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RESEARCH ARTICLE

A comparative study of vitamin – D level in preeclampsia, eclampsia and normotensive women

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ABSTRACT

Background: Preeclampsia is a disorder of unknown etiology, establishing the role of vitamin D in disease prognosis and treatment could bring a change in maternal mortality. **Objectives**: This study is to compare the level of vitamin D in the pregnancy of normotensive and pre-eclamptic women and to find the association between vitamin D level and severity of pre-eclampsia, maternal and perinatal outcome. **Method:** This was a prospective comparative observational study. This study included 100 normotensive women as control and 100 hypertensive women, consists of 69 mild pre-eclampsia, 25 severe pre-eclampsia and 6 eclampsia as cases. This study was conducted in Shyam Shah Medical College (MP). Single blood sample obtained from all the groups. Demographics and vitamin D levels compared between all the groups. **Results:** Vitamin D deficiency was low in all women; the incidence was more among pre-eclampsia, eclampsia group. Mean level of vitamin D was 13.31±7.5 ng/dl in normotensive, 8.31± 5.24 ng/dl in mild pre-eclampsia, 5.56± 1.95 ng/dl in severe pre-eclampsia and 4.97± 1.55 ng/dl in eclampsia. Mean vitamin D levels among the cases with good maternal outcome were 7.8±4.85ng/dl and 4.87±1.59 ng/dl in poor maternal outcome. Vitamin D deficiency can result in preterm deliveries and low birth weight babies. Mean vitamin D levels in women of healthy babies were 8.02±5.04 ng/dl, 5.45±1.25ng/dl in women of babies shifted NICU and 4.24±0.55 ng/dl among women of intra uterine death fetuses. **Conclusion:** Vitamin D deficiency during pregnancy can be associated with preeclampsia and poor maternal, fetal outcome.

Keywords: Vitamin D, pre-eclampsia, eclampsia.

Preeclampsia is a multisystem disorder specific to pregnancy, characterized by hypertension and proteinuria after 20th week of pregnancy. It is seen in about 5-15% of pregnancies and it is a major contributor of maternal and perinatal morbidity and mortality [1].

Pregnancy is a physiological state that can cause many alterations in metabolic, biochemical, hematological and immunologic processes. Pregnancy can induce hypertension in previously normotensive women and aggravate hypertension in those who were hypertensive before pregnancy. The National High Blood Pressure Education Program Working Group has classified hypertensive disorders during pregnancy into 4 categories: 1) chronic hypertension, 2) preeclampsia-eclampsia, 3) preeclampsia superimposed on chronic hypertension and 4) gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy). The most serious consequences for the mother and baby were result of pre-eclampsia and eclampsia [2]. Etiopathogenesis of preeclampsia is not well known and no effective preventive therapy is available. Multiple factor such as genetic factors, angiogenic factors, abnormal placentation, oxidation stress, immunological factors result in endothelial dysfunction and play important role in the pathogenesis of preeclampsia [3].

In many countries vitamin D deficiency (VDD) is considered as a public health problem and pregnant women identified as a high risk group, among whom the prevalence of VDD ranges between 20 and 40%. Though vitamin D

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deficiency is preventable many children are born with this deficiency. Hence more studies are needed to establish why and how vitamin D deficiency is related to pregnancy and the neonatal outcome.

Previously vitamin D was considered important for bone and calcium metabolism but recent studies have redefined its role. According to various studies vitamin D have role in immunomodulation and placental development. Vitamin D stimulates the activity of T regulatory cells, which are important in supporting placental implantation by favorable immune response. It enhances angiogenic properties in endothelial progenitor cells and mediate endothelial function and dysfunction in cell models. There is some evidence that low level of vitamin D is associated with the risk of preeclampsia but more studies are needed [4]. The study was done to determine the serum vitamin D levels in women having pre-eclampsia and healthy pregnant women, and to compare the maternal and fetal outcome among these women.

Methods

This was a prospective comparative observational study conducted in the Department of Obstetrics and Gynecology, Shyam Shah Medical College, Rewa (MP) from March 2020 to July 2021. Every fifth pregnant women who was diagnosed with pre-eclampsia, eclampsia attending labour room and OPD constituted the cases of study population. Among 552 hypertensive women enrolled after applying inclusion and exclusion criteria, 100 cases were chosen; similarly100 normotensive women were also chosen and created a study group of 200 women. All the women of the study group gave their informed consent to be included in the study. Complete history of the patient along with their demographic profile is noted during admission using a pretested questionnaire. General examination and obstetric examination conducted at the same time. Blood and urine samples for extensive investigations including complete blood count, kidney function test, liver function test, random blood sugar, serum uric acid, serum electrolytes and vitamin D was drawn and standards lab procedures used to estimate the serum level of these parameters.

