CORRELATION OF VITAMIN D AND BODY MASS INDEX IN TERM NORMOTENSIVE AND PRE -ECLAMPTIC WOMEN

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ABSTRACT

INTRODUCTION: Obesity is associated with alteration in the vitamin D levels and has been related to vitamin D status. Lower vitamin D levels in higher BMI individuals may be secondary to an alteration in tissue distribution resulting from an increase in adipose mass. Therefore women with higher BMI need higher vitamin D supplementation as compared to women with BMI within normal range.

MATERIAL AND METHOD: This was a case control study carried out in Department of Obstetrics and Gynaecology, ESIC-PGIMSR, New Delhi from August 2012-April 2014. A total of 100 patients were divided into two equal groups (control and study groups of 50 each). Control group had women with singleton uncomplicated term normotensive pregnant women in labour while the study group comprised of term preeclamptic women in labour.In all the patients their BMI was analysed .Blood samples for vitamin D, serum calcium, serum phosphorus, serum parathormone, serum alkaline phosphatase levels were drawn and subsequently their levels were evaluated in cord blood; correlation studied between vitamin D & BMI.

RESULTS: The mean BMI was relatively higher in the study group (26.34 ± 4.12)kg/m^2 than in the control group (24.24 ± 3.13)kg/m^2. Thus in our study a prevalence of higher BMI was seen in patients of preeclampsia. When all the 100 women are being considered, median vitamin D levels were found to be higher (6.6ng/ml) in normal BMI patients (n=55) as compared to levels (5.6ng/ml) in patients with higher BMI(n=45).

CONCLUSION: Vitamin D levels are related to maternal body mass index. Individuals with higher percentage body fat may require higher vitamin D intake to attain optimal 25(OH) D levels, compared with lean individuals and thereby may prevent pregnancy complications like Pre eclampsia.

KEYWORDS: Vitamin D, BMI

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INTRODUCTION

Obesity is associated with alterations in the vitamin D levels. The low levels of 25-hydroxyvitamin D (25-OHD) in obesity have been attributed to multiple factors like decreased exposure to sunlight because of limited mobility, negative feedback from elevated 1,25-hydroxyvitamin D and PTH levels on hepatic synthesis of 25-OHD , and excessive storage of vitamin D in the adipose tissue. The first evidence of a relationship between vitamin D and body fat was described by Lumb *et al* [1] in 1971. They hypothesized that vitamin D after absorption is sequestered and stored in tissues like fat and muscle and then released slowly into the circulation in which it is used biologically. Worstman *et al (2000)*[2] confirmed that obesity-associated vitamin D insufficiency most likely is due to decreased bioavailability of vitamin D3 from cutaneous and dietary sources because of its deposition in body fat compartments. Based on this evidence, it is expected that obese individuals need higher-than-usual doses of vitamin D for supplementation.

However, it still remains unclear whether adiposity (or percentage body fat) should be taken into consideration while assessing vitamin D requirements in the general population.

MATERIAL AND METHODS

This study was conducted in the Department of Obstetrics and Gynaecology, ESIC-PGIMSR, Basaidarapur, New Delhi. In our study 100 patients who gave informed written consent were enrolled .The patients were divided equally into study and control groups of 50 each. In the study group patients having preeclampsia (defined as BP≥140/90 mm Hg after 20wks of gestation and proteinuria ≥ 1+ dipstick) at term in labor were enrolled whereas normotensive patients at term in labor were included in the control group. On admission brief history and clinical examination was done. In all the patient's blood samples for vitamin D, serum calcium, serum phosphorus, serum parathormone, serum alkaline phosphatase levels were drawn during first stage of labor and subsequently their levels were evaluated in cord blood also.

Factors such as BMI, age, mode of delivery, birth weight of baby were studied in both the groups.

RESULTS

WHO criteria was used for Body mass index assessment with values in the range (18.5-24.9)kg/m^2 taken as normal and body mass index ≥25kg/m^2 defined as high (table 1).The mean BMI was relatively higher in the study group (26.34 ± 4.12)kg/m^2 than in the control group (24.24 ± 3.13)kg/m^2. The difference in the mean BMI of both the groups was found to be statistically significant with p value of 0.005. 58% of the patients in the study group were having high BMI as compared to 32% of the patients in the control group (fig. 1). There was again a statistically significant difference in the number of patients having higher BMI in both the groups (p value 0.009).Thus in our study a prevalence of higher BMI was seen in patients of preeclampsia.

