Original Article

Association of Maternal Serum Vitamin D Level with Preeclampsia

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ABSTRACT

Objective: To determine the relationship between pre-eclampsia and maternal serum vitamin D levels.

Study Design: Case control Study

Place and Duration of Study: This study was conducted at the department of Obstetrics and Gynae Unit- 2, DUHS, OJHA, Karachi from 10th December, 2021 to 10th May, 2022.

Materials and Methods: This study was conducted on 162 pregnant patients between the age 18 to 35 years having singleton pregnancy greater than 20 weeks. Patients were divided in two groups, group A comprised of cases i.e. women with preeclampsia and group B were controls i.e. normotensive pregnant women. The relationship of maternal serum vitamin D was determined among cases and control groups. Patients with multiple gestations, fetal anomaly, diabetic and already taking vitamin D were excluded.

Results: This study was conducted on 162 patients divided in two groups, cases and controls. The mean age in group A was 26.65±4.71 years 27.10±5.73 years in group B. In group A 68 (84%) patients had vitamin D deficiency and in group B 45 (55.6%) patients had vitamin D deficiency. The association was statistically significant.

Conclusion: Our study concludes that there is a relationship between Vitamin D levels and preeclampsia. Vitamin D deficiency was found in 84% patients in case group and 55.6% in control group. The difference was significant statistically (P = 0.0001)

Key Words: Preeclampsia, Vitamin D deficiency, Normotensive

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INTRODUCTION

After 20 weeks of pregnancy, up to 8% of pregnant women develop the pregnancy-specific syndrome known as pre-eclampsia, which is characterized by high blood pressure and proteinuria[1-2]. Preeclamptic women are more likely to have pulmonary edema, coagulation problems, hepatic or renal failure, and their condition may proceed to eclampsia, which can cause convulsions, brain hemorrhage, blindness, and even death[3]. An increase in the incidence of severe pre-eclampsia was shown to be connected with maternal midgestational vitamin D deficiency, according to a nested case control study carried out in two US states.

According to a study in the Iraqi Postgraduate Medical Journal, pre-eclamptics had lower vitamin D levels than healthy pregnant females[4-5]. Women who are pregnant and vitamin D deficient are five times more likely to develop preeclampsia, a potentially dangerous illness. Researchers emphasized that pregnant women with even slightly low vitamin D readings may have twice as much of a chance of developing the disease[6-7]. Pregnant women continue to be at high risk for the deficiency even with prenatal vitamins. According to a study in India in 2017, only 10% of pregnant females had suboptimal levels of vitamin D, while 90% were vitamin D deficient and the hypertensive group had lower average blood levels of vitamin D than the normotensive group[8]. Between January and December 2017, a study conducted in Karachi at Jinnah postgrqaduate Medical centre (JPMC) found a significant relationship between pre-eclampsia and low vitamin D levels[9]. According to a 2016 study from India in the Journal of Obstetrics and Gynecology of India, patients in both the control and study group were deficient in vitamin D. However, maternal vitamin D levels were lower significantly in the study group in comparison to the control group[10].

Since pre-eclampsia can be prevented by maintaining optimal vitamin D levels in pregnant females, the purpose of this analysis is to determine the association between maternal levels of serum vitamin D and the development of pre-eclampsia. It will also add data

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from our pregnant women and help predict pre-eclampsia in females with vitamin D deficiency.

MATERIALS AND METHODS

This Case control Study was conducted at department of Obstetrics and Gynae Unit-2, Dow University Hospital Ojha campus Dow University of health Sciences Karachi from 10th December, 2021 to 10th May, 2022. The patients with preeclampsia were included in the case group and pregnant patients with normal blood pressure and no proteinuria were included in the control group.

By taking vitamin D deficiency prevalence in pre-eclamptic patients (PI) =90% (5), vitamin D deficiency prevalence in normotensive patients (P2) =62% (5), power of test (I-Beta)=99%, 162 patients were selected with the help of Who software for sample size collection taking 95% CI, 81 patients will be taken from each group. The patients were included by non-Probability consecutive sampling technique.

