Maternal Serum Level of Vitamin D and the Incidence of Preeclampsia

Abdelsalam Youssef
Obstetrics and Gynecology department, Faculty of Medicine, Al-Azhar University, Egypt,
abdo_peace@hotmail.com

Hossam Al-Din Salem
Obstetrics and Gynecology department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt,
hoassameldinsalem.2062@azhar.edu.eg

abdelsattar farhan
Obstetrics and Gynecology department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt,
drabdsattar@gmail.com

Tarek El-Dahshan
Department of clinical pathology, Faculty of medicine, Al-azhar University, Cairo, Egypt,
drtarekakareim@gmail.com

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Maternal Serum Level of Vitamin D and the Incidence of Preeclampsia

Abdelsalam Mohamed Abdelsalam Youssef 1* M.B.B.Ch, Hosam Al-Din Hussein Kamel Salem 2 MD, Abdelsattar Mohamed Ebrahim Farhan 2 MD and, Tarek Abd Elkareim Eldahshan 3MD.

*Corresponding Author:
Abdelsalam Mohamed Abdelsalam Youssef
Abd_peace@hotmail.com

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1Resident of Obstetrics and Gynecology Department, El Galaa Teaching Hospital, Egypt.
2Obstetrics and Gynecology Department, Faculty of Medicine, Al-Azhar University Cairo, Egypt.
3Clinical Pathology Department, Faculty of Medicine, Al-Azhar University Cairo, Egypt.

ABSTRACT

Background: After 20 weeks of pregnancy, preeclampsia is a state marked by hypertension and proteinuria, affecting 2-8% pregnancy worldwide and is the major factor of maternal and foetal morbidity and death.

Aim of the work: To discover whether preeclamptic women had greater vitamin D deficiency than normotensive pregnant women.

Patients and methods: This research involved 90 pregnant women. Obstetrics and Gynecology and Clinical Pathology Departments of Bab-Elshaeria University Hospital, Faculty of Medicine, Al-Azhar University, and Galaa Teaching Hospital collaborated in the study.

Results: Between the two groups, there was no statistically substantial variance in vitamin content. D in PET group and normal group with p-value = 0.073; also the table shows that the percentage of patients with The normal group had a higher optimal level (33.3%) than the PET group (15.6%), with a significant difference between the two groups.

Conclusion: Vitamin D deficiency and its mechanism of development is correlated to the slowly progression of preeclampsia and needs to be subjected to more research. In terms of vitamin D deficiency, there was no statistically substantial variance between the normal and PET groups.

Keywords: Preeclampsia; proteinuria; pregnancy; vitamin D deficiency.

INTRODUCTION

Preeclampsia is a pregnancy-related disease characterised by hypertension and proteinuria after 20 weeks of pregnancy that affects 2-8% of all pregnancies globally and is the leading factor of maternal and foetal morbidity and death. It is a prominent cause of maternal death in affluent countries, accounting for up to 16% of all maternal deaths. 1 It’s a multisystem condition characterized by high blood pressure before or after 20 weeks of pregnancy, proteinuria of more than or equal to 300 mg/24 hours, or systolic blood pressure of more than 30 mmHg, or diastolic blood pressure of more than 15 mmHg. 2 Vitamin D deficiency has been linked to the development of preeclampsia, according to Wei et al. 3 Preeclampsia, gestational diabetes mellitus, and intrauterine growth restriction are all conditions that can occur during pregnancy. are three of the most common causes of pre-eclampsia, and perterm birth have all been linked to vitamin D deficiency during pregnancy. 4 Branno et al., 5 have discovered a link between vitamin D intake and other pregnancy outcomes. Vitamin D insufficiency in pregnant women has been frequently observed in a number of nations. 6 Maternal vitamin D may be influenced by several factors: diet, supplementation, sun exposure, skin pigmentation, and genetics. 7

Considering the abnormal trophoblastic invasion Liu et al. 8 by increasing inflammation, vitamin D deficiency is likely to contribute to the development of preeclampsia. The aim of the research was to discover out if vitamin D deficiency is more prevalent in preeclamptic women compared to normotensive pregnant women.

