

Association of Hypovitaminosis D with Hypertensive Disorder of Pregnancy

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ABSTRACT

Background: Pregnancy related hypertensive disorders have devastating outcome of pregnancy and cause many obstetrical complications during or after pregnancy. Hypovitaminosis D has been observed in many pregnant females having pregnancy induced hypertension. **Study Design:** Case control study. **Settings:** Department of Obstetrics & Gynecology, Lahore General Hospital, Lahore-Pakistan. **Duration:** 3 months from January 01, to March 30, 2019. **Methodology:** This Case control study was conducted at Department of Obstetrics & Gynaecology, for 6 months. Sample size of 100 patients were enrolled in the study through Non-Probability, Consecutive Sampling. Patients of age 18-40years, presented >24 weeks of pregnancy were included Then blood sample was taken and vitamin D level was noted. If level <20ng/ml, then hypovitaminosis D was labeled. Odds ratio was calculated and if OR>1, then significant association was considered. **Results:** The mean age of cases was 26.08±4.29years and mean age of controls was 29.84±2.96years. The mean gestational age of cases was 32.58±9.63weeks and controls presented at 36.71±10.11weeks. Mean serum vitamin D level was 24.9±7.72ng/ml among cases while 39.07±11.14ng/ml among controls. The difference was significant (p<0.0001). The hypovitaminosis D was observed in 43 (86%) cases while in 10 (20%) controls. The odds ratio was calculated as 24.57 (5% CI: 8.534 – 70.745, p<0.0001), which showed significant association of hypovitaminosis D with hypertensive disorder of pregnancy. **Conclusion:** There is significant association of hypovitaminosis D detected with preeclampsia or pregnancy induced hypertension in our study.

Keywords: Vitamin D deficiency, Hypovitaminosis D, Preeclampsia, Pregnancy induced hypertension, Blood pressure, Proteinuria.

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INTRODUCTION

Preeclampsia is still one of the major causes of maternal mortality in developed countries with an incidence of 15%-20%.¹ In Pakistan, preeclampsia was present in 21% pregnancies.² The prevalence of vitamin D insufficiency ranges from 9.3-41.4%, while vitamin D deficiency ranged 22.7-90.3% in pregnant females.³ Supplementation with a balanced protein and energy diet does not appear to reduce the risk of preeclampsia. Further, there is no evidence that changing salt intake has an effect.⁴ Supplementation with antioxidants such as vitamin C, D and E has no effect on pre-eclampsia incidence therefore, supplementation with vitamins C, E, and D is not recommended for reducing the risk of pre-eclampsia.⁴

Vitamins are chemicals that are needed by your body for good health. They are vital for everyone and ensure that body works well, is able to fight illness and heal well. Vitamin D deficiency during pregnancy has been linked with a number of serious short- and long-term health problems in offspring, including impaired growth, skeletal problems, type 1 diabetes, asthma, and schizophrenia. Yet few investigators have explored the role of maternal vitamin D status in adverse pregnancy outcomes.⁵ Vitamin D deficiency is highly prevalent in women of reproductive age and in pregnant mothers.⁶ If proven effective, the population level benefits of vitamin D supplementation would be substantial and likely to impact the long-term health of offspring.⁷ The association between maternal vitamin D supplementation and status with the risk of preeclampsia was

consistent across different types of studies, with evidence for benefits in prospective observational studies as well as in clinical trials. Two recent meta-analyses of observational studies also support an association between maternal serum 25(OH)D levels and preeclampsia.^{8,9}

The aim of the study is to determine the association of hypovitaminosis D with hypertensive disorder of pregnancy in females presenting in third trimester. It has been observed that in literature that there is significant association of hypovitaminosis D with hypertensive disorder of pregnancy and preeclampsia is a hazardous complication of pregnancy which may lead to severe morbidities and mortality of pregnant female as well as the fetus. With changing lifestyle and less screening of vitamin D in routine increases the chances of hypertensive disorder of pregnancy and preeclampsia which lead to complications of pregnancy. So, we want to conduct this study to attain the local evidence and implement the screening of pregnant females for vitamin D level in order to prevent hypertensive disorder of pregnancy / preeclampsia.

The objective of the study was to determine the association of hypovitaminosis D with hypertensive disorder of pregnancy in females presenting in third trimester.

METHODOLOGY

Study Design: Case control study.

Settings: Department of Obstetrics & Gynecology, Lahore General Hospital, Lahore-Pakistan.

Duration: 3 months from January 01, to March 30, 2019.

Sample Technique: Non-Probability, Consecutive Sampling.

Sample Size: Data of 100 females is calculated with 95% confidence level, 8.5% margin of error and taking expected percentage of hypovitaminosis D i.e. 22.7% in pregnancy in third trimester.

Inclusion Criteria: Patients of age 18-40years, presented >24 weeks of pregnancy were included. Cases were those females who had pregnancy induced hypertension (BP≥140/90mmHg) or preeclampsia (BP≥140/90mmHg along with proteinuria ≥+1 on dipstick method).