Inclusion Criteria:

CASES	CONTROL
Pre-eclampsia	Normotensive pregnant women With No Proteinuria
Singleton Pregnancy	Singleton Pregnancy
Pregnancy>20weeks	Pregnancy>20weeks
Pregnant females Between 18-35 Years of age	Pregnant females Between 18-35 Years of age
Primigravida And Multigravida	Primigravida And Multigravida

Exclusion Criteri:

- Multiple gestations confirmed by ultrasound.
- Major congenital fetal anomalies on ultrasound.
- Pregestational hypertension by history.
- Renal disease by Renal function tests.
- Diabetes Mellitus by fasting blood sugar levels.
- Patients already taking vitamin D supplements.

After obtaining consent, pregnant women admitted in ward/labor room of DUHS were enrolled on the basis of exclusion and inclusion criteria. After detailed history and comprehensive clinical examination, blood samples for vitamin D were sent to DOW Diagnostics Reference and Research Laboratory and their results were interpreted. Cases were patients with pre-eclampsia and controls were normotensive pregnant patients with no proteinuria.

Venipuncture was used to collect the blood aseptically, which was then allowed to clot before the serum was extracted. Prior to assaying, air bubbles were looked for and eliminated. 175 microL of volume are needed as a minimum. The LIAISON Analyzer family, which includes the LIAISON, LIAISON XL, and LIAISON XS, is a direct competitive CLIA for determining the amount of total 25 OH vitamin D in serum. 25 OH vitamin D separates from its binding protein during the first incubation and binds to a particular antibody on a solid phase. Tracer ~~was~~ introduced after 10 minutes, and after the second 10 minutes of incubation, unbound material is eliminated using a wash cycle. Then starter chemicals were included to start the flash chemiluminescence reaction. Between 4.0 and 150ng/ml of vitamin D are measured by the LIAISON 25 OH vitamin D test. Data were including maternal age, parity, height, weight, BMI, gestational age, residence, socioeconomic status, any addiction, preeclampsia present or not and vitamin D deficient or not.

Height was assessed by wall height chart and weight was determined by weight machine. BMI was determined by formula: weight (kg)/height (m 2). Gestational age was calculated by ultrasound.

All data were entered and analyzed using SPSS 23. Numerical variables such as age, parity, height, weight, BMI and gestational age were expressed as mean+/- standard deviation. Categorical variables such as residence, socioeconomic status, education, pre-eclampsia present or not, and vitamin D deficient or not were expressed as frequency or percentages (%). The association of pre-eclampsia and vitamin D deficiency was ascertained using chi-square test. The p value < 0.05 was considered significant. Effect modifiers such as age, parity, height, weight, and gestational age, residence, socio economic status, and any addiction were controlled through stratification.

RESULTS

This study was conducted on 162 patients comprising of cases and controls having 81 in each. The mean age in group A (cases) was 26.65±4.71 years 27.10±5.73 years in group B (controls). The mean height in group A was 1.65±0.33 meters and 1.65±0.33 meters in group B. The mean weight in group A was 74.56±2.83 kg and 74.33±2.64 kg in group B. The mean gestational age in group A was 29.91±6.1 weeks and 29.06±5.73 in group B. The mean parity was 3.38±1.15 in group A and 3.58±1.46 in group B. The mean BMI in group A was 27.18±1.44 kg/m2 and 27.04±1.45 kg/m2 in group B. (Table No. 1).

Regarding age distribution there were 33 (40.7%) patients in the age group of 18 to 25 years in group A and 37 (45.7%) in group B. In the age range of 26 to 35 years there were 48 (59.3%) patients in group A and 44 (54.3%) in group B. (Table No. 2).

In group A 68 (84%) patients had vitamin D deficiency and in group B 45 (55.6%) patients had vitamin D deficiency. The relationship was significant statistically. (Table No. 3).

