiency in the patients with hypertensive disorders of pregnancy and normal pregnant women in India and found that more than half of both cases and controls groups were urban residents but with no statistically significant difference.

Regarding level of education of the studied women, the present study revealed that more than half of the study group and less than half of the control group were illiterate and the difference wasn't statistically significant. This finding was similar to **(Sharma et al., 2020)** who reported that nearly two-thirds of both case and control group were illiterate with no statistical significant difference between both groups. This finding was contrary to a study conducted by **(Shahid et al., 2020)** who studied the association of vitamin D levels with preeclampsia in Pakistan and found that more than half constituted the illiterate study subjects while more than one-third constituted of secondary control subjects with highly statistical significant differences.

As regards to the occupation of the studied women, the current study revealed that the majority of the study and control group were housewives with no statistically significant difference between both groups. This finding was in the same line with **(Das et al., 2021)** who evaluated the association between maternal vitamin D deficiency and preeclampsia among Indian gravidas and stated that the difference between both groups was non-significant where the majority of the case and control groups were housewives. This was contradicted with **(Wei et al., 2021)** who studied the maternal vitamin D, oxidative stress and preeclampsia and reported that the majority of both case and control groups were employed but with no statistical difference.

Concerning the economic status of the studied women, the present study revealed that less than two-thirds of the study group hadn't enough income while more than half of the control group had enough income, but with no statistical significant difference. on the contrary, a study conducted by **(Serrano et al., 2018)** who studied the vitamin D deficiency and preeclampsia in Colombia: A case-control study and reported that the majority of both mothers with

preeclampsia and healthy normotensive mothers belonged to low socioeconomic status and the difference between both groups was statistically significant.

As regards to the family history of chronic diseases of the studied women, the present study revealed that more than one-third of the study group had family history of HTN compared to one-tenth of the control group with highly statistical significant difference between both groups. This finding was consistent with **(Mareg et al., 2020)** who studied the determinants of preeclampsia among pregnant mothers attending antenatal care and delivery service in Gedeo Zone, Southern Ethiopia: A case control study and indicated that nearly one-third of cases had a family history of HTN compared to one-fifth of controls and the difference was statistically significant.

On the contrary, a study conducted by **(Fondjo et al., 2021)** who reported that nearly one-tenth of both preeclamptic and normotensive women had a family history of HTN with no statistically significant difference. From the researcher's point of view, the similarity of this finding might be due to a similar design conducted on the population recruited from facilities and this was supported by biophysical evidence that preeclampsia was a highly heritable familial disease.

In relation to the gestational age of the studied women, the present study finding revealed that the mean gestational age was slightly lower in preeclampsia group when compared to control group (35.97 ± 2.54 and 36.05 ± 5.24 weeks respectively) where half of the study group had gestational age between 32 to 37 weeks while less than two-thirds of the control group had gestational age more than 37 weeks and the difference was highly statistical significance. This finding was supported by **(Seifer et al., 2022)** who studied the preeclampsia at delivery is associated with lower serum vitamin D and higher antiangiogenic factors: A case control study in the United States of America and reported that women with preeclampsia had earlier gestational age at delivery (37 ± 2.6 vs. 38.4 ± 2.3 weeks) than the women in the control group with highly statistically significant difference between both groups.

These results were contradicted with **(Richard et al., 2020)** who performed a case-control study constitute of 95 preeclamptic and 95 control group and indicated that there was no statistically significant difference between the preeclamptic group and control group regarding the gestational age as (34.1 ± 4.4 vs. 34.5 ± 3.4 weeks). From the researcher's point of view, this similarity in results might be related to induction of preeclamptic mothers in the earlier gestation than normotensive mothers due to fear of developing the severity of preeclampsia that has a worsening effect on both mother and fetus.

As regards to serum vitamin D level of the studied women, the present study finding revealed that women with preeclampsia had significantly lower mean vitamin D in comparison to normotensive women (19.85 ± 11.07 vs. 28.72 ± 7.59 ng/ml) with highly statistically significant difference between the two groups where nearly half of the study group had deficient vitamin D less than 20 ng/ml compared to less than a quarter of the control group and also, stated that there were 3-fold increased odds of developing preeclampsia in pregnant women who had vitamin D deficiency (<20 ng/ml) which clearly showed a strong significant

association of preeclampsia with vitamin D deficiency. In other words, vitamin D deficiency could be an independent risk factor for preeclampsia.

This finding was in agreement with **(Karpa et al., 2022)** who performed a case-control study and measured serum vitamin D levels for 100 case and 100 control group and revealed that the mean vitamin D level was significantly lower in preeclamptic group compared to healthy normotensive group (8.87 ± 4.66 vs. 25.83 ± 7.07) where the majority of preeclamptic group had significantly more vitamin D deficiency (<20 ng/ml) in comparison to a quarter of the healthy normotensive women with highly statistically significant difference in both groups.

