Original article:

Comparison of maternal serum vitamin D levels in cases with preeclampsia, eclampsia and healthy pregnant women in Churu District

Dr Gogaram¹#, Dr Hanuman Prasad²*, Dr Sarad Misha¹

#: First author; * : Corresponding author
1: Principal specialist, Obs &Gyn, DBH Churu; 2: Associate professor, Churu medical College.

ABSTRACT

Background: Vitamin D deficiency has been associated with various poor maternal and fetal outcomes and is proposed to be important in the pathogenesis of preeclampsia (PE). The question of interaction between PE and Vitamin D status in pregnant women of Churu district were not done earlier.

Aims: The aim of this study is to assess and compare maternal serum vitamin D levels in eclampsia, preeclampsia and healthy pregnant women and the role of vitamin D deficiency in the etiology of preeclampsia (PE).

Methods: This study was a cross section comparative study carried out on the pregnant women in the third trimester admitted for termination or in labour. 50 pregnant females with either pre-eclampsia or eclampsia were compared with equal number of normotensive pregnant females for serum vitamin D. They were followed up until delivery.

Results: Most pregnant females had vitamin D deficiency pointing towards universal prevalence. Only 10% had suboptimal to optimal vitamin D level while 90% had vitamin deficiency. The hypertensive group had lower mean serum vitamin D level (9.06±5.20 ng/ml) as compared to normotensive group (13.67±7.24 ng/ml). Neonatal outcome was poorer in the hypertensive group.

Conclusion: Vitamin D levels were lower in both preeclamptic and eclamptic patients compared to healthy normotensive pregnant women (P<0.001). Vitamin D supplementation is considered to decrease the risk of both preeclampsia and eclampsia in the patient population at risk for vitamin D deficiency.

Keywords: Preeclampsia, 25-hydroxy vitamin D, Vitamin D, eclampsia, hypertension.

INTRODUCTION:

Preeclampsia (PE) is a disease specific to pregnancy, affecting many bodily systems, characterized by high blood pressure and proteinuria after the 20th week of pregnancy, complicating 2-8% of pregnancies and increasing maternal and fetal mortality and morbidity.1,2 Several studies have examined the association between maternal lifestyle and risk of developing pre-eclampsia, however, the etiology of pre-eclampsia still remains unknown. Multiple factors, such as maternal constitutional factors, angiogenetic factors, endothelial dysfunction, syncytiotrophoblastic microparticles (STMP), and inflammatory activation, play a role in the development and progression of preeclampsia.3 The maternal diet is among the factors related to the etiology of preeclampsia; an insufficient diet, especially in terms of calcium, magnesium, selenium and vitamin A and C, is a contributing factor to preeclampsia.4,5
Some studies have shown increased proinflammatory cytokines such as TNF-α, IL-6, and interferon-γ among vitamin D-deficient pregnant women.\textsuperscript{7-10} In addition, hypertension is highly prevalent among individuals with vitamin D deficiency.\textsuperscript{8,11-14} Kidneys and placenta, major organs for conversion of 25-hydroxyvitamin D [25(OH)D] to its biologically active form 1,25-dihydroxyvitamin D [1,25(OH)\textsubscript{2}D], are affected physiologically and metabolically during pregnancy.\textsuperscript{15-17} Therefore, vitamin D has received great attention as a possible etiological factor in pre-eclampsia. Recent epidemiological studies have emphasized the role of vitamin D deficiency in the development of preeclampsia.\textsuperscript{18} Recent in vitro studies have demonstrated the improvement of angiogenesis and inhibition of release of adhesion molecules from endothelial cells by vitamin D.\textsuperscript{19,20} The role of vitamin D deficiency in immunomodulation and placental development has been emphasized in various studies and thus, they put the emphasis on vitamin D deficiency, regarding its possible role in the pathophysiology of preeclampsia.\textsuperscript{7,21-22}