Table No. 1: Descriptive statistics (n = 162)

Groups		Age in years	Height in meter	Weight in Kg	Gestational age (weeks)	Parity	BMI kg/m²
Group A (CASES) (Preeclampsia) n=81	Mean	26.65	1.6572	74.5612	29.91	3.38	27.1809
	Std. Deviation	4.712	.03385	2.83240	6.149	1.157	1.44150
Group B (CONTROLS) (Normotensive) n=81	Mean	27.10	1.6590	74.3363	29.06	3.58	27.0415
	Std. Deviation	5.739	.03345	2.64366	5.730	1.465	1.45303

Table No. 2: Age distribution

		Age distribution		Total
		18 to 25 years	26 to 35 years	
Groups	Group A (Preeclampsia)	33	48	81
		40.7%	59.3%	100.0%
	Group B (Normotensive)	37	44	81
		45.7%	54.3%	100.0%
Total		70	92	162
		43.2%	56.8%	100.0%

Table No. 3: Association of Vitamin D deficiency in both groups

		Vitamin D Deficiency		Total	P value
		Yes	No		
Groups	Group A (Preeclampsia)	68	13	81	0.0001
		84.0%	16.0%	100.0%	
	Group B (Normotensive)	45	36	81	
		55.6%	44.4%	100.0%	
Total			49	162	
		69.8%	30.2%	100.0%	

Table No. 4: Education status

		Education Status						Total
		Un-Educated	Primary	Secondary	Inter	Graduation	Post-graduation	
Groups	Group A (Preeclampsia)	18	11	19	14	15	4	81
		22.2%	13.6%	23.5%	17.3%	18.5%	4.9%	100.0%
	Group B (Normotensive)	10	18	22	13	11	7	81
		12.3%	22.2%	27.2%	16.0%	13.6%	8.6%	100.0%
Total		28	29	41	27	26	11	162
		17.3%	17.9%	25.3%	16.7%	16.0%	6.8%	100.0%

Table No. 5: Socioeconomic status

		Socioeconomic Status			Total
		Lower class (Salary <50000)	Middle class (Salary 50000 to 100000)	Upper class (Salary >100000)	
Groups	Group A (Preeclampsia)	37	29	15	81
		45.7%	35.8%	18.5%	100.0%
	Group B (Normotensive)	37	35	9	81
		45.7%	43.2%	11.1%	100.0%
Total		74	64	24	162
		45.7%	39.5%	14.8%	100.0%

Regarding the education status 18 (22.2%) were uneducated in group A and 10 (12.3%) in group B. 11 (13.6%) had primary education in group A and 18 (22.2%) in group B. 19 (23.5%) had secondary education in group A and 22 (27.2%) in group B. 14 (17.3%) had intermediate education in group A and 13 (16%) in group B. 15 (18.5%) had graduation in group A and 11 (13.6%) in group B. 4 (4.9%) had post-graduation in group A and 7 (8.6%) in group B (Table No. 4).

According to the residence status 32 (39.5%) were from urban areas in group A and 25 (30.9%) in group B. 23 (28.4%) were from peri-urban areas in group A and 31 (38.3%) in group B. 26 (32.1%) in group A were from rural areas and 25 (30.9%) in group B. In our study 37 (45.7%) patients were from lower class in group A and

37 (45.7%) in group B. 29 (35.8%) were from middle class in group A and 35 (43.2%) from group B. 15 (18.5%) were from upper class in group A and 9 (11.1%) in group B (Table No. 5).

Stratification of vitamin D deficiency w.r.t parity, weight, gestational age and socioeconomic status can be seen from table no 6 to table no 8.

Table 6: Stratification of vitamin D deficiency in both group w.r.t parity

Parity Groups			Vitamin D Deficiency		Total	P value
			Yes	No		
1 to 3	Groups	Group A (Preeclampsia)	33	4	37	0.001
			89.2%	10.8%	100.0%	
		Group B (Normotensive)	17	20	37	
			45.9%	54.1%	100.0%	
	Total		50	24	74	
			67.6%	32.4%	100.0%	
> 3	Groups	Group A (Preeclampsia)	35	9	44	0.09
			79.5%	20.5%	100.0%	
		Group B (Normotensive)	28	16	44	
			63.6%	36.4%	100.0%	
	Total		63	25	88	
			71.6%	28.4%	100.0%	

