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Serum vitamin D status in preeclamptic patients in comparison with normotensive pregnant controls: A rural based study

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Abstract
Aim of Study: To compare the serum vitamin D levels in preeclampsia and healthy pregnant women.
Design: Case control study.
Settings: Rajah Muthaih Medical College Hospital, Chidambaram.
Results: In this study of 55 antenatal cases, 30 cases of preeclampsia and eclampsia were selected as study group A&25 healthy pregnant women were selected as control group B. Maternal and fetal medical records were reviewed. Blood samples were collected from all cases. Demographic and 25(OH) D levels were compared & no significant difference was observed in age, gravidity, BMI between the groups. Majority were primigravida in both the groups. Mean vitamin D level in study group A were (24.72±12.49ng/ml) significantly lower than control group B(31.65±15.25ng/ml) (p<0.02). The rate of LSCS was found to be higher in preeclampsia and eclampsia to conclude, Vitamin D supplementation could decrease the risk of both preeclampsia and eclampsia in pregnancy& morbidity due to increase operative delivery.

Keywords: Vitamin D, preeclampsia, eclampsia normotensives

Introduction

Hypertensive disorders complicate 5 to 10 per cent of all pregnancies and together they are one of the members of the deadly triad along with haemorrhage and infection - that contributes greatly to maternal mortality & morbidity [1]. The preeclampsia syndrome, either alone or superimposed on chronic hypertension is the most dangerous. The new onset hypertension termed gestational hypertension is followed by signs and symptoms of preeclampsia almost half the time and preeclampsia is identified in 3.9% of all pregnancies [13]. WHO systematically reviews maternal mortality worldwide in developed countries & 16% of maternal deaths were reported to be due to hypertensive disorders. Hypertensive disorders also increase perinatal morbidity & mortality by means of diseases like FGR, LBW, preterm, RDS & admission to NICU.

Recent studies shows that 25 (OH)-D may play a role in implantation and placental function potentially due to angiogenic, immunomodulatory and anti-inflammatory effects [2]. It could also interfere with many mechanisms involved in PE pathogenesis including trophoblastic invasion as well as blood pressure control and proteinuria. Our study also aimed to assess Vit. D levels in patients with eclampsia, preeclampsia in comparison with normotensive pregnant controls [3].

Materials and Methods

After obtaining the Institutional ethical Committee approval and informed written consent, the study was conducted over a period between Nov 2016 and Oct 2018 in the Department of Obstetrics and Gynaecology at Rajah Muthiah Medical College, Chidambaram, Tamil Nadu. This is a prospective cross sectional case control study. The diagnosis of preeclampsia was made using RCOG guidelines. Based on this criteria, the patients with SBP≥140 mm Hg / DBP≥90 mm Hg (4-6hrs apart) with proteinuria are diagnosed as PE & those above criteria with GTCS diagnosed as eclampsia.

Thirty antenatal cases with PE/E are selected as group A and twenty five normal mothers are selected as group B with gestational age more than 20 weeks. All cases with H/o previous metabolic disorders, chronic HT, GDM, BMI >30, TB drugs intake (asprin, omeprazole, steroids, multivitamins) were excluded from this study.

All detailed history and clinical information are obtained from the patient Venous blood samples were collected from all groups (A/B) and sent for 25(OH) D level estimation by Enzyme linked immunosorbent assay.

Both groups were compared for baseline demographic parameters like age, GA, booked status, systolic & diastolic blood pressure, BMI, U/A, adverse maternal outcome, fetal outcome like LBW.

All data tabulated analysed in appropriate manner with involvement of statistician from the department of biostatistics, Annamalai University. The statistical analysis was done using SPSS-21 and applying chi square test of independence and association, parametric and non-parametric (mann Whitney 'U' test), student's 't' test and pearson correlation coefficient.

