

## Research Article

# Vitamin D Deficiency during Pregnancy and its Relationship with Pre-Eclampsia, Eclampsia and Gestational Hypertension

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**Abstract**

**Objective:** To assess frequency of vitamin D deficiency during pregnancy and its relationship with Pre-eclampsia, Eclampsia and Gestational Hypertension.

**Methods:** A case control study was conducted between Jan to Dec 2014 at Abbasi Shaheed hospital, Karachi. It included 104 pregnant women with singleton fetus at or after 24 weeks gestation, 52 women with Pre-eclampsia, Eclampsia and Gestational Hypertension and 52 controls matched for age, gestation, gravidity and socio-economic status. Serum Vitamin D level was assessed after informed consent.

Data entry was on SPSS 17 and statistical tests chi square and t test were applied.

**Results:** All 104 participants had subnormal Vitamin D levels (<30 ng/ml), 2(1.92%) had Vitamin D insufficiency (21-29 ng/ml) and 102(98%) had Vitamin D deficiency (<20 ng/ml). Of the total, 71(75.96%) had severe deficiency (<10 ng/ml). Mean Vitamin D level was 6.78 in cases and 9.43 in controls (p 0.002). Vitamin D level <10 ng/ml was seen in 86.5% hypertensive's and 65.4% controls, values between 10-29 ng/ml were noted in 13.5% hypertensive's and 34.6% controls (p 0.012;OR 3.403). Vitamin D deficiency was associated with Pre-eclampsia/Eclampsia (p=0.045; OR 3.706) and Gestational Hypertension (p=0.025; OR 4.235).

**Conclusion:** Severe Vitamin D deficiency is common in pregnant Pakistanis and is associated with hypertensive disorders of pregnancy.

**Keywords:** Vitamin D deficiency; Pre- Eclampsia; Eclampsia; Gestational Hypertension; Pakistan

## Introduction

In the face of rampant worldwide Vitamin D deficiency [1] and its frightening implications [2], research in this field continues relentlessly.

Vitamin D is a fat soluble vitamin which plays a very important role in bone mineralization. However, low levels of Vitamin D have been associated not only with Osteoporosis but with Coronary artery disease, Diabetes, obesity and cancer [2]. In pregnancy, Vitamin D status is important for maternal and fetal health. A fall in serum Vitamin D during pregnancy results in poor fetal bone mineralization as early as 19 weeks gestation [3].

Our previous work on urban Pakistani pregnant women revealed that 78% women were Vitamin D deficient and 88% of the newborns were deficient at birth [4].

Hypertension complicates 6 to 12% of all pregnancies whereas Pre-eclampsia occurs in one out of every 10 primigravidae [5]. In the UK, 5/1000 maternities are complicated with severe Pre-eclampsia and 5/10,000 maternities have Eclampsia [6]. These are serious conditions associated with high maternal and fetal mortality particularly in the developing world where pregnant women are already compromised

by health issues such as poor nutrition and anemia. Much research has been done to determine the pathophysiology of hypertensive disorders in pregnancy, but exact etiology is still unclear. It seems that it results from inadequate placental perfusion that causes the placenta to release chemicals and toxins in maternal circulation that damage the endothelial lining of blood vessels [5,7]. Apart from known risk factors such as stress, obesity, diabetes, and advanced age, low antioxidants, variations in trace metals and electrolyte disturbances have been linked with the pathogenesis of pre eclampsia [8,9].

It has been proposed that Vitamin D influences pathways instrumental in pathogenesis of Pre eclampsia and low levels of this vitamin in early and mid pregnancy are associated with subsequent development of Pre eclampsia [10,11] whereas other studies have demonstrated no difference in occurrence of hypertensive disorders of pregnancy with low Vitamin D levels [12].

Hypertension is one of the leading causes of maternal mortality worldwide [13] but few effective preventive strategies for these conditions are available. Demonstration of a link between Pre eclampsia and Vitamin D levels will open up a pathway for prevention of hypertension in pregnancy.

