

# Correlation between Serum Vitamin D levels and hypertensive disorders in pregnancy in primigravida in third trimester

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## Abstract

**Background:** Hypertension related to pregnancy is a common obstetric complication observed in 7-8% of the antenatal cases in India. Vitamin D is involved in the development of the placenta and feto-maternal wellbeing, thereby helping in prevention of obstetric complication like hypertension in pregnancy. It modulates various biochemical reactions in the body to prevent abnormal placentation preventing pregnancy related hypertension. **Materials and methods:** A cross sectional observational study was conducted on 120 antenatal women between April 2017 – March 2018 in Mahatma Gandhi Medical College and Research Institute. Based on blood pressure, primigravidas were classified as Mild (Group 1) and Severe (Group 2). Investigations for hypertensive disorders of pregnancy and serum Vitamin D were done. Serum Vitamin D levels were classified into deficiency, insufficiency (20-30ng/ml) and sufficiency (30-100ng/ml). Statistical analysis was done using SPSS-17. **Results:** In this study, among the primigravidas with hypertensive disorders of pregnancy 67.5% were Vitamin D deficient, 24.2% had insufficiency and 8.3% had sufficient serum Vitamin D levels. It was also observed that the serum Vitamin D levels were significantly low with an increase in the pre-pregnancy BMI (P value – 0.002) and increase in blood pressure (P value – 0.004). There was significant negative correlation seen between serum vitamin D and blood pressure as we moved from the mild to the severe hypertension group. **Conclusion:** With lower levels of serum vitamin D, more was the severity of hypertension in pregnancy. Obesity was also associated with severe vitamin D deficiency in the present study.

**Keywords:** Hypertensive disorders of pregnancy, Obesity, Exposure to sunlight, Vitamin D

## Introduction

Vitamin D is a precursor for several biochemical reactions in the body and mainly involved in calcium-phosphorus metabolism and mineralisation of the bones. Vitamin D unlike other vitamins does not require daily supplementation; sunlight exposure replenishes the body stores. It is commonly observed when people are subjected to inadequate sunlight exposure, poor dietary habits, bedridden individuals and extremes of age.

Vitamin D is also involved in the development of the placenta and feto-maternal wellbeing, thereby helping in prevention of obstetric complication like hypertension in pregnancy[1]. Hypertension in pregnancy is a common obstetric complication leading to signs like thrombocytopenia, elevated liver enzyme, haemolysis, seizures and bleeding manifestations which account for the high maternal morbidity and mortality. There have been

several studies done to find an association between hypertension related to pregnancy and levels of calciferol in the body. Observations made by Bodnar LM et al and Burris et al have suggested that low calciferol levels have associated with an increased chance of developing gestational diabetes, preterm births and preeclampsia [2,3]. Merewood A et al found association of Vitamin D deficiency with increased rates of caesarean section[4].

Bener A et al studied that hypovitaminosis D was associated with 5 times higher chance of developing hypertension during pregnancy [5]. The risk of the mothers giving birth to neonates which were small for gestation age was also much higher when they had suboptimal Vitamin D levels [6]. Vitamin D has a regulatory action on centrally acting vasodilating agents and has been found to regulate blood pressure. Vitamin D has also been found to modulate various immunological agents and suppress autoimmune antibodies so as to prevent abnormal placentation thereby preventing hypertension related to

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pregnancy [7]. But on the contrary Anupama Dave et al (2016) felt that there was no causal relationship between low vitamin D level and adverse maternal and neonatal outcome in terms of hypertension, anaemia, caesarean section rates, diabetes or bony pain[8]. Hence an effort was made to establish the relationship between serum level of vitamin D in hypertensive disorders in pregnancy and if a correlation exists between the serum level of vitamin D and the severity of hypertensive disorder in pregnancy.

**Aims**

To find the correlation of serum Vitamin D levels with hypertensive disorder in pregnancy.

**Objectives**

1. To estimate the serum Vitamin D levels in primigravida with gestational age 28-40 weeks with hypertensive disorders of pregnancy.
2. To find a correlation between serum Vitamin D levels and severity of hypertensive disorders of pregnancy.

**Materials and Methods**

**Place of study:** Dept. of Obstetrics and Gynecology, Mahatma Gandhi medical college and research institute, Puducherry.

