

## Comparison of Maternal Serum Vitamin D Levels in Pregnancy with Preeclampsia and Healthy Pregnant Women

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Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 02-05-2024

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Conflict of interest: Nil

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### Abstract:

**Background:** Preeclampsia is a pregnancy specific multisystem disorder of unknown etiology. Vitamin D deficiency is proposed to be important in the etiopathogenesis of preeclampsia.

**Aim:** To assess and compare maternal serum vitamin D levels in preeclamptic patients and healthy pregnant women for early prediction and prevention of preeclampsia.

**Materials and Methods:** This study was a comparative cross sectional study, carried out on 100 pregnant women with gestational age  $\geq 20$  weeks. 50 clinical cases of preeclampsia were compared with equal number of healthy normotensive pregnant women for serum vitamin D levels.

**Results:** Mean serum vitamin D level in preeclamptic women was  $9.76 \pm 3.19$  ng/ml as compared to healthy normotensive pregnant women  $19.57 \pm 6.37$  ng/ml. The difference in Serum vitamin D in two groups was statistically significant with p-value  $< 0.001$ .

**Conclusion:** The result showed significantly low levels of vitamin D in preeclamptic cases as compared to healthy normotensive pregnant women of the study population. Hence it is advised to supplement pregnant lady with vitamin D to decrease the risk of preeclampsia.

**Keywords:** Preeclampsia, Vitamin D, Hypertension, Healthy pregnant women.

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### Introduction

Preeclampsia is a transient multisystem disorder of unknown etiology. Preeclampsia is defined as the onset of hypertension to the extent of 140/90 mmHg or more with proteinuria, usually after the 20th week of pregnancy in a previously normotensive and nonproteinuric women and resolving completely after the sixth week of delivery. It is associated with increased maternal and fetal mortality and morbidity. Generally the incidence of Preeclampsia is in the range of 2-8% of all pregnancies [1-3]. Although its incidence has fallen in the developed countries due to improved antenatal care, but its incidence is still high in the developing countries [4].

Deficiency of vitamin D has been associated with various poor maternal and fetal outcomes and is proposed to be important in the etiopathogenesis of preeclampsia. Various studies emphasize the role of vitamin D in immunomodulation and placental

development [5-7]. Recent in vitro studies shows that vitamin D is associated with improvement of angiogenesis by promoting angiogenic properties in endothelial progenitor cells [8-9]. Vitamin D has been emphasized to play a major role in signal and gene regulations in the development of placental trophoblasts in the placental growth phase [10-11]. Decrease level of vitamin D has been suggested to cause excess activity of inflammatory cytokines like TNF-alpha and to decrease immunological tolerance for implantation and to trigger preeclampsia. Antiinflammatory role of vitamin D has been revealed in some studies [12]. These results may confirm that vitamin D is a biomarker that can play a role in the pathophysiology of preeclampsia. Once the diagnosis of preeclampsia has been established treatment options are limited. For this reason, much attention has recently been focused on preeclampsia prediction and prevention.

**Aim**

To assess and compare maternal serum vitamin D levels in preeclamptic patients and healthy pregnant women for early prediction and prevention of preeclampsia.

**Material and Method**

**Study Design:** The study was a comparative cross sectional study.

**Place and Period of Study:** The study was carried out in the Department of Biochemistry in collaboration with the Department of Obstetrics and Gynecology, Nalanda Medical College and Hospital, Patna, Bihar in a time duration of January 2020 to January 2021.

**Study Population:** The study was carried out on 100 pregnant women with gestational age  $\geq 20$  weeks coming for antenatal assessment in the OPD or admitted under the department of Obstetrics and Gynecology, Nalanda Medical college and Hospital, Patna. The work was carried out after due clearance and approval from institutional ethical committee. Study subject had participated in the study after informed consent and after taking history (age, gravidity, parity, gestational age etc.), general examination (pallor, oedema, blood pressure, weight etc.), routine urine examination.

For statistical significance and comparison all antenatal cases were divided in two groups:

**Group 1 (Study group):** Includes a total of 50 clinical cases of preeclampsia with  $\geq 20$  weeks of gestation in the age group of 18 – 35 years.

**Inclusion Criteria:** The diagnosis of preeclampsia was confirmed using the Report of American college of Obstetricians and Gynecologist, Task force on hypertension in pregnancy criteria. Based on these criteria, patients with systolic blood pressure  $\geq 140$  mmHg and / or diastolic blood pressure  $\geq 90$  mmHg (measured after a period of rest of four hours, twice daily) and proteinuria  $\geq 300$  mg protein / 24 hours, were diagnosed as preeclampsia.

**Exclusion Criteria:** All maternal complications in pregnancy without preeclampsia were excluded eg – Presence of UTI, History of hypertension, Diabetes mellitus, Liver, cardiac or renal disease, Multifetal gestation, Drug intake, Alcoholism, Any other major illness.