This study aimed to see if vitamin D insufficiency is more common in preeclamptic women than in normotensive pregnant women.

PATIENTS AND METHODS

This research involved 90 pregnant women. Obstetrics and Gynecology and Clinical Pathology Departments of Bab-Elshaeria University Hospital, Faculty of Medicine, Al-Azhar University, and Galaa Teaching Hospital collaborated in the study.
Preeclamptic and non-preeclamptic patients were separated into two groups, each with 45 cases.

Inclusion criteria (Delimitations): Nulliparous women, singleton pregnancy, aged from 18-40 and gestational age from 32-40 weeks.

Exclusion criteria (Limitations): Women with rheumatoid arthritis, parathyroid disease, renal or hepatic malfunction, metabolic bone disease, diabetes, impaired absorption, and systemic lupus erythematosus, as well as women who have had multiple pregnancies, have a history of taking medications that affect bone, vitamin D, or calcium metabolism in the previous six months, such as antiepileptics, theophylline, or antitubercular drugs.

Preeclamptic group (patient’s group) based on: Blood pressure: After 20 weeks of pregnancy, two blood pressure readings of higher than or equal to 140 mmHg systolic and greater than or equal to 90 mmHg diastolic must be taken four hours apart at least (Roberts et al., 2013). Proteinuria is defined as a 24-hour protein excretion of 300 mg or greater.

Non preeclamptic group (control group): All of them are hypertensive, with a blood pressure of less than 140/90 and no proteinuria.

Consent: A written informed consents were taken from all subjects (patients & controls) of two groups after full demonstration of steps and significance of this study.

Methods: All cases in the previously mentioned two groups were subjected to:

History: Full history was taken from all subjects (patients & controls) of two groups.

Examination: General examination: Vital signs: Pulse: counted in one complete minute, blood pressure: measured using Mercury sphygmomanometer, temperature, yellowish discoloration of the sclera (in day light) and Lower limb edema (by pressure at the ankle and lower tibia against bone).

Abdominal examination: Inspection for shape, pigmentation and scars, fundal level, fundal grip and pelvic grip. Obstetric ultrasound examination: Trans-abdominally to certify: Gestational age, number of fetuses, amniotic fluid index is a measurement of the amount of amniotic fluid (by the four quadrant technique), IUGR (measured by biparietal diameter, femur length, and head circumference/absentia circumference ratio), and defined as birth weight less than the 10th centile for gestation and placental location.

Laboratory investigations: Urine analysis was done to detect proteinuria by dipstick screening test, Some of the tests available are CBC. All of these tests, as well as liver and kidney function testing, are indicated.... and both liver kidney functions are performed on automated response 920 analyzer.

Estimation of Vitamin D in maternal blood: Vitamin D assay: enzyme immunoassay test kit was used to detect and screen: All samples for 25(OH) Vitamin D total in human serum and plasma by using special antibodies to capture both 25 hydroxy-vitamin D3 and D2. This test is used to detect the total 25(OH) vitamin D concentration in human blood and plasma, which can help with the diagnosis of vitamin D deficiency.

Status of 25(OH) vitamin D and expected values: In recent literature, the following classification ranges for 25(OH) vitamin D statuses have been proposed.

Statistical Analysis: The data was collected, edited, coded, and input into IBM SPSS software version 23. (Statistical Package for Social Science). Non-parametric data was represented by the median with inter-quartile range, whereas quantitative data with a parametric distribution was represented by the median, standard deviations, and ranges (IQR). Qualitative features were also represented using numbers and percentages.

### RESULTS

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Normal group</th>
<th>PET group</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median ± SD</td>
<td>No. = 45</td>
<td>No. = 45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranges</td>
<td>27.04 ± 4.84</td>
<td>29.51 ± 5.96</td>
<td>-2.155</td>
<td>0.034</td>
<td>S</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>27 (23 – 30)</td>
<td>28 (26 – 33)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-values 0.01: highly significant (HS)

*PET preeclampsia pregnant women.