This finding was contradicted with **(Masnavi et al., 2022)** who studied the relationship between vitamin D and preeclampsia: A descriptive comparative study (180 case vs. 200 control) in Iran and indicated that there was no statistically significant difference between the serum levels of the vitamin D in women with preeclampsia and healthy pregnant women and the serum levels of vitamin D had a similar distribution in the case and control groups.

From the researcher's point of view, the reason behind these conflicting results may be due to issues with the study design, methodology, lack of adjustment of confounders and methods of measuring vitamin D levels. In addition, other factors might justify the differences in the results of studies conducted in this regard, including prevention of using vitamin D supplements, different eating habits, ethnicity, smoking and seasonal changes. Hence, a more comprehensive assessment of the role of vitamin D in the prevention and treatment of hypertensive disorders is needed and may be recommended performing clinical trials to investigate this issue further.

As regards to studying the relation of 25(OH) vitamin D between normal pregnancy and the severity of preeclampsia, the present study revealed that there was a highly statistically significant difference in serum level of vitamin D between mild, severe preeclampsia and control groups where serum vitamin D level was significantly lower in cases of severe preeclampsia than mild preeclampsia and control groups.

This result was in accordance with **(Jindal et al., 2019)** who studied the association of deficiency of maternal vitamin D levels with severity of preeclampsia in Northern India and reported that the mean serum vitamin D level was found to be lower in the preeclampsia with severe features as compared to preeclampsia without severe features and normotensive patients in addition to, this difference was statistically significant. From the researcher's point of view, severe preeclampsia has been more closely linked to vitamin D deficiency which required more attention to it.

The current study revealed that there was a highly statistically significant relation between serum vitamin D and both degrees of preeclampsia where the majority of severe preeclampsia cases had vitamin D deficiency less than 20 ng/ml compared to less than one-third of mild preeclampsia cases. On the other hand, no one case

of severe preeclampsia had normal vitamin D ≥ 30 ng/ml compared to less than one-third of mild preeclampsia cases.

This result was consistent with **(Alsaeed et al., 2020)** who reported that all cases of severe preeclampsia had vitamin D deficient less than 30 ng/ml in comparison to nearly two-thirds of mild preeclampsia cases with highly statistically significant relationship between 25(OH) vitamin D and severity of preeclampsia. This result was inconsistent with **(Ali et al., 2018)** who studied the ratio between low serum maternal 25-Hydroxy vitamin D concentration and the risk of preeclampsia in Egypt and indicated that there was no statistically significant relation between vitamin D and severity of preeclampsia. In the researcher's opinion, these differences in results needed additional data to approve this affirmation.

According to the correlation between serum vitamin D and preeclampsia, the present study revealed that there was a highly negative significant strong correlation between serum vitamin D and (systolic blood pressure, diastolic blood pressure and proteinuria) as when the vitamin D level decreases, the severity of preeclampsia increases. This result was matched with **(Gupta and Patel., 2021)** who studied the evaluation of vitamin D levels in pregnancy induced hypertension in India and stated that there was a significant strong negative correlation between systolic and diastolic blood pressure and vitamin D levels in hypertensive pregnant females.

This result disagreed with **(Ali et al., 2018)** who reported that there was no statistically significant correlation between systolic and diastolic blood pressure and vitamin D levels. From the researcher's point of view, this may be proven that vitamin D deficiency is a risk factor for severe preeclampsia and has a role in developing PE that requires more attention from the health care providers.

Conclusion

In light of the current study, there is a relationship between vitamin D deficiency and preeclampsia, suggesting that vitamin D deficiency may be a risk factor for preeclampsia and a helpful tool for early detection of preeclampsia and its severity. So, the results of the current study answered the research question.

Recommendation

Based on the results of this study, the following recommendations were proposed:

- Early measurement of vitamin D in all pregnant women may be a screening tool for early detection of preeclampsia.
- Conducting awareness sessions on vitamin D importance and its deficiency effect on the pregnant women to improve pregnancy outcomes.
- Development of educational program for antenatal nurses about vitamin D and prevention of preeclampsia.

Further studies

- Further studies are needed to document the role of vitamin D supplementation in the prevention of preeclampsia either alone or in combination with calcium.
- Establishing and prescription of vitamin D supplementation as an intervention strategy for all pregnant women in antenatal care protocol.
- Further studies regarding the relationship between vitamin D deficiency and preeclampsia on a large sample from different geographic areas in Egypt in order to generalize the results and improve the power of finding.

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