**Table 1:** Study Characteristics of the participants.

	Cases (n=52)	Controls (n=52)	P-value
Age, years	28.73 ±4.36	28.71 ±4.37	0.980
Gestational Age, weeks	35.26 ±2.15	36.11 ±2.19	0.050
Gravida	2.38 ±1.03	2.38 ±1.03	0.999
Housewife	29 (43.9%)	37 (56.1%)	0.146
SBP, mmHg	154.8 ±15.3	108.3 ±9.1	0.001
DBP, mmHg	96.3 ±7.4	71.9 ±6.9	0.001
Hb, mg/dL	9.3 ±1.5	9.4 ±1.5	0.657
Vitamin D Level, ng/mL	6.78 ±3.55	9.43 ±4.86	0.002

\*Presented in n (%), numeric data presented in mean ±SD, chi-square for categories and independent t -test for mean difference was used to calculate the p-values.

This study aims to assess the frequency and severity of Vitamin D deficiency in pregnant Pakistani women and explore the association of vitamin D deficiency and pregnancy hypertensive disorders in an urban population of Karachi. The ultimate aim is correction of vitamin D deficiency in a timely manner, thus reducing the morbidity and mortality of hypertension in pregnancy.

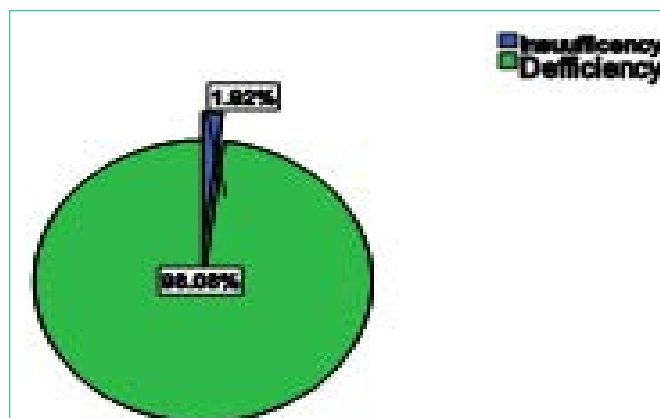
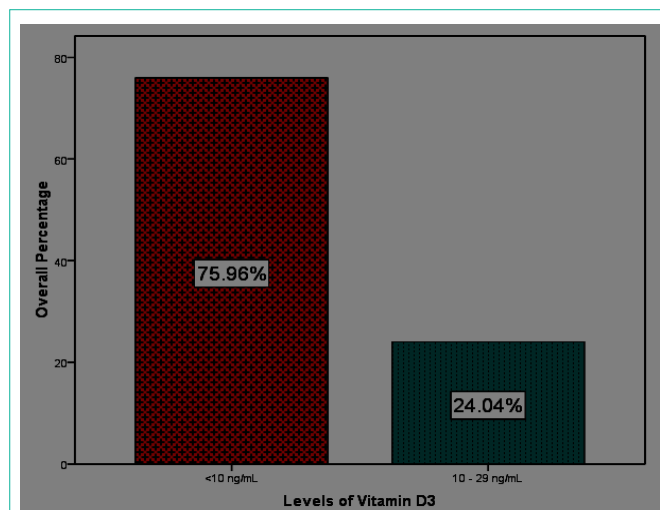
## Materials and Methods

The study was conducted in the Obstetrics and Gynecology Department of Karachi Medical Dental College and Abbasi Shaheed Hospital, a tertiary care public sector hospital catering mostly to the poor population of Karachi. It was an observational case control study. From Jan 2014 to Dec 2014, 104 pregnant women fulfilling the entry criteria and with singleton fetus at 24 or more weeks gestation were enrolled. These included both antenatal and intrapartum women attending the hospital. Written informed consent was obtained. 52 cases enrolled were women affected by Gestational Hypertension, Pre eclampsia or Eclampsia as per standard definition [5]. For each case, a non hypertensive control was chosen of the same age group, gestational age, gravidity and socio economic status. Ages were grouped as <20, 20 to 25 years, 26 to 30 years, 31 to 35 years, 36 and above. Gestational age groups were 24 to 28 weeks, 29 to 32 weeks, 33 to 36, 37 to 40 and >40 weeks confirmed by early scan. Gravidity was matched exactly. All women at the hospital belonged to the same socio economic status with monthly per capita income of Rs.3000-5000 per family member.