**Table 1:** In terms of maternal age, the normal and PET groups are comparable: A statistically significant variance was discovered. Among normal group and PET group regarding to age with p-value = 0.034. Table (1)

<table>
<thead>
<tr>
<th>Platelet count (x 10^9/L)</th>
<th>Normal group</th>
<th>PET group</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median ± SD</td>
<td>No. = 45</td>
<td>No. = 45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranges</td>
<td>225.84 ± 62.30</td>
<td>194.24 ± 73.87</td>
<td>2.194*</td>
<td>0.031</td>
<td>S</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>134 – 370</td>
<td>63 – 302</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>205 (180 – 280)</td>
<td>200 (180 – 260)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-values 0.01: highly significant (HS)

*PET preeclampsia pregnant women.

**Table 2:** In terms of platelet count, there is a comparison between the normal and PET groups.

In terms of platelets, there was a statistically significant variance among the normal and PET groups. count with p-value = 0.031. Table (2)
There was no statistically significant variance in the level of vitamin D in PET group and normal group, where the percentage of patients with deficient vitamin D level with p-value = 0.073; also the table shows that the percentage of patients with optimum level was found to be greater in the normal group (33.3%) than in the PET group (15.6%), with a substantial variance between the two groups with p-value < 0.05. The percentage of patients with insufficiency vitamin D level was found to be higher in the PET group (42.2%) than in the normal group (20.0%), with a p-value = 0.05. There was no statistically significant variance in the vitamin D level in the PET group and normal group in terms of vitamin D deficiency percentage of patients with deficient vitamin D level with p-value = 0.671. Table (3)

### Table 3: A comparison of vitamin D levels and the proportion of patients with normal and abnormal (deficient) levels was made between the normal group and the PET group.

### Table 4: Correlation between vitamin D levels and the other variables investigated

Apart from the substantial negative association between vitamin D level and AST level, there was no statistically substantial correlation between vitamin D level and the other examined parameters among the studied cases. Table (4)

### Table 5: Relation of vitamin D level with mode of delivery, symptomatic findings and urine analysis (dipstick)

There was no substantial relationship found between vitamin D level and mode of delivery, visual, headache, epigastric pain and urine analysis with p-value = 0.264, 0.748, 0.226, 0.548 and 0.424 respectively. Table (5)

### Table 6: Comparison between patients with deficient, insufficient and optimum vitamin D level regarding demographic data and characteristics

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)

*Chi-square test; •: Independent t-test

---

<table>
<thead>
<tr>
<th>Vitamin. D</th>
<th>Normal group</th>
<th>PET group</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. = 45</td>
<td>No. = 45</td>
<td>19.84</td>
<td>0.05</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamin D Deficient (Abnormal) (&lt; 20 ng/ml)</th>
<th>Median ± SD</th>
<th>Range</th>
<th>Median (IQR)</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal vitamin D level (&gt; 20 ng/ml)</td>
<td>Normal group</td>
<td>PET group</td>
<td>3.850</td>
<td>0.05</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4: Correlation between vitamin D levels and the other variables investigated

Apart from the substantial negative association between vitamin D level and AST level, there was no statistically substantial correlation between vitamin D level and the other examined parameters among the studied cases. Table (4)

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<table>
<thead>
<tr>
<th>Vitamin D</th>
<th>Normal group</th>
<th>PET group</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. = 45</td>
<td>No. = 45</td>
<td>19.84</td>
<td>0.05</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamin D Deficient (Abnormal) (&lt; 20 ng/ml)</th>
<th>Median ± SD</th>
<th>Range</th>
<th>Median (IQR)</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal vitamin D level (&gt; 20 ng/ml)</td>
<td>Normal group</td>
<td>PET group</td>
<td>3.850</td>
<td>0.05</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

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P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)

*Chi-square test; •: Independent t-test
There was no substantial relationship found between vitamin D level and demographic data of the studied patients. Table (6)