Exclusion Criteria: Controls were the females without hypertension. Chronic conditions including diabetes, chronic hypertension, renal dysfunction, bleeding disorders, females already taking vitamin supplements, anemia were excluded.

Data Collection Procedure: 100 patients fulfilling the above-mentioned inclusion criteria were enrolled in this study from OPD. Informed consent was obtained and patient demographic information was recorded. Then blood pressure was noted at presentational and proteinuria was assessed by using dipstick method. Patients were divided in two groups on the basis of blood pressure i.e. cases with hypertension and controls with normal blood pressure. Then blood sample was taken through a 5cc disposable syringe and sent to the laboratory of the hospital of assessment of vitamin D level. Reports were assessed and vitamin D level was noted. If level <20ng/ml, then hypovitaminosis D was labeled. Females with hypovitaminosis D were managed as per standard protocols. Data was recorded on proforma and analyzed by using SPSS version 22. Odds ratio was calculated and if OR>1, then significant association was considered.

RESULTS

The mean age of cases was 26.08±4.29years and mean age of controls was 29.84±2.96years. The mean gestational age of cases was 32.58±9.63weeks and controls presented at 36.71±10.11weeks. There were 23 (46%) primigravida, 27 (54%) multigravida (1-4) and 0 (0%) grand multigravida among cases while 14 (28%) primigravida, 34 (68%) multigravida (1-4) and 2 (4%) grand multigravida among controls. Among cases, 24 (48%) were primiparous and 26 (52%) were multiparous while among controls, 14 (28%) were primiparous and 36 (72%) were multiparous. Table 1

Table 1: Demographics of patients

		Group	
		Case	Control
n		50	50
Age (years)		26.08±4.29	29.84±2.96
Gestational age (weeks)		32.58±9.63	36.71±10.11
Gravida	Primigravida	23 (46%)	14 (28%)
	Multipara	27 (54%)	34 (68%)
	Grand multipara	0 (0%)	2 (4%)
Parity	Primiparous	24 (48%)	14 (28%)
	Parity 1-3	26 (52%)	36 (72%)

The mean SBP of cases was 166.6±22.78mmHg while 115.20±9.53mmHg for controls. The mean DBP of cases was 102.8±8.27mmHg while 72.8±6.07mmHg for controls. Among cases, proteinuria was 1+ in 4 (8%) cases, 2+ in 23 (46%) cases, 3+ in 12 (24%) cases while nil in 11 (22%) cases. Among controls, proteinuria was nil in all cases (100%). Among cases, pregnancy induced hypertension was observed in 11 (22%) cases while 39 (78%) had preeclampsia. Mean serum vitamin D level was 24.9±7.72ng/ml among cases while 39.07±11.14ng/ml among controls. The difference was significant (p<0.0001). Table 2

Table 2: Hemodynamics of patients

	Group	
	Cases	Control
n	50	50
Blood pressure (mmHg)		
SBP	166.6±22.78	115.20±9.53
DBP	102.8±8.27	72.80±6.07
Proteinuria		
+	4 (8%)	0 (0%)
++	23 (46%)	0 (0%)
+++	12 (24%)	0 (0%)
Nil	11 (22%)	50 (100%)
Type of hypertensive disorder		
Pregnancy induced hypertension	11 (22%)	Nil
Preeclampsia	39 (78%)	
Serum vitamin D level (ng/ml)	24.9±7.72	39.07±11.14*

* = p-value < 0.0001 (Significant)

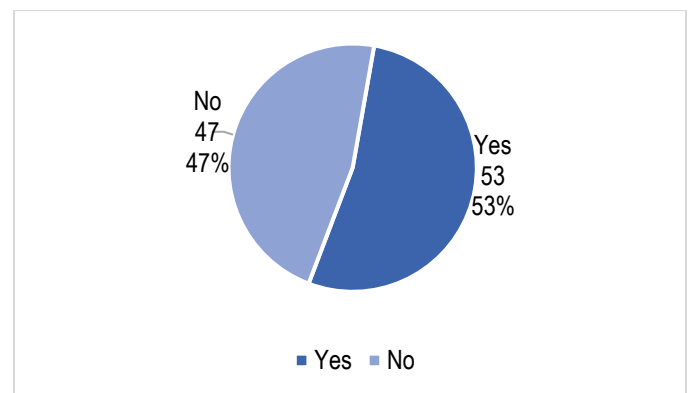


Fig 1: Hypovitaminosis D

The hypovitaminosis D was observed in 43 (86%) cases while in 10 (20%) controls. The odds ratio was calculated as 24.57 (5% CI: 8.534 – 70.745, p<0.0001), which showed significant association of hypovitaminosis D with hypertensive disorder of pregnancy. Table 3

Table 3: Association of hypertensive disorder of pregnancy with hypovitaminosis D

Hypovitaminosis D	Group	
	Case	Control
Yes	43 (86%)	10 (20%)
No	7 (14%)	40 (80%)
Total	50 (100%)	50 (100%)

Odds ratio = 24.57 (95% CI: 8.534 – 70.745, p-value < 0.0001)

DISCUSSION

The exact mechanism of how preeclampsia worsen maternal and fetal outcome remains to be elucidated. Uncontrolled inflammation, typical of preeclampsia, might be related to the development of intrauterine pathologies.¹⁰

Risk factors for pre-eclampsia include obesity, prior hypertension, older age, and diabetes mellitus. It is also more frequent in a woman's first pregnancy and if she is carrying twins. The underlying mechanism involves abnormal formation of blood vessels in the placenta amongst other factors. Most cases are diagnosed before delivery.