Women with multiple pregnancy, chronic hypertension, type 2 diabetes mellitus, epilepsy, thyroid disorders and other medical disorders which cause seizures were excluded from the study. Pregnant women with blood pressure more than 140/90 mmHg with proteinuria (more than 300mg/dl in 24 hours urine) on 2 or more occasions at least 6 hours apart, after 20 weeks of gestation was diagnosed as pre-eclampsia. Severe pre-eclampsia diagnosed as per the criteria of International society for the study of hypertension in pregnancy, blood pressure >160/110 mmHg and related complications. Diagnosis of eclampsia was based on presence of tonic – clonic seizures in patients with no systemic disease that may cause seizures.

Venous blood samples for 25(OH) vitamin – D estimation was collected after 12 hours overnight fasting, protected from light, stored at 20^0C until analysis, 25(OH) vitamin – D estimation was done using chemiluminiscent immunoassay (CLIA).

Classification of clinical categories of vitamin D level: -

- Severely deficient 0-10 ng/mL
- Deficient 11-20 ng/mL
- Insufficient 21-32 ng/mL
- Adequate 33-49 ng/mL
- Optimum 50-60 ng/mL
- Toxic >60 ng/mL [4]

Follow up of these women was done until delivery and early postpartum period. Follow up of all the delivered babies was done, during the early neonatal period (0-6 days) for complications. Apgar at one minute after birth was noted and complications like preterm delivery, low birth weight, NICU admission, stillbirth and intrauterine death were studied. All the information was recorded in a pre-structured proforma, entered in MS excel spreadsheet and analyzed by appropriate statistical method.

Quantitative data will be expressed as mean ± SD (standard deviation) categorical variable was expressed as number and percentage. Categorical variables compared using Pearson Chi – square test. P value <0.05 is considered as significant.

Results

In this study 200 patients, 100 patients each from normotensive and pre-eclampsia eclampsia group compared. Among those patients, cases were again divided into 69 pre-eclampsia, 25 severe pre-eclampsia and 6 eclampsia for the easy comparison. Socio demographic profile of all these women was assessed. The age of the study group ranges from 28 to 40 years. There was no statistical correlation observed between vitamin D levels of the study group and age (p=0.984) and parity (p=0.564) (table 1). Most of the women of this study have normal body weight. Among the eclampsia patients 83.33% were overweight. Only one obese patient of this study had severe pre-eclampsia. 40.77 % of women with severe vitamin D deficiency were overweight. In obese patients one woman had severe vitamin D

Table 1: Demographic characteristic features of patients

Categories	Vitamin D Category								P value
	Severely deficient (0-10 ng/mL)		Deficient (>10-20ng/mL)		Insufficient (>20-32ng/mL)		Adequate (>32-49ng/mL)		
Age group	N	%	N	%	N	%	N	%	
Up to 20 years	33	25.38	13	27.08	6	28.57	0	0.00	0.984
21-25 years	60	46.15	21	43.75	10	47.62	1	100.00	
26-30 years	21	16.15	7	14.58	1	4.76	0	0.00	
31-35 years	9	6.92	3	6.25	2	9.52	0	0.00	
36-40 years	7	5.38	4	8.33	2	9.52	0	0.00	
Weight status									
Underweight	0	0.00	0	0.00	0	0.00	0	0.00	
Normal	76	58.46	32	66.67	12	57.14	1	100.00	
Overweight	53	40.77	16	33.33	9	42.86	0	0.00	0.009
Obese	1	0.77	0	0.00	0	0.00	0	0.00	
Socioeconomic status									
Lower	18	85.7	3	14.2	0	0.00	0	0.00	Less than
Lower Middle	14	77.7	1	5.55	3	16.6	0	0.00	0.001
Upper Lower	83	63.3	36	27.4	11	8.3	1	0.07	
Upper Middle	15	50	8	26.6	7	23.3	0	0.00	
Literacy status									
Illiterate	28	82.35	6	17.64	0	0.00	0	0.00	
Primary	12	70.5	4	23.52	1	5.88	0	0.00	
Middle	23	60.52	7	18.42	8	21.05	0	0.00	0.032
Hr. Sec	54	63.52	25	29.41	5	5.88	1	1.11	
Graduate/PG	13	50	6	23.07	7	26.92	0	0.00	
Obstetric history									
Multigravida	36	27.7	17	35.4	8	38.1	0	0.0	
Primigravida	94	72.3	31	64.6	13	61.9	1	100	0.564

deficiency. There was more prevalence of vitamin D deficiency and hypertensive disorders in overweight women.