**Group 2 (Control):** A total of 50 healthy normotensive pregnant women with comparable parameters with the study group were included in the control group.

The two groups were matched according to age, gravidity, parity, maternal weight, gestational age.

**Blood Sample Collection and Analysis:** With all aseptic and antiseptic measures approx. 5 ml of venous blood was collected (10 -12 hours fasting) in red capped clot activator vial and properly labelled. Blood sample was allowed to clot by placing in a rack at room temperature for at least 30 minutes. Then it was centrifuged at 2000 rpm for 10 minutes within 2 hours of collection.

Biochemical analyses of serum vitamin D was done on Chemiluminescence Immunoassay Analyser.

**Reagent Used:** The Elecsys vitamin D total assay employs a vitamin D binding protein (VDBP) as capture protein to bind vitamin D3 (25-OH) and vitamin D2 (25-OH).

**Calculation:** The analyzer automatically calculates the analyte concentration for each sample in ng/ml. The results obtained were further analysed for Mean, SD and p-value. Student's t-tests was employed to examine the differences among the preeclampsia and the control group. A p-value  $<0.05$  was considered as statistically significant.

**Result**

The study was done as a comparative cross sectional study conducted on 50 preeclamptic patients as case and 50 healthy normotensive pregnant women as control group.

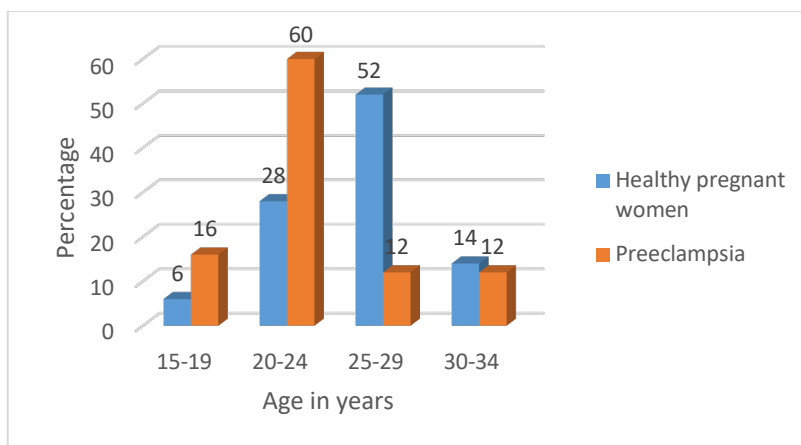


Figure 1: Age (yrs) distribution in healthy pregnant women and preeclamptic women

This figure I shows maximum incidence of preeclampsia in the age group of 20-24 years. Mean age of preeclamptic women was 22.72±4.38 and healthy pregnant women was 25.56±3.85. The difference in age was significant with p<0.001.

Table 1: Table showing distribution of cases according to gravida in healthy pregnant and preeclamptic women.

Gravida	Healthy pregnant women		Preeclampsia	
	Cases	%	Cases	%
G1	14	28	35	70
G2	17	34	10	20
G3	16	32	3	6
G4	2	4	2	4
G5	1	2	0	0

This table shows that maximum incidence of preeclampsia 70% was in first gravida.

Table 2: Table showing levels of serum vitamin d (ng/ml) in healthy pregnancy and in preeclamptic women

Group	Range	Mean	SD
Healthy pregnancy	8.92-32.48	19.57	6.37
Preeclampsia	4.06-16.89	9.76	3.19

p-value <0.001 Significant\*\*\*

This table shows that levels of serum vitamin D in preeclamptic women were in the range of 4.06-16.89 ng/ml. Mean value was 9.76 ng/ml. In healthy pregnancy range of serum vitamin D was

8.92-32.48 ng/mL. Mean value was 19.57 ng/mL. The difference in Serum vitamin D in two groups was significant with p-value <0.001.

Table 3: Table showing comparison of mean levels of serum vitamin d (ng/ml) between the two groups in each age interval

Age interval (In yrs)	Group	No.	Mean	SD	t-value	p-value	Sig.
15-19	N	3	12.23	0.65	1.97	<0.05	*
	P	8	9.79	3.31			
20-24	N	14	18.62	3.95	7.32	<0.001	***
	P	30	9.50	3.22			
25-29	N	26	20.86	6.82	5.02	<0.001	***
	P	6	10.58	3.79			
30-34	N	7	22.41	7.85	3.83	<0.001	***
	P	6	10.14	2.95			

N: Normal healthy pregnant women P: Preeclamptic women

This table shows the comparative study of Serum Vitamin D in different age groups of normal

healthy pregnant women and preeclamptic women. In each age group mean Serum Vitamin D levels

were found to be significantly low in preeclamptic women compared to normal pregnant women.