**Type of study:** Cross sectional observation study

**Sampling methods:** Consecutive sample

**Inclusion criteria**

- Primigravida with gestational age between 28-40 weeks.
- Maternal age 19-35 years of age
- Patients diagnosed to have hypertensive disorder in pregnancy

**Results**

This observational comparative study was conducted in the Department of obstetrics and gynaecology, Mahatma Gandhi Medical College and Research Institute, Puducherry. The demographic characteristics are described in Table.1. The total number of participants in the study were n=120. Among the participants, 67.5% had vitamin D deficiency, 24.2% had Vitamin D insufficiency and 8.3% had Vitamin D sufficiency. It was observed that 75% of the studied population had mild hypertension and 25% had severe hypertension based on ACOG 2014 guidelines. In the population studied, 67.5% had Vitamin D deficiency irrespective to the age, exposure to sunlight and first trimester BMI.

Age and exposure to sunlight did not bear any significance to the levels of serum Vitamin D. On comparing the mean serum Vitamin D levels in the three BMI groups, the obese group had significantly lower mean serum vitamin D levels when compared to the over weight and normal groups. On comparing the mean serum Vitamin D levels in the two blood pressure groups, the blood pressure group 2 has significantly lower mean serum vitamin D levels when compared to group 1. (Table.2) Overall, there was a significant negative correlation between serum Vitamin D levels with systolic blood pressure (p value- 0.015), diastolic blood pressure (P value- 0.005) and mean arterial pressure (p value – 0.006) respectively which was statistically significant (p value = 0.015). This implies that with an increase in systolic, diastolic and mean arterial blood pressure levels among primigravida in the third trimester with hypertensive disorders of pregnancy, there is significant reduction in serum Vitamin D levels. (Table.3) In Group 1, there was a significant negative correlation between serum

**Exclusion criteria**

- Patient with diabetes known cases of hypo or hyperthyroidism and auto immune diseases.
- Chronic hypertension

**Sample collection:** Primigravidas were classified as Mild (Group 1) and Severe (Group 2) based on blood pressure [Group 1 - 140/90mm-159/109mm of Hg and Group 2 – greater than and equal to 160/110mm of Hg] as per ACOG guidelines 2014.

Patients with Group 1 form of hypertension were observed for 6 hours after admission and if the blood pressure continues to be  $\geq$ 140/90mm of Hg, they were diagnosed to have hypertensive disorder of pregnancy and were considered for the study.

Among these primigravidas, based on the inclusion and exclusion criteria, informed consent was obtained and single blood sample of 5ml was collected for estimation of serum Urea, serum Creatinine, serum Uric acid, serum Bilirubin, serum Proteins, SGOT, SGPT, ALP, LDH and serum Vitamin D was done by chemiluminescence assay.

Result obtained were analysed. Serum Vitamin D levels were classified into deficiency where value of vitamin D less than 20ng/ml, insufficiency (20-30ng/ml) and sufficiency (30-100ng/ml).

**Statistical methods:** Statistical analysis used Student T test, Chi square test and Pearson's correlation coefficient to compare between two variables.

A p value <0.05 was considered significant.

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Vitamin D levels with systolic blood pressure (P value- 0.032) but not with diastolic blood pressure and mean arterial pressure respectively. In Group 2, there was a significant negative correlation between serum Vitamin D levels with systolic (P value – 0.007) and diastolic blood pressure (p value- 0.002) respectively but not with mean arterial pressure. Fig.1 scatter plot shows a 5% variability in the Vitamin D levels, explained by the linear relationship between systolic blood pressure and Vitamin D. It is seen that 6% of the variability in the Vitamin D levels is explained by the linear relationship between diastolic blood pressure and Vitamin D. (Fig. 2) It is seen that 6% of the variability in the Vitamin D levels is explained by the linear relationship between mean arterial blood pressure and Vitamin D (Fig.3)

**Table-1: Distribution of all variables: (n=120)**

<b>Maternal factors</b>	<b>Characteristics</b>
Age in years - Mean ( $\pm$ SD)	24.9 ( $\pm$ 3.5) years
Exposure to sunlight	
Outdoor workers	14(11.7%)
Indoor workers	106(88.3%)
BMI- Mean ( $\pm$ SD) in kg/m <sup>2</sup>	29.82( $\pm$ 5.75)
BMI- n, (%)	
Normal	25(20.8%)
Overweight	51(42.5%)
Obese	44(36.7%)
POG in weeks - Median(range)	38 (28-40) weeks
<b>Blood Pressure Factors</b>	<b>Characteristics</b>
Systolic in mm of Hg- Mean( $\pm$ - SD)	149.1 ( $\pm$ 10.6) mm of Hg
Diastolic in mm of Hg – Mean( $\pm$ - SD)	95.3 ( $\pm$ 6.7) mm of Hg
Mean arterial pressure (MAP) in mm of Hg – Mean ( $\pm$ - SD)	113.2 ( $\pm$ 7.5) mm of Hg
Blood Pressure group- n, (%)	
Group 1*	90(75%)
Group 2**	30(25%)