Rarely, pre-eclampsia may begin in the period after delivery. While historically both high blood pressure and protein in the urine were required to make the diagnosis, some definitions also include those with hypertension and any associated organ dysfunction. Blood pressure is defined as high when it is greater than 140 mmHg systolic or 90 mmHg diastolic at two separate times, more than four hours apart in a woman after twenty weeks of pregnancy. Pre-eclampsia is routinely screened for during prenatal care.¹¹⁻¹⁴

In our study, the hypovitaminosis D was observed in 43 (86%) cases while in 10 (20%) controls. The odds ratio was calculated as 24.57 (5% CI: 8.534 – 70.745, p<0.0001), which showed significant association of hypovitaminosis D with hypertensive disorder of pregnancy. In a study by Mere wood et al, the risk of preeclampsia was 5-fold increased among women with 25(OH)D levels below 15 ng/mL at a pregnancy duration of up to 22 weeks.¹⁵ Similarly, Powe et al. reported that first-trimester 25(OH)D levels of less than 15 ng/mL were related to the development of preeclampsia.¹⁶ In a case-control study, women with early-onset (before 34 weeks) severe preeclampsia displayed lower serum 25(OH)D levels (median 18 ng/mL, IQR 13–31 ng/mL) than did healthy controls (median 32, IQR 20–44 ng/mL).¹⁷

One study has reported that there was a significant increase in the risk of pre-eclampsia among those with vitamin D (25(OH)D) level <50nmol/l compared with those without at 24–26 weeks of gestation (8.1% versus 2.5%, P = 0.001).¹⁸ One more study has reported that there was a significant increase in the risk of pre-eclampsia among those with vitamin D (25(OH)D) level <50nmol/l compared with those without at 24–26 weeks of gestation (58.9% versus 33.8%, P = 0.001).¹⁷ But another study reported that there was an insignificant increase in the risk of pre-eclampsia among those with vitamin D (25(OH)D) level

<50nmol/l compared with those without at 24–26 weeks of gestation (1.67% versus 1.2%, P = 0.6947).¹⁹

A new study finds that women who develop severe preeclampsia tend to have lower blood levels of vitamin D than healthy pregnant women raising the possibility that the vitamin plays a role in the complication. Preeclampsia rates are elevated during winter months, when sunlight-dependent 25(OH) D productions are reduced. Vitamin D supplementation reduces preeclampsia risk, compared to unsupplemented controls.²⁰

Two clinical trials support a potential role of vitamin D in the prevention of preeclampsia, although neither of these treated with vitamin D supplements alone. In an uncontrolled trial, supplementation with a multivitamin/mineral supplement and halibut liver oil (containing 900 IU/d vitamin D) provided at 20 wk gestation reduced the odds of preeclampsia by 32% (95% CI, 11–47%). Vitamin D supplementation in early pregnancy should be explored for preventing preeclampsia and promoting neonatal well-being.²¹

Two clinical trials support a potential role of vitamin D in the prevention of preeclampsia, although neither of these treated with vitamin D supplements alone. In an uncontrolled trial, supplementation with a multivitamin/mineral supplement and halibut liver oil (containing 900 IU/d vitamin D) provided at 20 wk gestation reduced the odds of preeclampsia by 32% (95% CI, 11–47%). Vitamin D supplementation in early pregnancy should be explored for preventing preeclampsia and promoting neonatal well-being.²¹

CONCLUSION

Though this study, we found significant association of hypovitaminosis D detected with preeclampsia or pregnancy induced hypertension. Now, we have got the local evidence and now we recommend the females for regular antenatal check-up during pregnancy and screening for vitamin D levels in order to balance vitamin D level in blood and prevent preeclampsia or hypertensive disorders in pregnancy.

LIMITATIONS

Study was carried out on hundred females; fifty in each group. However, authenticity of results can improve with larger sample size and more findings can be elaborated. Only one vitamin level was checked in this study, but not the other vitamins during pregnancy which may also associated with preeclampsia. Also females were not followed-up for prolonged time till delivery, as that was not part of study and obstetrical outcome with Hypovitaminosis D was also not observed.

SUGGESTIONS / RECOMMENDATIONS

Further studies can be done on larger sample size to obtain more authentic results. Other vitamins should also be screened during pregnancy in order to find the association of preeclampsia with other vitamins as well. Females with Hypovitaminosis D can be followed-up for prolonged time till delivery, and obstetrical outcomes with Hypovitaminosis D can also not observed.

CONFLICT OF INTEREST / DISCLOSURE

No conflict of interest to be declared by any author involved in the research.

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