Exclusions included women with co-morbidities such as essential or pre existing hypertension, diabetes, thyroid disease, renal disease or any other medical illness, and multiple pregnancy.

Data collection proforma included demographic and other data, i.e., age, height, weight, occupation, socio economic status, gravidity and gestation age. The BP of each participant was recorded three times and average noted. In addition to routine investigations such as Complete Blood Count and Hypertension profile (if indicated), venous blood sample was drawn for 25 (OH) vitamin D analysis by radioimmunoassay. In accordance with our previous work, maternal Vitamin D level >30 ng/ml was regarded as normal, 21-29 ng/ml insufficient and <20 ng/ml deficient [4]. For the purpose of analysis, a level <10 ng/ml was considered severe deficiency.

Data entry was done on SPSS17 and statistical tests chi square for categories and independent t test for mean difference were used.

**Figure 1:** Vitamin d status amongst the study population (n=104).**Figure 2:** Level of vitamin d deficiency in study population (n=104).

The study was approved by the institutional Ethical Review Board prior to commencement.

## Results

Total 104 pregnant women attending the Abbasi Shaheed hospital for antenatal and intrapartum care enrolled in the study. Demographical characteristics of participants are shown in Table 1. The mean age of cases was 28.73 and controls 28.71, average gestational age of cases 35.26 and controls 36.11. Gravidity was same in both groups i.e., 2.38. 29 (43.9%) cases and 37 (56.1%) controls were housewives. Mean systolic and diastolic blood pressures were 154.8 and 96.3 mm Hg respectively in cases, whereas systolic and diastolic blood pressures were 108.2 & 71.9 mm Hg respectively in controls. Mean Haemoglobin level was 9.25 in cases and 9.38 in controls. All participants belonged to the same socio-economic class.

Mean Vitamin D level in cases (n= 52) was 6.78 ng/ml and in controls (n=52) was 9.43 ng/ml, p value 0.002.

None of the 104 participants had normal Vitamin D levels (>30 ng/ml). Only 2 (1.92%) had Vitamin D insufficiency (21-29 ng/ml) and 102 (98.08%) had Vitamin D deficiency (<20 ng/ml) (Figure 1). Overall 71 (75.96%) patients were severely deficient (Vitamin D level

<10 ng/ml) and 33 (24.04%) belonged to mild to moderate Vitamin D deficient group (10-20 ng/ml) (Figure 2).

Severe Vitamin D deficiency was seen in 45 (86.5%) cases and in 34 (65.4%) controls and difference was found significant (p-value 0.012; OR3.403). Values between 10-29 ng/ml were seen in 7(13.5%) hypertensives and 18(34.6%) controls (Table 2).

One of the hypertensives was excluded from further analysis as patient refused urinalysis and differentiation between Pre-eclampsia and Gestational Hypertension was uncertain. The remaining 51 hypertensive population of the study comprised of 27 with Gestational Hypertension and 24 with Pre-eclampsia and Eclampsia. On stratification of severity of Vitamin D deficiency between cases and controls (Table 3), a statistically significant association was seen between severity of Vitamin D deficiency and Gestational Hypertension (p-value 0.025; OR4.235) as well as between Vitamin D deficiency and Pre-eclampsia/Eclampsia (p-value 0.045; OR3.706). 88.9% of Gestational Hypertensives and 87.5% of pre Eclampsia/Eclampsia had severe deficiency whereas 65.4% of controls had severe Vitamin D deficiency.