<table>
<thead>
<tr>
<th></th>
<th>Deficiency vitamin D &lt;20</th>
<th>insufficiency vitamin D 21-30</th>
<th>Optimum vitamin D level &gt;30 ng/ml</th>
<th>Test value</th>
<th>P-value</th>
<th>Si. g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood</td>
<td>Median ± SD</td>
<td>153.16 ± 10.57</td>
<td>156.84 ± 12.50</td>
<td>148.57 ± 13.45</td>
<td>1.327*</td>
<td>0.276</td>
</tr>
<tr>
<td>pressure</td>
<td>Range</td>
<td>140 – 180</td>
<td>140 – 180</td>
<td>130 – 170</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood</td>
<td>Median ± SD</td>
<td>101.58 ± 8.34</td>
<td>101.05 ± 8.09</td>
<td>98.57 ± 10.69</td>
<td>0.318*</td>
<td>0.730</td>
</tr>
<tr>
<td>pressure</td>
<td>Range</td>
<td>90 – 120</td>
<td>90 – 120</td>
<td>90 – 110</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Platelet count</td>
<td>Median ± SD</td>
<td>205.16 ± 63.67</td>
<td>183.00 ± 64.01</td>
<td>195.14 ± 76.83</td>
<td>0.417*</td>
<td>0.662</td>
</tr>
<tr>
<td>AST</td>
<td>Median (IQR)</td>
<td>30 (20-40)</td>
<td>24 (14-40)</td>
<td>21 (15-22)</td>
<td>3.109*</td>
<td>0.211</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>10 – 65</td>
<td>10 – 98</td>
<td>10 – 30</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>Median (IQR)</td>
<td>13 (11-21)</td>
<td>12 (11-18)</td>
<td>11 (9-15)</td>
<td>1.720*</td>
<td>0.423</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>7 – 45</td>
<td>6 – 83</td>
<td>6 – 15</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>Mean ± SD</td>
<td>0.96 ± 0.16</td>
<td>1.02 ± 0.16</td>
<td>0.94 ± 0.08</td>
<td>1.116*</td>
<td>0.337</td>
</tr>
<tr>
<td>level</td>
<td>Range</td>
<td>0.7 – 1.3</td>
<td>0.9 – 1.4</td>
<td>0.9 – 1.1</td>
<td>S</td>
<td></td>
</tr>
</tbody>
</table>

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)
•: Independent t-test; †: Mann Whitney test

Table 7: Comparison between patients with deficient, insufficient and optimum vitamin D level regarding blood pressure, liver function and kidney function.

There was no statistically substantial relation found between vitamin D level and blood pressure, liver function and kidney function of the studied patients. Table (7)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Deficiency vitamin D &lt; 20</th>
<th>insufficiency vitamin D 21-30</th>
<th>Optimum vitamin D level &gt; 30</th>
<th>Test value</th>
<th>P-value</th>
<th>Si. g.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>1250 (450 – 1825)</td>
<td>624 (425 – 3100)</td>
<td>525 (450 – 555)</td>
<td>1.115*</td>
<td>0.573</td>
</tr>
<tr>
<td>Headache</td>
<td>Range</td>
<td>409 – 4000</td>
<td>409 – 4000</td>
<td>409 – 4000</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>Median (IQR)</td>
<td>11 (57.9%)</td>
<td>13 (68.4%)</td>
<td>2 (28.6%)</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>5 (1.5%)</td>
<td>1 (5.3%)</td>
<td>2 (28.6%)</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>proteinuria gm/24 H</td>
<td>+</td>
<td>12 (63.2%)</td>
<td>9 (47.4%)</td>
<td>5 (71.4%)</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Urine analysis (dipstick)</td>
<td>++</td>
<td>6 (31.6%)</td>
<td>9 (47.4%)</td>
<td>0 (0.0%)</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Fetal weight</td>
<td>Median ± SD</td>
<td>2.62 ± 0.50</td>
<td>2.65 ± 0.44</td>
<td>2.87 ± 0.53</td>
<td>0.739*</td>
<td>0.483</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>1.8 – 3.5</td>
<td>1.7 – 3.5</td>
<td>1.7 – 3.2</td>
<td>S</td>
<td></td>
</tr>
</tbody>
</table>

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)
*:Chi-square test; •: Independent t-test; †: Mann Whitney test

Table 8: Comparison between patients with deficient, insufficient and optimum vitamin D level regarding symptoms, proteinuria, urine analysis and fetal weight.