\*Group 1 – MILD HYPERTENSION - BP - 140/90 – 159/109 mm of Hg

\*\*Group 2 – SEVERE HYPERTENSION - BP -  $\geq$ 160/110 mm of Hg

**Table-2: Distribution of Serum Vitamin D groups among the other variable groups.**

<b>Variable Groups</b>	<b>N(%)</b>	<b>Vitamin D Deficient N(%)</b>	<b>Vitamin D Insufficiency N(%)</b>	<b>Vitamin D Sufficiency N(%)</b>	<b>P Value</b>
<b>Age group</b>					
<30 years	107	72(67.3%)	28(26.2%)	7(6.5%)	0.152
$\geq$ 30 years	13	11(84.6%)	1(7.7%)	1(7.7%)	
<b>Exposure to sunlight</b>					
<b>Outdoor workers (More exposure)</b>	14	8(57.1%)	4(28.6%)	2(14.3%)	0.513
<b>Indoor workers (Less exposure)</b>	106	75(70.8%)	25(23.6%)	6(5.7%)	
<b>BMI group</b>					
<b>Normal</b>	25	16(64%)	7(28%)	2(8%)	0.002
<b>Overweight</b>	51	34(66.67%)	13(25.5%)	4(7.8%)	
<b>Obese</b>	44	33(75%)	9(20.5%)	2(0.5%)	
<b>Blood pressure group</b>					
<b>Group 1 (Mild)</b>	90	57(63.3%)	25(27.8%)	8(8.9%)	0.004
<b>Group 2 (Severe)</b>	30	26(86.7%)	4(13.3%)	0(0%)	
<b>Total</b>	120	62(62%)	31(31%)	7(7%)	

\*the mean difference is significant at 0.05

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Table-3: Correlations between systolic and diastolic blood pressure and serum Vitamin D levels.

Blood pressure	Vitamin D levels in Group 1 (Mild hypertension)	Vitamin D levels in Group 2 (Severe hypertension)	Vitamin D (Overall)
Systolic - r(p value)	-0.163 (0.032)	-0.328 (0.007)	-0.223 (0.015)
Diastolic - r(p value)	0.013 (0.910)	-0.363 (0.002)	-0.252 (0.005)
Mean arterial pressure	-0.129(0.227)	0.044(0.819)	-0.248(0.006)

'r' is the Pearson's correlation coefficient. \*the mean difference is significant at 0.05

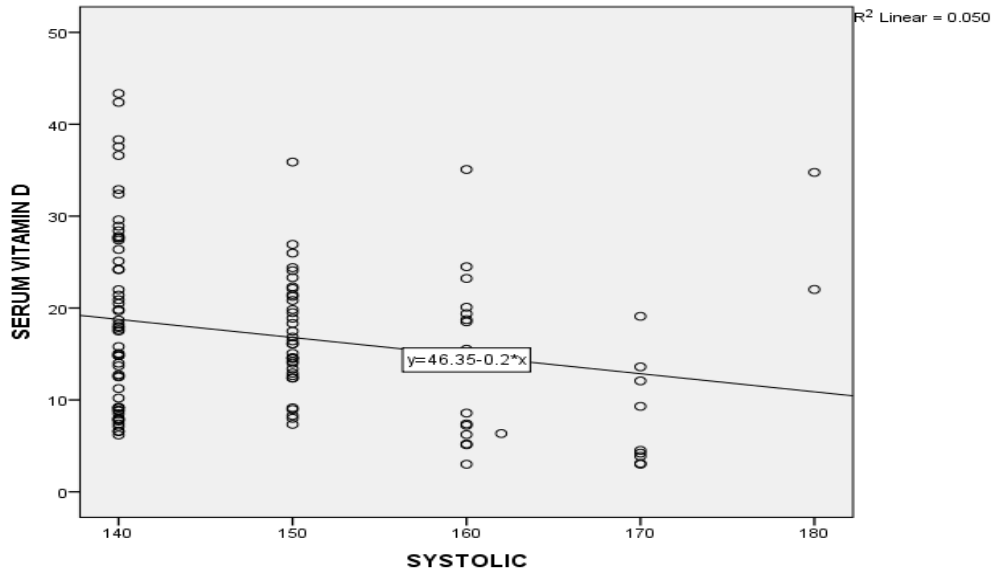


Fig-1: Scatter plot shows the linear relationship between systolic blood pressure and serum Vitamin D levels. N =120