Up to now, controversial results have been obtained concerning the relationship between vitamin D and preeclampsia. Some previous studies have shown a relationship between the reduced risk of preeclampsia and higher 25(OH) D levels in pregnancy.\textsuperscript{23-26} However, some recent findings have indicated no association between plasma 25(OH) D concentrations and preeclampsia.\textsuperscript{27,28} The results of the study by Oken et al. demonstrated an association between higher dietary intakes of vitamin D and increased risk of gestational hypertension during pregnancy.\textsuperscript{28} In another study that included a large sample size, it was shown that low vitamin D concentrations at 24–26 of gestation weeks was associated with 3.2 times greater risk of pre-eclampsia.\textsuperscript{18}

**MATERIAL AND METHODS:**

This study was conducted at the district hospital Churu. A total of one hundred volunteers (50 preeclamptic and eclamptic pregnant women and 50 healthy pregnant women) were included in the study. The diagnosis of preeclampsia was confirmed using the “Report of the American College of Obstetricians and Gynecologists’ Task Force on Hypertension in Pregnancy” criteria.

The inclusion criteria of the patients were: singleton pregnancy, gestational age between 24 and 28 weeks based on the first trimester ultrasound exam, no history of chronic hypertension, not using any type of multivitamins, having lived in Churu district during the previous 2 years, and no history of recognized internal diseases, such as kidney disease, diabetes, thyroid, etc., during the pregnancy. Hypertension was defined as systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg on two occasions within at least 6 h apart. It should be mentioned that none of the participants had high blood pressure at the beginning of the study.

**Collection and Analysis of Samples:** we followed the standard protocol of sample collection and analysis. The serum samples were assessed for 25(OH) D using chemiluminescence immuno assay. All the participants were followed every 2 weeks from the 24th until the 33th weeks, each week up to delivery, and until 2 days after the delivery. Subjects were classified into four categories according to serum vitamin D level:

- $>$20ng/ml: suboptimal to optimal
- 10-20 ng/ml: mild deficiency
- 5-10ng/ml: severe deficiency and
- $<$5 ng/ml : very severe deficiency
Statistical Analysis: Results are expressed as Mean ± SD. Data are analyzed with the help of Microsoft excel 2007, using student’s t-test and chi-square test. A p-value < 0.05 was considered as statistically significant.

RESULTS:
No statistically significant differences were found in age (p=0.792) and habituation between the two groups. The level of education (p=0.015) and socioeconomic status (p=0.023) was significantly lower in the preeclamptic and eclamptic group compared to the normotensive pregnant women. The preeclampsia and eclampsia group had either irregular or no ANC (p <0.001). Systolic and diastolic blood pressures were significantly higher in the eclamptic and preeclamptic patient groups compared to the healthy pregnant women (P<0.00). (Table 1)

### Table 1
Comparison of sociodemographic profile between study (pre-eclampsia/eclampsia) and control group (Normotensive)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-eclampsia and eclampsia group</th>
<th>Control group</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>23.42±3.36</td>
<td>23.28±3.58</td>
<td></td>
<td>0.792</td>
</tr>
<tr>
<td>Booked</td>
<td>8</td>
<td>34</td>
<td>42</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Irregular ANC</td>
<td>29</td>
<td>10</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>No ANC</td>
<td>13</td>
<td>6</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td>0.015</td>
</tr>
<tr>
<td>Illiterate</td>
<td>18</td>
<td>10</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Upto high school</td>
<td>28</td>
<td>35</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Above high school</td>
<td>4</td>
<td>5</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
<td></td>
<td></td>
<td>0.023</td>
</tr>
<tr>
<td>Lower</td>
<td>11</td>
<td>9</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Lower middle</td>
<td>16</td>
<td>8</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Upper lower/middle</td>
<td>22</td>
<td>30</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Gestation weeks</td>
<td>38.5±1.43</td>
<td>35.3±2.94</td>
<td></td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Systolic BP(mmHg)</td>
<td>114.5(140-90)</td>
<td>156(179-146)</td>
<td></td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>68.9±8.77</td>
<td>105.7±6.62</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

There was universal prevalence of vitamin D deficiency among the pregnant females, but the level of serum vitamin D was significantly lower in the preeclamptic and eclamptic group. 18 percent of the patients in the hypertensive group with either preeclampsia or eclampsia were found to have very severe deficiency (<5 ng/ml) as compared to 6 percent in healthy normotensive group. Among all pregnant mothers, with suboptimal to optimal (20 ng/ml) serum vitamin D, only 6% were from the hypertensive group and rest 14% were from normotensive group. The mean
serum vitamin D level was 9.06±5.20 ng/ml in diseased group compared to 13.67±7.24ng/ml in healthy pregnant group which was statistically significant (Table 2).