Results

In the present work serum Vitamin 'D' levels in preeclampsia, eclampsia is compared with that of healthy pregnant women. A total of 30 cases with preeclampsia, eclampsia women were selected and catagorized as group 'A'. A total of 25 health pregnant women were selected as control and assigned as Group 'B'. 50% study group 'A' and 40% in control group 'B' were of the age group between 20-25yrs. The mean age of group 'A' was 24.5 3±3.62 yrs and it was 26.9±4.86yrs for group 'B'. The chi square test of independence is insignificant (t=1.15) (P=.76). Hence both group 'A' are age matched.

The most of women in group 'A' were unbooked (90%) whereas unbooked women in group 'B' was 68%. The chi-square test of independence is statistically significant (x2=4.13, P=.04). Therefore booked status is significantly higher in group B.

The majority of women in group 'A' (66.6%) as well is in group 'B' (56%) were primi gravida The BMI distribution was statistically Insignificant between the groups (x2=.47, P=.49).Most of women in both the groups were (group A-93.34%), (group B-88%) are overweight.

Table 1: Systolic Blood Pressure Comparison

SBP	N	Mean mmHg	S.D	Independence Sample Test	
				Z value	'P'
A	30	153.33	12.13	6.51	.001
B	25	126	7.07		

Table 2: Diastolic Blood Pressure Comparison

DBP	N	Mean mmHg	S.D	Independence Sample Test	
				Z value	'P'
A	30	99.33	10.8	6.58	.001
B	25	78	4.08		

The mean Systolic blood pressure was 153.33±12.13mmHg in group 'A' whereas it was 126±7.07mmHg in group 'B'. The difference is statistically significant (z=6.51, p=.001). The mean Diastolic blood pressure was 99.33±10.8mmHg in group 'A' and it was 78±4.08mmHg for group 'B' the difference was again statistically significant (Z=5.58, P=.001). Systolic & Diastolic BP have negative weak pearson correlation with serum vitamin D levels in both groups.

Table 3: Comparison of urine albumin in group A

Urine albumin	Group 'A'		Chi square test	
	N	%	Value	'D'
1+	6	19.9	55	.001
2+	16	53.2		
3+	6	19.9		
4+	2	6.6		
Total	30	100		

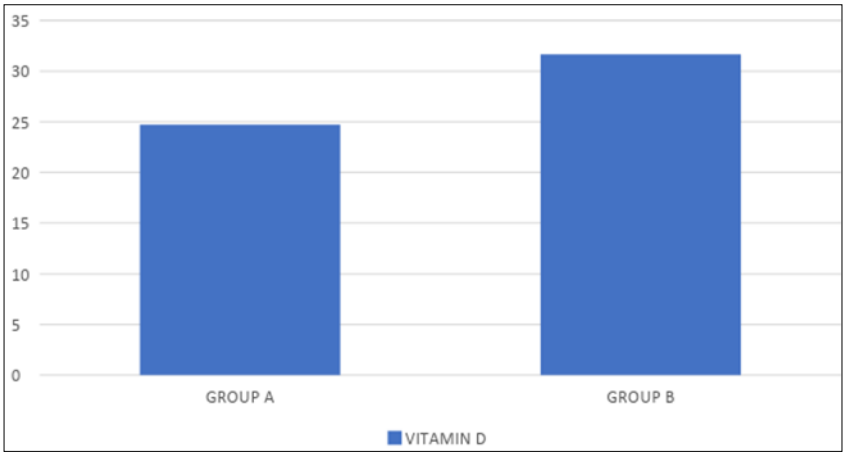
In group 'A' urine albumin was 2+ for 53.28%, 1+ for 19.9%, 3+for 19.9% and 4+ for 6.6%. The chi-square test of independence was statistically significant (Z-55) (P-.001). Therefore, urine albumin was found to be significantly higher in group 'A' than in group 'B'.

Table 4: Comparison of Vitamin 'D' levels

Sr. Vitamin D (Ng/ml)	Group 'A'		Group 'B'		Independent sample test	
	N	%	N	%	't'	'p'
<10(deficient)	-	-	1	4	1.85	.034
10-30 (insufficient)	21	70	15	60		
30-100 (sufficient)	9	30	9	36		
Total	30	54.5	25	45.5		
Mean	24.72		31.02			
S.D	12.49		14.99			

70% of group 'A' women & 60% of group 'B' women were found in sufficient. In the Vitamin D level between 30-100ng/ml sufficient, group 'A' had 30% and group 'B' had 36%.