Out of 21 women of lower socio-economic status 85.7% have severe vitamin D deficiency (table 1). In contrast only 50 % of upper middle-class women have severe vitamin D deficiency. It has been statistically proven that a vitamin D deficiency and hypertensive disorder of pregnancy was more prevalent among low socioeconomic status.

Among normotensive women 90% had normal vaginal delivery 10% had caesarian section. But 30% of hypertensive women underwent caesarian section. Out of 40 caesarian sections, 37 (92.5%) women were severely vitamin D deficient. In this study it is observed that incidence of caesarian section is more among hypertensive and vitamin D deficient women.

In this study assessment of induction of labour was done. Induction of labor was not quite commonly seen among the normotensive women; only 7% of them have undergone induction. But when coming to the hypertensive group 50 % of eclampsia cases, 27.54 % of pre-eclampsia cases and 36% of severe pre-eclampsia cases under gone induction. This suggests that waiting for natural onset of labor becomes difficult in hypertensive women because termination of pregnancy is always the key to management.

Among 100 cases 16.67% of eclampsia, 26.09% of pre-eclampsia and 44% of severe pre-eclampsia patients has been undergone caesarian section and out of 100 normotensive patients only 10 % of them had caesarian section (table 2). On applying Chi square test to this study P value came as 0.001, suggesting that there was more incidence of caesarian section among hypertensive women than that of normotensive women. Among 40 caesarian sections 37 women had severe vitamin D deficiency. In 160 women who had normal vaginal delivery 93 women had severe vitamin D deficiency but their vitamin D level was higher than the patient who had cesarean. One mother with adequate vitamin D level had normal vaginal delivery. On statistical assessment the P value was found to be 0.001, suggesting that there is an increased incidence of LSCS in vitamin D deficiency (table 2).

Vitamin D deficiency was prevalent among all the subjects off this study. Hence the degrees of deficiencies among both groups were compared to assess its relation to severity of the hypertensive disease of pregnancy. In this study it is observed that 100% women of eclampsia and severe pre-eclampsia group were severely deficient of vitamin D with a blood level between 0 and 10 ng/dl. Severe vitamin D deficiency is also seen among 81.16% pre-eclamptic and 43% of normotensive women. 38 % of normotensive and 14.49 % of mild preeclampsia women had deficient (11-20ng/dl) levels of vitamin D (figure 1). Among 200 women only 1 woman from control group had adequate (33-49ng/dl) level of vitamin D. P value of this study came as less than 0.0001 suggesting vitamin D deficiencies are

Table 2: Clinical characteristics features of cases and controls patients

Mode of delivery	Controls		Cases					
	Normotensive		Mild Pre-eclampsia		Severe preeclampsia		Eclampsia	
	N	%	N	%	N	%	N	%
LSCS	10	10.00	18	26.09	11	44.00	1	16.67
NVD	90	90.00	51	73.91	14	56.00	5	83.33
Chi square = 16.89; P = 0.001								
Vitamin D levels among study group according to classification								
Vit. D Category	N	%	N	%	N	%	N	%
Severely deficient	43	43.00	56	81.16	25	100.00	6	100.0
Deficient	38	38.00	10	14.49	0	0.00	0	0.00
Insufficient	18	18.00	3	4.35	0	0.00	0	0.00
Adequate	1	1.00	0	0.00	0	0.00	0	0.00
Optimum	0	0.00	0	0.00	0	0.00	0	0.00
High (>60ng/mL)	0	0.00	0	0.00	0	0.00	0	0.00
Less than 0.0001								
Cases and controls according to status of the baby								
Status of baby	N	%	N	%	N	%	N	%
Healthy	94	94.00	63	91.30	16	64.00	0	0.00
Shifted NICU	6	6.00	5	7.25	8	32.00	3	50.00
IUD	0	0.00	1	1.45	1	4.00	3	50.00
Chi square = 86.14; P <0.0001								
Cases and controls according to birth weight of the baby								
Birth Weight	N	%	N	%	N	%	N	%
Normal (≥2.5 kg)	100	100.00	56	81.16	12	48.00	1	16.67
LBW (<2.5 kg)	0	0.00	13	18.84	13	52.00	5	83.33
Chi square = 65.44; P <0.0001								

Vitamin D levels among study group according to mode of delivery								
Mode of delivery	Severely deficient (0-10 ng/mL)		Deficient (>10-20ng/mL)		Insufficient (>20-32ng/mL)		Adequate (>32 - 49ng/mL)	
	N	%	N	%	N	%	N	%
LSCS	37	28.46	2	4.17	1	4.76	0	0.00
NVD	93	71.54	46	95.83	20	95.24	1	100.00
P = 0.001								

associated with occurrence and severity of pre-eclampsia. In this study the mean level of Vitamin D was 13.31±7.5 ng/dl in normotensive, 8.31± 5.24 ng/dl in pre-eclampsia, 5.56± 1.95 ng/dl in severe pre-eclampsia and 4.97± 1.55 ng/dl in eclampsia women, clearly stating the difference in vitamin D levels can contribute to the severity of pre-eclampsia.

