ASSOCIATION OF VITAMIN-D INSUFFICIENCY DURING PREGNANCY WITH MATERNAL & PERINATAL MORBIDITY AND MORTALITY

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ABSTRACT

Objective: To determine the association of Vitamin-D insufficiency during pregnancy with maternal & perinatal morbidity and mortality.

Study Design: Prospective cohort study.

Place and Duration of Study: This study was conducted at Obstetrics and Gynaecology Department, PNS Shifa Karachi, from Dec 2017 to Dec 2018.

Methodology: A total of 585 pregnant females who fulfilled the inclusion criteria were booked at or before 20 weeks of gestation. Serum vitamin–D3 levels [25(OH)D], Doppler studies and serial measurements of blood pressures were done and the patients were observed for intrauterine growth restriction (IUGR), low birth weight (LBW), development of pregnancy induced hypertension (PIH) and outcomes of pregnancy like still birth and neonatal intensive care unit (NICU) admissions.

Results: A total of 585 patients were enrolled in the study out of which 394 (67.4%) were found to be vitamin–D deficient. Sixty seven babies (11.5%) had IUGR [31=vitamin-D deficient mothers, 36=non-deficient mothers] (RR=0.660). Increased Doppler indices were seen in 108 (18.5%) of the babies [87=Vitamin-D deficient mothers, 21=non-deficient mothers] (RR=1.25). A total of 128 babies (22%) were low birth weight (LBW) [93=vitamin D deficient mothers, 35=non-deficient mothers] (RR=1.103). Two (0.34%) still births were seen in vitamin-D deficient patients (RR=1.48). 14% babies required neonatal intensive care [53=vitamin-D deficient mothers, 28=non-deficient mothers] (RR=0.967). Eighty three (14.2%) cases of maternal hypertension [54=vitamin-D deficient mothers, 29=non-deficient mothers] (RR=0.961).

Conclusion: Increased doppler indices, low birth weight and still birth had statistically significant association with vitamin D deficiency.

Keywords: Vitamin-D, Perinatal outcome, Pregnancy.

INTRODUCTION

Maternal nutritional status plays a critical role in creating an optimal intra-uterine environment and could be linked to various maternal and perinatal outcomes[1]. Vitamin D is a micronutrient that is vital for maintaining calcium homeostasis and regulation of bone mineralization in the body, and hence plays a very important role in fetal development[2]. Vitamin D or cholecalciferol, is a fat soluble vitamin produced by exposure to sunlight. 7-dehydrocholesterol in the skin absorbs UV B radiation and is converted to previtamin D3 which then isomerizes to vitamin D3.

Vitamin D is metabolized first in the liver into 25-hydroxyvitamin D which is a major circulating form and then hydroxylated in the kidneys into 1, 25-dihydroxyvitamin D which is the biologically active form of vitamin D[3]. Low maternal vitamin D levels during pregnancy may be responsible for reduced fetal growth and may adversely affect neonatal development[4]. It is also linked to adverse maternal outcome like development of pre-eclampsia[5], gestational diabetes mellitus[6] and a four-fold increase in the risk of primary caesarean section[7]. There is a high prevalence of vitamin D insufficiency during pregnancy but limited trials have been done for vitamin D supplementation in relation to specific clinical outcomes[1].

The high prevalence of Vitamin D deficiency globally[8] deemed it relevant to assess the associa-

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tion between vitamin D insufficiency and the various parameters of perinatal morbidity and mortality. In this prospective study we tried to establish the association between low maternal vitamin D levels and Intrauterine growth restriction (IUGR), pregnancy-induced hypertension (PIH) and outcome of pregnancy like still birth, low birth weight (LBW) and neonatal intensive care unit (NICU) admissions. The results of this study could help the obstetricians to emphasize on the vitamin-D supplementation in the antenatal period to reduce the perinatal morbidity and mortality in our community.

METHODOLOGY

This study was conducted at Obstetrics and Gynaecology Department, PNS Shifa Karachi, from December 2017 to December 2018. Approval of study was taken from Ethical Review Board and consent taken from patients. A total of 585 patients were recruited by consecutive non-probability technique from those reporting to Obstetrics and Gynaecology OPD. During this study the patients in the age group of 20-35 Years, booked at or before 20 weeks of gestation, had uncomplicated pregnancy with no history of IUGR or PIH in the previous pregnancies were included. Patients with known comorbidities such as essential hypertension, diabetes, thyroid disease, renal disease, anti-phospholipid Syndrome (APS), Systemic Lupus Erythematosus (SLE) or any other medical illness, multiple pregnancies or history of IUGR in the previous pregnancy were excluded from the study. The demographic data was collected on a questioner like age, occupation, gravidity and gestational age. The Blood Pressure of each participant was recorded twice at each antenatal visit and the patient was observed for development of hypertension. In addition to routine investigations, venous blood sampling was done for 25 (OH) vitamin D done at 22 weeks of gestation and analyzed by Radio-immunoassay. Vitamin D insufficiency was defined as a 25 (OH) D concentration of <30 ng/mL (75 nmol/L)[9,10]. Doppler studies (abdominal circumference, uterine artery and umbilical artery doppler