Table 2
Comparision of maternal serum vitamin D (ng/ml) between study and control group

<table>
<thead>
<tr>
<th>vitamin D (ng/ml)</th>
<th>Pre-eclampsia and eclampsia group N (%)</th>
<th>Control group N (%)</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>9(18)</td>
<td>3(6)</td>
<td>12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 to 10</td>
<td>30(60)</td>
<td>15(30)</td>
<td>45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10 to 20</td>
<td>8(16)</td>
<td>25(50)</td>
<td>33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;20</td>
<td>3(6)</td>
<td>7(14)</td>
<td>10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>9.06±5.20</td>
<td>13.67±7.24</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

DISCUSSION:
Factors that play a role in the pathogenesis of preeclampsia and eclampsia have not yet been fully determined. Calcitriol exerts the hormonal action via binding to nuclear vitamin D receptors, which are present throughout the body, including pregnancy-specific tissues such as the placenta and uterine placental bed (decidua). During pregnancy, vitamin D may play a role in implantation and placental function potentially due to angiogenic, immunomodulatory, and anti-inflammatory effects. Vitamin D is considered as having a major role in the synthesis and regulation of genes that are effective in the early developmental phase of the placenta.\textsuperscript{21,22} Immunomodulatory properties of vitamin D have been reported to play a key role in the development of immunological tolerance in pregnancy and the presence of a sufficient level of vitamin D has been emphasized to have a role in the management and prevention of PE.\textsuperscript{29} Low vitamin D levels has been associated with increased IL-6 concentrations through stress induced kinase, p35 inactivation, and inhibition of inflammatory cytokines of tumor necrosis factor alpha.\textsuperscript{30,31} Moreover, vitamin D play a major role in the endothelial cell function and dysfunction in cell culture models by modulating endothelial progenitor cells.\textsuperscript{32} The placental growth factor (PIGF) was detected to be significantly decreased. Vitamin D has been thought to play a potent endocrine suppressor role in renin biosynthesis for the regulation of the renin-angiotensin system. In addition, hypertension is suggested to be tied to preeclampsia and eclampsia. Various studies have shown the relationship between preeclampsia and vitamin D to be complicated. They have shown a low vitamin D level in the second trimester to be an indicator of preeclampsia.\textsuperscript{24,33-35} In the present study although serum vitamin D deficiency was invariably present in both the groups, it was more severe in the mothers with preeclampsia and eclampsia. Robinson et al carried out a study to assess the levels of total 25-hydroxyvitamin D (25-OH-D) at diagnosis of early-onset severe preeclampsia and found reduced total 25-OH-D levels in comparison to healthy controls (P<0.001).
Hypponen et al did a systematic review and meta-analysis and concluded that low maternal serum 25(OH)D levels lead to an increased risk of preeclampsia whereas vitamin D supplementation lowered this risk. Bakacak M et al also found similar results. All the patients enrolled in both the study and control group were found to be vitamin D deficient. They found more incidence of severe vitamin D deficiency (90%) in preeclamptic patients as compared to normotensive patients (62%). This difference in the median maternal vitamin D levels of both the groups was found to be statistically significant.

**CONCLUSIONS:**

Present study establishes a consistent association of maternal serum vitamin D deficiency with hypertensive disorders, preeclampsia and eclampsia. However, since the size of study group was very small, it needs to be studied further with groups. The present study serves as a need for larger randomized controlled studies and meta analyses to confirm the findings. Our study also suggests that vitamin D support in patients with a history of preeclampsia in previous pregnancies may decrease the risk of preeclampsia and eclampsia during the current pregnancy.

**REFERENCES:**