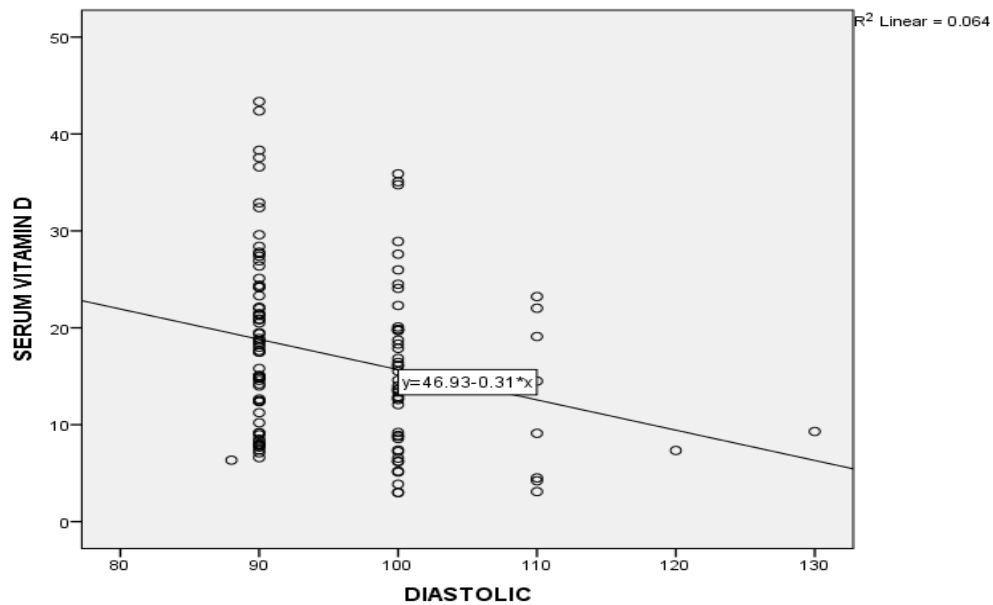
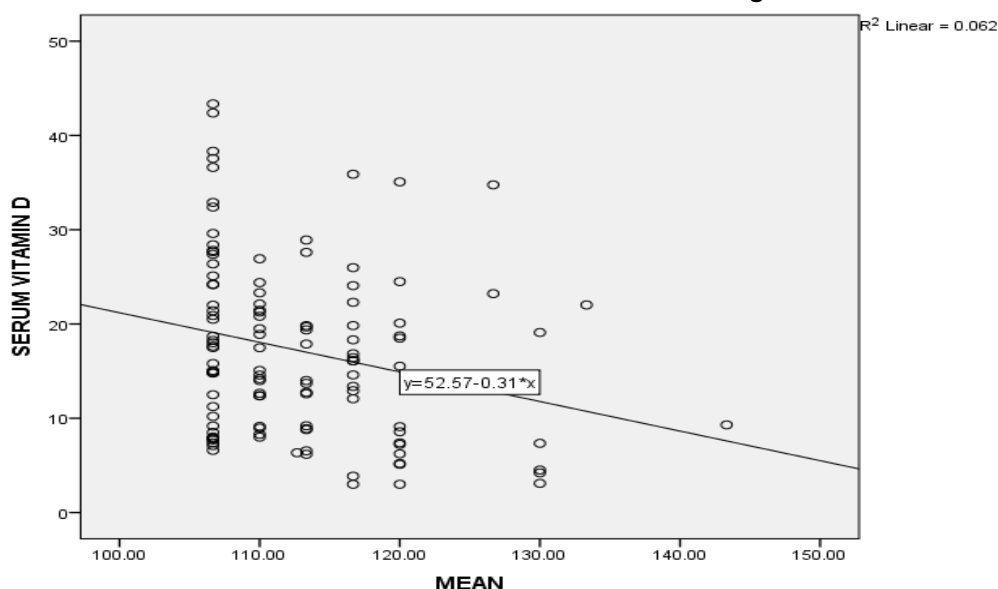