indices) were done and the patients were observed for IUGR and outcome of pregnancy like still birth, LBW (LBW=term or preterm neonates with birth weight <2500 gr)[11], and NICU admissions. The data was compiled and statistically analyzed by SPSS-21. Descriptive analytical tests were applied to calculate the frequencies, means, standard deviations and relative risk (RR) for associations with confidance interval (CI= 95%). A relative risk (RR) of >1 was considered statistically significant. Attributable risk was found using the formula [(RRR-I) = (1-RR) ×100]. Patients were called for follow-up regularly at 3 weeks interval.

RESULTS

A total of 585 patients were enrolled in the study with maternal age (Mean ± SD) 28.59 ± 3.1 out of which 394 (67.4%) were found to be vitamin–D deficient while 191 (32.6%) had normal levels of serum vitamin-D (table-I & II). Demographic data showed that most of the women were house wives (72.6%) while the working women were 27.4%, primigravidas (34%), multigravidas (66%), spontaneous vaginal deliveries (61.7%), cesarean sections (38.3%) (table-I). 67 babies (11.5%) had IUGR out of which 31 were of vitamin-D deficient mothers while 36 were of mothers who had no vitamin D deficiency (RR= 0.660). Increased doppler indices (DI) were seen in 108 (18.5%) of the babies, 87 from vitamin-D deficient mothers while 21 from the non-deficient mothers (RR=1.25). 128 babies (22%) were low birth weight (LBW) out of which 93 were born to the vitamin D deficient mothers while 35 were born to mothers with normal vitamin D levels (RR=1.103). Two (0.34%) still births were seen in vitamin-D deficient patients (RR= 1.48). 14% babies required neonatal intensive care, 53 from the vitamin D deficient mothers and 28 from the normal ones (RR=0.967). Eighty three (14.2%) of the patients were found to be hypertensive out of which 54 had vitamin-D deficiency while 29 had normal vitamin-D levels (RR=0.961) (table-III). Increased doppler indices (RR=1.25), LBW (RR=1.103) and still birth (RR=1.48) had statistically significant association with vitamin D defi-

ciency however, no statistically significant association was found between vitamin D deficiency and IUGR (RR=0.660), NICU admissions (RR=

Table-I: Demographic variables.

Maternal variables	n (%)
Maternal age (Mean ± SD)	28.59 ± 3.1
Primigravida	199 (34%)
Multigravida	386 (66%)
Birth by SVD	361 (61.7%)
Birth by C-sections	224 (38.3%)
House wives	425 (72.6%)
Working	160 (27.4%)

Table-II: Frequency of vitamin D Insufficiency.

Total no. of cases(n)	Vitamin D Insufficiency	n=585	%
585	yes	394	67.4
	no	191	32.6

Table-III: Variables under study.

Variables	n (%)	Vitamin D Insufficiency		RR	RRR(I): [(1-RR)×100] %
		Yes	No		
Intrauterine growth restriction	67 (11. 5)	31	36	0.660	34
Increased DI	108 (18 .5)	87	21	1.252	25
Maternal HTN	83 (14. 2)	54	29	0.961	3.9
Low birth weight	128 (21 .9)	93	35	1.103	10.3
Still birth	2 (0.3)	2	-	1.487	48
NICU admissions	81 (13. 8)	53	28	0.967	3.3

0.967) and the development of maternal hypertension (RR=0.961).

DISCUSSION

Vitamin D deficiency has been reported to be very high among the women in Pakistan despite its sunny climate and sub-tropical location. About 90% of the females of reproductive age group are Vitamin D deficient[12]. The purpose of this study was to find out the prevalence of vitamin D deficiency among the pregnant patients reporting to our hospital and establishing an association between the low maternal serum vitamin D levels and the various perinatal morbidity and mortality indicators. Vitamin D insufficiency was found in 67.4% of the pregnant ladies in our study. Such a high frequency of Vitamin D insufficiency is a point of serious concern. This might be due to