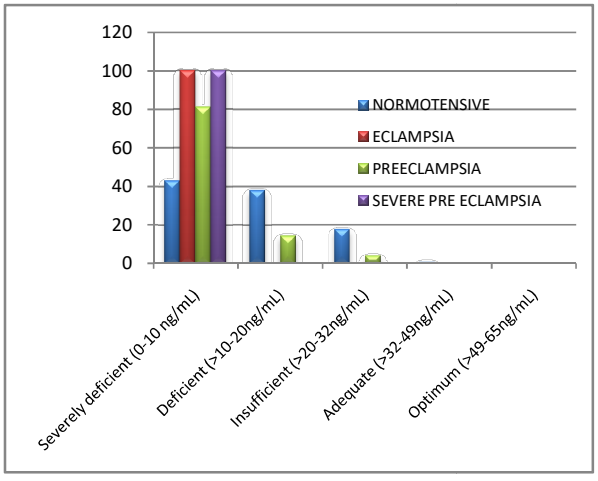

Figure 1: Distribution of vitamin D levels among study group according to classification

Table 3: Distribution of cases according to maternal complication

Maternal complications	Number of cases
Abruption	1
ARDS	1
DIC	0
HELLP	3
Mortality	1
PPH	4
PRESS	1
Pulmonary edema	2
Retinopathy	1
ARF	2
No complications	84

On observing the maternal outcome of cases 84 cases had good maternal outcome without any complications (table 3). But 3 cases developed HELLP, 3 developed PPH and 2 patients had acute renal failure and pulmonary edema. One case of each abruption, ARDS, PRESS and retinopathy seen among the cases. One case died during the study period due to complications from pre-eclampsia. Mean vitamin D levels among the cases with good maternal outcome was 7.8±4.85ng/dl and 4.87±1.59ng/dl in poor maternal outcome.

The p value of this study came as 0.033 indicating women with sufficient vitamin D levels have better maternal outcome.

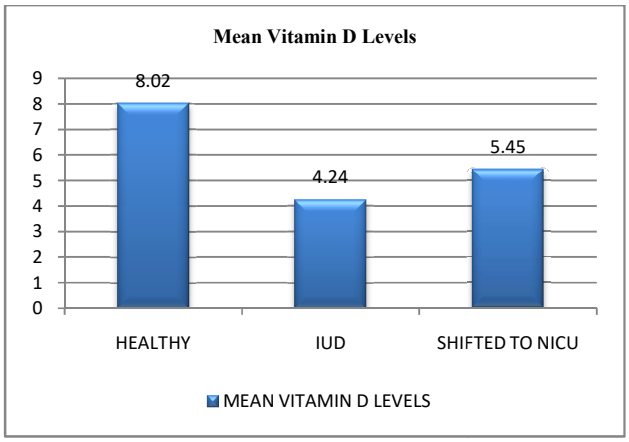

Figure 2: Distribution of cases according to fetal outcome with comparison of vitamin D levels

Mean vitamin D levels in women of healthy babies were 8.02±5.04 ng/dl, 5.45±1.25ng/dl in women of babies shifted NICU and 4.24±0.55 ng/dl among women of intrauterine death fetuses (figure 2). On assessment vitamin D levels in relation to the birth weight of the baby it was observed that mean vitamin D level among the normal birth weight babies (> 2.5 Kg) was 8.13±4.97ng/dl 85 and 5.23±3.42ng/dl in low birth weight babies (table 4). In this study on comparing vitamin D level of normal and low birth weight babies p value came as 0.0215, suggesting that maintaining a higher level of vitamin D during pregnancy can result in good perinatal outcome. On assessing the perinatal outcome of this study, it is observed that 94% of babies born to normotensive women were healthy and only 6% of them were shifted to NICU. No intrauterine deaths were seen in this group.