Fig-2: Scatter plot shows the linear relationship between diastolic blood pressure and serum Vitamin D levels. N =120



**Fig-3: Scatter plot shows the linear relationship between mean arterial blood pressure and serum Vitamin D levels. N =120**

### Discussion

The present study was undertaken to establish an association between Vitamin D levels and hypertension in pregnancy in primigravidas between 28 – 40 weeks admitted to Mahatma Gandhi Medical College and Research Institute between April 2017 and Mar 2018. 120 cases who were admitted from the obstetrics and gynaecology OPD with high blood pressures were taken and Vitamin D levels were assessed.

In the present study, it was observed that majority of the subjects had suboptimal levels of serum Vitamin D. Almost 92% of the patients recruited had Vitamin D levels less than 30 ng/ml. In northern India, Jain V et al (2011)[9], Goel P et al (2016)[10], Agarwal S et al (2016) [11] and Kumari et al (2017)[12] observed that the serum levels of Vitamin D of most of their subjects had low values of vitamin D during the last few weeks of gestation. (Table 4) The mean age observed among the cases was 24.9±3.5 years and Vitamin D deficiency was more when the age was greater than and equal to 30 years (84.6%) when compared the population less than 30 years (65.4%). Goel P et al (2016) observed that the mean age among women with hypertensive disorders of pregnancy was 25.48 years and that 83.3% of those subjects were Vitamin D deficient[10] Dave A et al (2017) observed that pregnant women below 30 years of age had higher odds of developing deficiency of Vitamin D compared to the older population[8]. The sunlight exposure was also considered based on the whether the woman’s occupation involved outdoor (more exposure) or indoor (less exposure) work. The number of cases with vitamin D deficiency was compared. In the present study, 88.33% had less exposure to sunlight which suggests that a majority of our patients were involved with indoor work whereas only 11.67% had more exposure. Bener et al observed that 36.6% had more exposure and 63.4% had less exposure [13]. In India, Dave A et al (2016) and Kumari et al (2017) et al observed that 38.1% and 35% had good exposure to sunlight and 61.9% and 65% had less exposure respectively[8,12].

**Table-4: Table showing the distribution of serum Vitamin D levels in the patients in our study when compared to others.**

	Jain V et al (2011)	Goel P et al (2016)	Agarwal S et al (2016)	Kumari et al (2017)	Our study
<b>Vitamin D deficiency</b>	81.1%	92%	83.4%	77.09%	67.5%
<b>Vitamin D insufficiency</b>	11.6%	6%	11.1%	22.91%	24.2%
<b>Vitamin D sufficiency</b>	7.3%	2%	5.53%		8.3%

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In the present study, on the basis of BMI, 36.67% were obese. It was seen that among the obese subjects, 72.7% and 20.45% were Vitamin D deficient and insufficient respectively which was significant (p value - 0.002). Hence an inverse relationship between Vitamin D and BMI was observed which could have been due to the fact that higher levels of body fat hampered vitamin D absorption. It was also seen that the finding from our study was in congruence with several other studies as described. Bodnar et al (2007) also described that among the cases studied, there was an increased rate of subnormal levels of Vitamin D among the obese subjects (p value < 0.05) [14]. Zad ND et al (2014) observed that 38% of their subjects fell under the obese category and that there was a moderate negative correlation (p < 0.001) between BMI and serum levels of Vitamin D during the first trimester [15]. Agarwal S et al (2016) observed in their study that among the obese cases, 100% were Vitamin D deficient [11]. Pena HR et al (2015) observed that among the obese subjects with normal blood pressure, 32.5% were Vitamin D deficient and 47.5% had insufficient Vitamin D levels. But when along with obesity, preeclampsia was also considered, then 47.7% were Vitamin D deficient, 47.7% had Vitamin D insufficient (P value -0.002) [16]. This showed that obesity by itself was an independent risk factor for Vitamin D deficiency but when obese individuals had associated preeclampsia, the risk only worsened.