the dietary insufficiency and other contributing factors like less exposure to sunlight, use of sun screen or high parity. Similar results were seen in a study conducted at Department of Obstetrics & Gynaecology, Liaquat National Hospital in 2011-12 which showed 69.6% of mothers to be vitamin D deficient[13]. A recent cross-sectional study done in Mangalore revealed Vitamin D deficiency in 41.2% of the mothers[14] while a study done at Abbasi Shaheed Hospital, Karachi also showed a very high prevalence of Vitamin D deficiency among the pregnant women[15]. Demographic data showed that most of the women who suffered from hypovitaminosis D were house wives (72.6%) and only 27.4% were working women. This could probably relate to exposure to the sunlight which is more in the working women going out as compared to the house wives who spend most of their time at home in our country. Multigravidas (66%) were found to be more Vitamin D deficient than the primigravidas (34%) which can be explained by the generalized micronutrients deficiency found in multigravidas due to repeated cycles of pregnancy and lactation. Similar results were found in another study done in Gujrat, India[16]. Spontaneous vaginal deliveries were 61.7% of the total deliveries while 38.3% ladies were delivered by cesarean sections.

Furthermore after finding the frequency of vitamin D insufficiency, an effort was made to find the association between vitamin D insufficiency and various outcomes of pregnancy. We found a significant association between LBW and maternal vitamin D deficiency (RR=1.103) which shows that vitamin D deficient mothers have a

10% more risk of giving birth to LBW babies as compared to mothers having normal levels of serum vitamin D. Our findings were in agreement with Morley et al[17], Dave et al[18] and a study conducted in Iran which reported a high prevalence and a greater risk of LBW in babies born to vitamin D deficient mothers[19]. Results from a large population-based prospective cohort study suggested that second trimester lower maternal vitamin D concentrations are associated with low birth weight and small-size for gestational age at birth[20]. However, our observations were in contrast with an earlier randomized controlled trial of antenatal vitamin D supplementation in Pakistani women which failed to substantiate the association of maternal Vitamin D and LBW[21]. WHO states the role of micronutrients including vitamin D, in improving the birth weight by about 77 gr and decreasing the incidence of LBW by 25%[22]. In our study we adjusted the confounders such as age and gestational age. Females who were less than 20 years or more than 35 years of age were excluded. Similarly pregnancies at or beyond 22 weeks with no risk factor for hypertension or any other comorbidities were selected and those with known medical illnesses were excluded.

We found statistically significant relationship between low maternal serum vitamin D levels and increased Doppler indices (RR=1.25) and still births (RR=1.48) which is in agreement with another study conducted on maternal and fetal outcome[18].

Our study failed to establish a causal relationship between maternal vitamin D deficiency and adverse perinatal outcome in terms of IUGR (RR=0.660) and NICU admissions (RR=0.967) which is compatible with a recent study conducted in China which shows a negative correlation between the vitamin D level and the incidence of adverse perinatal outcomes in pregnant women[23]. In recent years, maternal vitamin D deficiency has been suggested as a modifiable risk for hypertensive disorders of pregnancy. An accrual body of studies relates hypertensive disorders of pregnancy to maternal vitamin D deficiency. A systemic review showed a consistent evidence of association between low maternal vitamin D levels and adverse pregnancy induced hypertension outcomes[24]. A similar significant relation was found between Vitamin D deficiency and hypertension in pregnancy in a study done in Karachi[15]. However our study failed to substantiate the association of Vitamin D deficiency and development of maternal hypertension (RR= 0.961) which is consistent with a randomized controlled trial of antenatal vitamin D supplementation in Pakistani Women which failed to impact on the incident preeclampsia through vitamin D supplementation[21].

The explanation of this study results was that pregnant ladies who suffered from hypovitaminosis D had increased chances of poor pregnancy outcomes like increased Doppler indices, LBW and still birth. This calls for an active vitamin D supplementation program to be implemented during antenatal period so that these adverse pregnancy outcomes could be prevented. Efforts to educate women and create awareness among masses about the unmet need to ensure adequate vitamin D intake would certainly contribute to their increased knowledge about the importance of vitamin D in pregnancy and potential harmful effects of its deficiency which would ultimately reduce maternal and fetal risks of hypovitaminosis D. Pregnant ladies should also be counselled for adequate exposure to sunlight however the effectiveness of vitamin D supplementation over sun exposure cannot be sidestepped[25]. Many areas still need to be evaluated like the effect of early supplementation of vitamin D during antenatal period and the changes in vitamin D metabolism during pregnancy which could prove fruitful in devising a strategy for vitamin D supplementation during pregnancy and preventing the adverse maternal and fetal outcome.

CONCLUSION

Increased doppler indices, low birth weight and still birth had statistically significant association with vitamin D deficiency.

CONFLICT OF INTEREST

There is no conflict of interest to be declared by any author.

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