## Discussion

Considering the high prevalence of Vitamin D deficiency globally [1] and its suggested association with hypertensive disorders of pregnancy [10,11] it was considered relevant to assess this relationship in Pakistan where hypertension in pregnancy is a major contributor to maternal mortality [14].

The study enrolled women attending the Abbasi Shaheed hospital, Karachi, for antenatal and Intrapartum care. This tertiary care center caters to the underprivileged community of Karachi and majority of Obstetric patient's book late for antenatal care. Uncontrolled hypertension is therefore more common than in other centers of Karachi. Our previous work revealed that 78% pregnant women delivered at this hospital had subnormal Vitamin D [4] as in the previous study, 25 hydroxy vitamin D level in blood was measured for this analysis.

The results indicate rapidly worsening frequency and severity of Vitamin D deficiency in pregnant women of Karachi. In comparison to earlier study [4] where 22% women were Vitamin D sufficient and 32% insufficient, in this study, none were found to be sufficient and only 1.92% had Vitamin D insufficiency. As the vast majority (98%) were deficient, these were further categorised as severely deficient (<10 ng/ml) and deficient (10-20 ng/ml) for the purpose of analysis.

The fact that almost 70% of the study population had severe Vitamin D deficiency in this study is a matter of concern. Previous data suggests that maternal Vitamin D deficiency predisposes to Pre Eclampsia, [10,15] particularly if it persists into mid gestation [16]. In a case control study, nulliparous women who were Vitamin D deficient in early pregnancy subsequently developed pre-eclampsia [10]. Our study differs from previous data as we adjusted confounders amongst cases and controls such as age, gravidity and gestational age. Pregnancies at or beyond 24 weeks with no risk factor for Preeclampsia were chosen and those with known hypertension and medical illnesses excluded. All women belonged to low socio economic status and were mildly anemic.

**Table 2:** Degree of vitamin d deficiency in cases & controls.

	Group of Patients		P-value	Odds Ratio
	Cases (n=52)	Controls (n=52)		
<b>Vitamin D Level</b>				
<10 ng/mL	45 (86.5%)	34 (65.4%)	0.012	3.403
10-29 ng/mL	7 (13.5%)	18(34.6%)		

**Table 3:** Association of vitamin d deficiency with gestational hypertension and pre-eclampsia/eclampsia.

	Vitamin D Deficiency Groups		P-value	Odds Ratio
	<10 ng/mL	10-29 ng/mL		
<b>Cases (Gestational Hypertension), n=27</b>	24 (88.9%)	3 (11.1%)	0.025	4.235
<b>Controls, n=52</b>	34 (65.4%)	18 (34.6%)		
<b>Cases (Pre-eclampsia/Eclampsia), n=24</b>	21 (87.5%)	3 (12.5%)	0.045	3.706
<b>Controls, n=52</b>	34 (65.4%)	18 (34.6%)		

To our knowledge, Vitamin D deficiency has not been linked with occurrence of Gestational Hypertension. Exploration of this link seems valid too as all hypertensive disorders carry high risk of maternal mortality [17] and can be superimposed with Pre Eclampsia, a much more dangerous condition.

Results of this study clearly indicate a statistically significant relationship between severe Vitamin D deficiency and hypertension in pregnancy highlighting the importance of the problem. As prior work has related maternal Vitamin D status with Pre Eclampsia predominantly [10,13,11], we attempted to analyze deficiency of this important vitamin in the 2 major categories of hypertension in pregnancy. Severity of Vitamin D deficiency is significantly associated both with Gestational Hypertension and with Pre eclampsia/Eclampsia in this analysis inspite of few numbers. A larger group study will further clarify the association.

It remains clear that Vitamin D levels are crucial in pregnancy with relevance to maternal hypertension and its life threatening sequelae. Considering the significance of Vitamin D deficiency, recommendations for normal intake of this vitamin in pregnancy have been modified in the Developed World [18]. Dedicated serious intervention prior to and during pregnancy is required in the developing world also in order to reduce maternal hypertension, morbidity and death.

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