In the present study, we found that the mean systolic blood pressure was 149.1 ( $\pm$  10.6) mm of Hg and the mean diastolic blood pressure was 95.3 ( $\pm$  6.7) mm of Hg. Among the group 1 subjects (mild hypertension), we found that 91% had suboptimal Vitamin D levels, whereas in group 2 (severe hypertension) 100% of the subjects had suboptimal serum Vitamin D levels (P value < 0.001). The initial research studied the likelihood of development of preeclampsia on the basis of exposure to sunlight as it varies every season. It was proposed that the amount of exposure to sunlight was directly proportional to the Vitamin D produced in the body. Magnus et al (2001) suggested that the chances of developing preeclampsia was more during the winter months like December compared to the summer due to lesser exposure to sunlight during the winter [17].

Whereas Algert et al (2010) had a different concept as he felt that the amount of sunlight exposure mattered more around the time of delivery which decreased the odds of developing preeclampsia and not around conception. Algert et al also felt that the prevalence of preeclampsia was less in less among those who conceived in autumn compared to spring [18]. The studies conducted later emphasised more on the circulating serum levels of Vitamin D in the body along with sunlight exposure to include the groups who were at risk of developing Vitamin D deficiency. Bodnar et al (2007 and 2014), Aghajafari et al (2009), Robinson et al (2010), Bener et al (2013) and Hyppönen et al (2014) studied the relationship between serum Vitamin D levels and various maternal outcomes comparing similar parameters in different parts of the world. They all arrived at similar conclusions wherein they observed that suboptimal Vitamin D in mothers can lead to gestational diabetes mellitus, various forms of hypertensive disorders of pregnancy and pregnancy induced anaemia [19,20,21,5,6]. Aghajafari et al (2009) and Gernand et al (2014) studied the neonatal outcomes along with the maternal complications and concluded that maternal Vitamin D deficiency had a higher risk of preterm infants and babies which were small for the gestational age (SGA) [20,6]. Robinson et al (2010) and Bodnar et al (2014) noted that their cases with severe preeclampsia were associated with extremely low levels of vitamin D.

The former observed that 54% and 22% was Vitamin D deficient and insufficient respectively (p value - 0.005); they also observed that a 10 ng/mL increase in Vitamin D was associated with a 63% less chance of developing preeclampsia [21]. Whereas the latter observed that when patients attained Vitamin D of more than 50nmol/L, there was a 40% less chance in developing severe preeclampsia [2]. Bakacek Murat et al (2015) studied the Vitamin D with respect to the severity of hypertensive disorders of pregnancy but obtained no significant difference between the mild and the severe forms although there were statistically significant findings when compared to the controls [23]. When compared to our study, similar findings were reported by Kumari et al (2017) in northern India such that in cases with mild and severe preeclampsia, 95% and 100% had suboptimal Vitamin D levels respectively with a combined p value of < 0.05. They also found a negative correlation between Vitamin D at term and blood pressure with a significant P value [12]. But contrary to all the above mentioned studies, Dave A et al in a study conducted in northern India concluded that their study showed no causal relationship between suboptimal Vitamin D levels and maternal or neonatal complications [8].

**Conclusion**

Based on our results, it can be concluded that there is a significant negative correlation between the serum vitamin D levels and hypertensive disorders in pregnancy. The lower the serum vitamin D levels, more is the severity of hypertension in pregnancy. It was also

observed that obesity is associated with severe vitamin D deficiency which is evident from the drop in serum vitamin D levels as we move from the normal to the obese BMI group. Hence there is a need for supplementation of calciferol during pregnancy in order to reduce the risk of

serious maternal or neonatal outcome. Proper guidelines which can recommend the apt dosage of supplementation when vitamin D deficiency is diagnosed at different periods of gestation is required.

#### Author contributions:

**Dr. Ashwin Rao** is the principal investigator who conducted the study.

**Dr. Seetesh Ghose** guided the principal investigator during the process of the study.

**Dr. Setu Rathod** helped the principal investigator in the process of the study and manuscript preparation.

We are grateful to all the patients for their cooperation during the study process.

**Scope for knowledge:** Vitamin D deficiency is a predisposing factor for hypertensive disorders of pregnancy, gestational diabetes mellitus, preterm births and various adverse obstetric outcomes. We were able to correlate the grade of Vitamin D deficiency with the severity of hypertensive disorders of pregnancy. This study also opens the scope for other studies to come up with guidelines for proper supplementation of Vitamin D right from the preconceptional period to prevent adverse obstetric outcomes.

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**Permission from IRB:** Yes

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