There was no statistically substantial correlation found between vitamin D level and symptoms, proteinuria, urine analysis and fetal weight. Table (8)

**DISCUSSION**

The aim of our study was to find out if vitamin D deficiency is more prevalent in preeclampsia women compared to normotensive pregnant women, in addition to confirming if there is a relation between serum maternal level of vitamin D and development of preeclampsia. This study was held in Galaa Teaching Hospital and Bab El Shaareya University Hospital in pararrel.

Measurement of Vitamin D status is determined by its circulating form, 25-hydroxyvitamin D which is considered optimum when level above 30ng/mL. A level between 21 and 30 ng/mL is considered insufficient and deficient if less than 20 ng/mL. 

In this study, measurement of serum vitamin D in normotensive pregnant patients was compared to preeclampsia group and were found to be with no significant statistically difference between both groups with calculated means ± SD were 22.21 ± 9.35, 18.49 ± 8.43. The calculated p value was 0.050, despite that the level of vitamin D was less in preeclampsia group cases than normotensive cases.

Several studies have examined such association and relation between maternal serum vitamin D in normotensive pregnant patients in relation to preeclampsia group but the results are fluctuating between agreement and confliction. In agreement to our results; Powe et al. USA 10 which is a nested case control study recruited on 39 preeclampsic women and 131 normotensive pregnant women i.e.: there was no substantial correlation between vitamin D and Preeclampsia is the progression of pre-eclampsia. Vitamin D in the bloodstream is almost fully attached to vitamin D binding protein, which doubles during pregnancy. Total vitamin D levels were similar in cases and controls (P=0.435). We
should respect that we select our cases without measurement of vitamin D binding receptors, and increase in vitamin D binding protein may be an explanation to our results. Also, Ringerose et al. A case-control study was done on preeclamptic women (n=78) and normotensive pregnant women (n=109). Serum vitamin D was measured in all participants. Both cases and controls were more likely to be vitamin D deficient with (p=0.002). On the same hand, Yu et al. UK did prospective study as case control study on 48 pregnant women 11 pregnant women was later diagnosed as preeclamptic women (p = 0.22). In agreement with our results; Fernandez- Alonzo et al. Spain the relation between vitamin D and preeclampsia was no significant with p value = 0.91 so. The third-trimester vitamin D levels were measured in a subset of women (n=148).

In contrast to our results; Abedi et al., Iran There were 59 pre-eclamptic pregnant women and 59 healthy pregnant women in this case-control research. Pre-eclampsia shows a statistically significant link to vitamin D deficiency. Iranian women's serum vitamin D levels appear to be low as a result of their unique lifestyle. And the same case control study was done at (2015) in Iran by Mohaghegh et al. with (p = 0.001), i.e: there was significant between vitamin D and preeclampsia. He recruited 41 preeclamptic and 50 normotensive healthy women. Although Iran has the same lifestyle as ours with the same diet intake, so we can need more studies on larger number of cases to Determine whether there is a link between vitamin D and preeclampsia.Pashapour et al. In Urmia, Iran, researchers conducted a case-control study on Preeclamptic women (n = 80) had lower total vitamin D levels than healthy control women, according to a study of 80 preeclamptic women and 80 healthy pregnant women. According to these findings, there was a statistically substantial link between vitamin D insufficiency and preeclampsia. However, this result is against our study, but it may be due to using chemiluminescence for measuring viDT level.

And against our study; Benachi et al. In France, 83 cases of preeclampsia were matched with 319 controls in a nested case-control study.

High vitamin D levels throughout the third trimester were linked to a lower risk of preeclampsia (p = 0.008).

We should respect that difference in society, life style and diet which are the main risk factors that are responsible for the great effect of variation of results from one study to another.

**CONCLUSION**

Vitamin D deficiency and its mechanism of development is correlated to the slowly progression of preeclampsia and needs to be subjected to more research. In terms of vitamin D deficiency, the variance between the normal and PET groups was not statistically significant.

Conflict of interest : none

**REFERENCES**