Table 4: Distribution of cases according to birth weight with comparison to vitamin d levels

Birth weight	Number of cases	Mean vitamin D levels	Standard deviation
Normal (≥2.5 kg)	69	8.13	4.97
LBW (<2.5 kg)	31	5.23	3.42

Perinatal morbidity and mortality were more among hypertensive group. In eclampsia women no healthy babies were seen. 3 intrauterine deaths and 3 babies got shifted to NICU. Among severe pre-eclampsia group 64% babies were healthy, 32% got shifted to NICU and 4% were intrauterine death. 91.30% healthy babies, 7.25% NICU shifted babies and 4% intra uterine deaths were seen among mild pre-eclampsia group. P value of this parameter was less than 0.0001 implying that there was a poor perinatal outcome among hypertensive women. In this study no low birth weight babies were seen among normotensive women. In eclampsia group 83.3 % babies had low birth weight. 52% of low birth weight babies were seen among severe pre-eclampsia and only 18.84% was seen among mild pre-eclampsia. The p value of this study was less than 0.0001. Thus, indicating an increased severity of pre-eclampsia can lead to low birth weight and poor perinatal outcome. This is mainly due to termination of the pregnancy always improves maternal outcome as pathology of the disease lies in placenta. Hence health care fraternities prefer to terminate the pregnancy irrespective of the gestational age as the severity of pre-eclampsia increases.

Discussion

Pre-eclampsia is a disease specific to pregnancy. It is a major contributor to maternal and perinatal morbidity and mortality. Vitamin D is also known to have anti-inflammatory, antiatherogenic and immune boosting properties. It is now accepted that vitamin D plays a role in many organs, especially in the placenta, through the regulation of the expression of key associated development genes.

Most of the patients in present study and in various studies to compare vitamin D level in preeclamptic and normotensive women were in the range of 20 – 30 years [5, 6]. There was no statistical correlation between vitamin D deficiency and age as well as parity. Majority of patients in our study was having normal BMI but 40.77% of patients with vitamin D deficiency were overweight. There was more prevalence of vitamin D deficiency and eclampsia in overweight women. In a study by Abedi et al found that there is no significant relationship between BMI and preeclampsia as most of the patients in both groups had normal BMI. In this study it has been seen that vitamin D deficiency was much more, among preeclampsia - eclampsia mothers and severity of disease has a positive relation with vitamin D deficiency. Vitamin D deficiency was more prevalent in obese, illiterate and low socioeconomic status groups [7].

In preeclampsia - eclampsia cases incidence of preterm deliveries was high in comparison to normotensive women. Only 3% of cases were preterm among normotensive women but it was 11.59% in mild preeclampsia, 56% in severe preeclampsia and 66.67 % in eclampsia. The findings were in good agreement with Shaikh S et al [8], where 64% cases had gestational age between 31 to 37 weeks and 35% of patients had term pregnancy. In the study group among

preterm mother vitamin D deficiency was more, indicating vitamin D deficiency can lead to preeclampsia and preterm deliveries.

Termination of pregnancy being the key in the management of pre-eclampsia, more caesarian sections was seen in pre-eclampsia group. It was observed that the vitamin D deficiency can attribute to the increased incidence of caesarean section. In a study conducted by Ching Ming Liu in Taiwan on maternal complications and perinatal outcomes associated with gestational hypertension and severe pre-eclampsia reported 48.62% caesarean section rate [9].

Vitamin D deficiency can be associated with poor perinatal outcome and also contributes to the low birth weight in neonates. Present study has showed mean vitamin D levels of healthy, NICU shifted and IUD babies were 8.02± 5.04ng/dl, 5.45 ±1.25ng/dl and 4.24 ±0.55ng/dl respectively. In the study of Nasrin Khalessi et al in 2015, mean maternal vitamin D level of LBW neonates was 25.05nmol/L against 38.13nmol/L in normal birth weight babies [10].

Mean vitamin D levels among the cases with good maternal outcome were 7.8±4.85 ng/dl and 4.87±1.59 ng/dl in poor maternal outcome. The P value of this study came as 0.033 indicating sufficient vitamin D levels helps in improving the maternal outcome. Similar result was seen in the study of Mahija Sahu and Nidhi Chaudhary et al [11, 12]. Various studies being conducted in relation to vitamin D level in pregnancy found that even normotensive women were deficient in vitamin D level and in hypertensive women vitamin D level was much more reduced, leading to complications [13 - 15].

Conclusion

The present study has shown that there is an association between preeclampsia - eclampsia and vitamin D deficiency in women of reproductive age group. Vitamin D deficiency can result in hypertensive disorders of pregnancy and it may complicate the pregnancy through poor maternal and perinatal outcome. Vitamin D supplementation during pregnancy can be helpful in prevention of preeclampsia. There is a need for further studies and meta-analysis to confirm the findings.

Conflict of interest: None. **Disclaimer:** Nil.

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