Table No. 7: Stratification of vitamin D deficiency in both group w.r.t weight

Weight groups			Vitamin D Deficiency		Total	P value
			Yes	No		
70 to 75 kg	Groups	Group A (Preeclampsia)	47	9	56	0.001
			83.9%	16.1%	100.0%	
		Group B (Normotensive)	32	25	57	
			56.1%	43.9%	100.0%	
	Total		79	34	113	
			69.9%	30.1%	100.0%	
76 to 80 kg	Groups	Group A (Preeclampsia)	21	4	25	0.02
			84.0%	16.0%	100.0%	
		Group B (Normotensive)	13	11	24	
			54.2%	45.8%	100.0%	
	Total		34	15	49	
			69.4%	30.6%	100.0%	

Table No. 8: Stratification of vitamin D deficiency in both group w.r.t gestational age

Gestational Age Groups			Vitamin D Deficiency		Total	P value
			Yes	No		
20 to 30 weeks	Groups	Group A (Preeclampsia)	32	8	40	0.01
			80.0%	20.0%	100.0%	
		Group B (Normotensive)	26	21	47	
			55.3%	44.7%	100.0%	
	Total		58	29	87	
			66.7%	33.3%	100.0%	
31 to 40 weeks	Groups	Group A (Preeclampsia)	36	5	41	0.02
			87.8%	12.2%	100.0%	
		Group B (Normotensive)	19	15	34	
			55.9%	44.1%	100.0%	
	Total		55	20	75	
			73.3%	26.7%	100.0%	

DISCUSSION

Vitamin D3, also known as calciferol, is a prohormone essential for bone health and calcium homeostasis, in adding to neuromuscular effects[11]. According to several studies, maternal vitamin D deficiency is related with poor outcomes for both the fetus and mother. In the previous two decades, the non-classical role of vitamin D has been assumed; it controls a significant number of

human genes (about 200 genes), causing different autocrine effects in various tissues. For example, vitamin D regulates cell growth, differentiation, and death[12]. It regulates innate and acquired immunity, influencing immune responses. This explains the relation between vitamin D deficiency and the likelihood of developing many diseases, including depression, high blood pressure, diabetes, multiple sclerosis, cancer, asthma, allergies, infectious and autoimmune diseases[13].

Hypertension disorders are the most common medical consequence of pregnancy and it is important to discuss their relationship with vitamin D deficiency. Hypertension problems affect 7 to 15 percent of pregnancies, which can have consequences for both the mother and the fetus. Conditions covered include pre-eclampsia, eclampsia, chronic hypertension and pre-eclampsia in addition to chronic hypertension.

Discordant pathological and molecular data suggested a two-stage disease[14]. The etiology of preeclampsia is characterized by abnormal trophoblastic invasion of the spiral arteries, an exaggerated inflammatory response and inappropriate activation of endothelial cells. Severe pre-eclampsia affects black women more often than white women, suggesting that it may be related to vitamin D. Some hypotheses claim that pre-eclampsia and eclampsia are caused by the mother's immune system being unable to tolerate the growing fetus. Vitamin D, a steroid prohormone, has an immediate effect on various molecular processes such as trophoblast invasion and immunomodulation. Vitamin D may affect implantation and placental function during pregnancy due to its angiogenic and anti-inflammatory properties[15]. It is essential in immune adaptation to enhance immune responses at the fetal-placental interface and reduce the risk of infection and inflammation[16].

Insufficient vitamin D is related with many harmful health outcomes, counting gestational diabetes, high blood pressure problems, risk of infection, caesarean section and reduced fetal development. Knowledge on this subject is growing rapidly[17]. Numerous studies have shown a convincing link between pre-eclampsia and vitamin D and have shown that pre-eclampsia can be detected by low levels of vitamin D in the 2nd trimester of pregnancy[18]. Recent studies, although not standardized, have shown that the acceptable level of vitamin D deficiency when assessing the amount of vitamin D in the serum is now 20 ng/ml, above the previously recognized threshold of 15 ng. /ml[19].

CONCLUSION

According to the results of our study, pre-eclampsia and maternal serum vitamin D levels are related. 84% of patients in the case group were deficient in vitamin D in comparison to 55.6% in the control group. P = 0.0001 indicates that the variance is statistically significant.

Author's Contribution:

Concept & Design of Study:	Ambreen Shahid
Drafting:	Afshan Shahid, Riffat Jaleel
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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