The Chi-square test of association is statistically significant (x2=1.85, p=.034). The mean Vitamin D of group 'A' was 24.72±12.49ng/ml whereas it was 31.02±14.99ng/ml for group 'B'. The difference is statistically significant (t=-1.85, p=.034).



In group 'A' 49.9% of women had gestational age of greater than 37 weeks whereas most of the women (80%) in group 'B' had gestational age greater than 37 weeks. In group 'A' 43.3% of women had gestational age between 29-36 weeks whereas in group 'B' only 17.4% of women were of gestational age between 29-36 weeks. In group 'A' 6.3% were of gestational age between 20-28 weeks. The chi-square test of association is statistically significant (x2=6.51, p=.03). Hence gestational age of group 'A' is significantly less than group 'B'.

In group 'A' 75% underwent LSCS whereas in group 'B' only 48% underwent LSCS. Normal vaginal delivery was observed on 25% of group 'A' women and 52% of group 'B' women. The chi-square test of independence is statistically significant (x2=4.09, p=.04).

Discussion

The etiopathology of PE/E Still is not clearly understood & complex process. stage-1 off the Two Stage Model [7] of Preeclampsia is the result of failed remodelling of intervillous vessels which leads to reduced placental perfusion & release of toxins (free radicals, oxidizedlipids, cytokines, sVEGFR-1, pro inflammatory transcription nuclear factor (NF-kB), IL-6, ↓VDR, & 1α-hydroxylase) cause endothelial dysfunction ultimately the clinical features of Preeclampsia & eclampsia which is stage 2. The disorder remains a challenge with no preventive therapy & effective treatment is limited to delivery or termination of pregnancy. Our aim is to identify maternal Vitamin d deficiency is linked with ↑ed risk of PE & eclampsia [4-6].

Vitamin D in Pregnancy

Vitamin D is a pleotrophic steroid hormone mainly involved in calcium uptake and bone metabolism [17]. Recent studies show that it is involved in immune function, cell proliferation and disease prevention. Prevalence of Vitamin D deficiency in India is from 15%-80% [8-10]. The human decidua and placenta synthesize 1, 25(OH)D. Low levels of vit D3 impair Th1 to Th2 cytokine balance, affecting the immunological tolerance of embryo implantation, oxidative stress & subsequent development of PE. Vit D deficiency causes SGA & LBW in babies who also suffer from asthma, type1DM, schizophrenia, autism in later life [11].

A study performed in Norway by Haugen *et al*., an increase in 25nmol/L in maternal vit d level gives 63% ↓ incidence of PE with early onset. The risk of PE ↓ by 27% who received vit d in a dose of 400-600IU daily [12].

In our study only single measurement of Vitamin D was done in late pregnancy, after the PE had developed. So evaluation of potential role of vit D during early pregnancy was limited, reverse causality could not be ruled out [14-15]. Preconceptional & pregnancy dietary intake or maternal baseline vit d levels could not be assessed because these patients were admitted at the time diagnosis of PE. In our study out of 6 eclampsia patients one developed HELLP syndrome & two developed pulmonary edema. Even though our study revealed that the vit D status was significantly lower in PE& Eclampsia compared with normotensives [16]. It did not show significant difference between PE/E.

Conclusion

Despite adequate exposure to sunlight throughout the year, vitamin D deficiency is common in our country. Many of our Indian women are in vit D deficient or insufficient state and most of them have insufficient knowledge about importance of vit D in pregnancy & its dietary source. Our study strongly shows that the maternal vitamin D level in sufficient range might play a role in etiology & pathophysiology of PE [18-19]. Adequate vitamin D supplementations during antenatal period may decrease the incidence of PE, eclampsia associated complications of current pregnancy, also with H/O previous pregnancy with preeclampsia [20].

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