NB: NS = Not significant, \* = Significant at 5% level

\*\* = Significant at 1% level \*\*\* = Significant at 0.1% level

**Table 4: Showing comparison of mean level of serum vitamin D (mg/dl) between the two groups for each gravida**

Gravida	Group	No.	Mean	SD	t-value	p-value	Sig.
G1	N	14	16.86	4.71	5.005	<0.001	***
	P	35	9.95	3.31			
G2	N	17	20.53	6.56	6.49	<0.001	***
	P	10	8.68	2.80			
G3	N	16	20.98	6.85	4.78	<0.001	***
	P	3	10.22	2.52			
G4 & more	N	3	19.19	8.68	1.32	<0.01	**
	P	2	10.98	5.14			

N: Normal healthy pregnant women

P: Preeclamptic women

This table shows the comparative study of serum vitamin D in different gravida of normal pregnant women and preeclamptic women. In each gravida mean serum vitamin D levels were found to be low in preeclamptic women compared to normal pregnant women. The difference in the mean levels of serum vitamin D were significant in two groups for each gravida.

#### Discussion

The level of serum Vitamin D in preeclampsia women were in the range of 4.06 – 16.89 ng/ml with mean  $\pm$  SD of 9.76 $\pm$ 3.19 ng/ml. In normal pregnant women the range were 8.92 – 32.48 ng/ml with mean  $\pm$  SD of 19.57 $\pm$ 6.37 ng/ml (Table II). The age wise difference in serum Vitamin D between two groups (Table III) shows that in each age group mean serum Vitamin D levels were found to be low in preeclamptic women compared to normal pregnant women. The difference in the mean levels of serum Vitamin D were significant in the two groups for each age interval.

Gravida wise distribution of cases in the two groups (Table IV) shows that for primigravida (G1) mean  $\pm$  SD of serum Vitamin D in preeclamptic women was 9.95 $\pm$ 3.31 ng/ml, and in normal pregnant women was 16.86 $\pm$ 4.71 ng/ml. For G2 the mean  $\pm$  SD in preeclamptic was 8.68 $\pm$ 2.80 ng/ml, whereas in normal pregnant women level was 20.53 $\pm$ 6.56 ng/ml. In G3 mean  $\pm$  SD of serum Vitamin D in preeclamptic was 10.22 $\pm$ 2.52 ng/ml, and in normal pregnant women was 20.98 $\pm$ 6.85 ng/ml. This study shows that for each gravida mean serum Vitamin D levels were found to be significantly low in preeclamptic women compared to normal pregnant women.

All the above results for comparative study between two groups have shown that the mean level of serum Vitamin D were found to be significantly low in preeclampsia in comparison to

normal pregnant women. 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. Robinson et al carried out a study to assess the levels of 25-OH-D at diagnosis of early –onset severe preeclampsia and found reduced total 25-OD-D levels in comparison to healthy controls (p<0.001). Hypponen et al. (2014) 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. Backack M et al. (2015) [13] also found similar results. Their study concluded that vitamin D levels were lower in both preeclamptic and eclamptic patients compared to healthy normotensive pregnant women (p<0.001). This study demonstrates that vitamin D plays a role in the etiology and pathophysiology of preeclampsia. Mehta S. et al (2016) [14] conducted a case control study and concluded that vitamin D level is lower in women with hypertensive disorder of pregnancy as compared to healthy pregnant women also the level of vitamin D decreases with severity of HDP. A prospective case control study conducted by J Arunmaikannu et al. (2017) [5]. They found mean Vitamin D level in preeclamptic women was 16.97 $\pm$ 2.70 ng/ml and in controls it was 19.74 $\pm$ 3.82 ng/ml. This low vitamin D level in preeclamptic women was statistically significant (p<0.05). A cross sectional comparative study was carried out by Dr Gogaram et al.(2018) [15], their study concluded that vitamin D levels were lower in both preeclamptic and eclamptic patients compared to healthy normotensive pregnant women (p<0.001).

#### Conclusion

It is concluded from this study that significantly low levels of vitamin D are found in the serum of preeclamptic cases as compared to normotensive healthy pregnant women of the study population.

Hence it is advised to supplement pregnant lady with vitamin D. The present study suggests low levels of serum vitamin D could be possible contributors in the etio-pathophysiology of preeclampsia. Our study also suggest that vitamin D support in patients with a history of preeclampsia in previous pregnancies may decrease the risk of preeclampsia during the current pregnancy. But role of vitamin D supplementation in prevention of preeclampsia is not proven beyond doubt. Further studies are needed to document the adequate dose of vitamin D supplementation to prevent preeclampsia for improving maternal and fetal outcome.

#### Acknowledgement

We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staffs of hospital who were involved in patient care of the study population.

**Source of funding:** No funding received.

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