Table 1: Showing Comparison of BMI between Study and Control Group

BMI (kg/m^2)	Control Group		Study Group		P Value
	No. of cases	%	No. of cases	%	
18.5 - 24.9	34	68%	21	42%	0.009*
≥ 25	16	32%	29	58%	
Total	50	100%	50	100%	
Mean ± SD	24.24 ± 3.13		26.34 ± 4.12		0.005*

(* =Shows statistically significant)

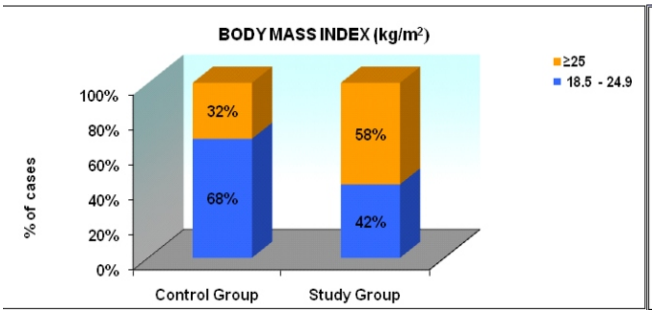

Figure 1: Shows Comparison of BMI (kg/m^2) Between Study and Control Group.

In the normal BMI range (18.5-24.9)kg/m^2 95.2% of the preeclamptic patients had severe vitamin D deficiency (<10ng/ml) while 58.8% of normotensive patients with normal BMI had severe vitamin D deficient status. This difference among the two groups in terms of number of severely vitamin D deficient patients across normal BMI range was statistically significant with p value of 0.012 . When the two groups were compared for the number of severely vitamin D deficient patients across higher BMI ranges (>25kg/m^2) ,the difference between the two groups slightly narrowed down with 86.2% of study group patients being severely vitamin D deficient as compared to 68.8% in the control group. Though here also the difference was statistically significant (p value 0.043) but to a lesser extent than that in case of comparison across normal BMI range. (Table2; Figure 2)

Table 2: Showing Distribution of Maternal Vitamin D Levels at normal and high
BMI in Study And Control Group

BMI (kg/m^2)	Vitamin D Levels (ng/ml)	Control Group		Study Group		P Value
		No. of cases	%	No. of cases	%	
18.5 - 24.9	<10	20	58.8%	20	95.2%	0.012*
	10 - 20	10	29.4%	1	4.8%	
	>20	4	11.8%	0	0.0%	
	Total	**34**	**100%**	**21**	**100%**	
≥ 25	<10	11	68.8%	25	86.2%	0.043*
	10 – 20	1	6.2%	4	13.8%	
	>20	4	25%	0	0.0%	
	Total	**16**	**100%**	**29**	**100%**	

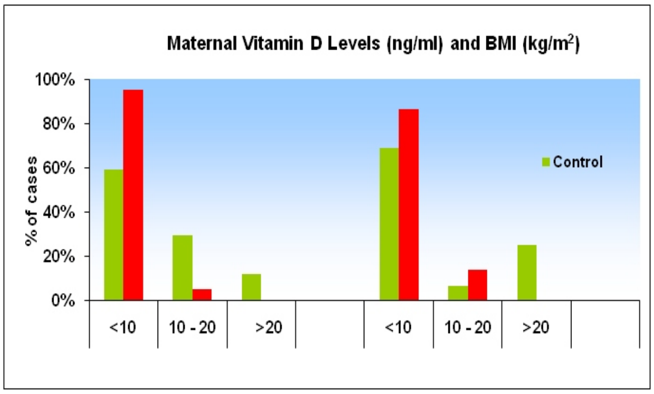

Figure 2: Shows Distribution of Maternal Vitamin D Levels at normal and high BMI in Study And Control Group.

Median vitamin D levels were found to be higher (6.6ng/ml) in normal BMI patients as compared to levels (5.6ng/ml) in patients with higher BMI. The difference was not significant with p value of 0.914. (Table 3; Fig. 3)

Table 3. Showing Median Maternal Vitamin D Level in Normal (18.5 - 24.9) kg/m^2 and High BMI(≥ 25)kg/m^2 patients

	Normal BMI patients(18.5 - 24.9) kg/m^2 (n=55)		High BMI patients(≥ 25)kg/m^2 (n=45)		P Value
	Median	IQR	Median	IQR	
Vitamin D Level (ng/ml)	6.6	3.2 - 10	5.6	3.4 - 9.05	0.914

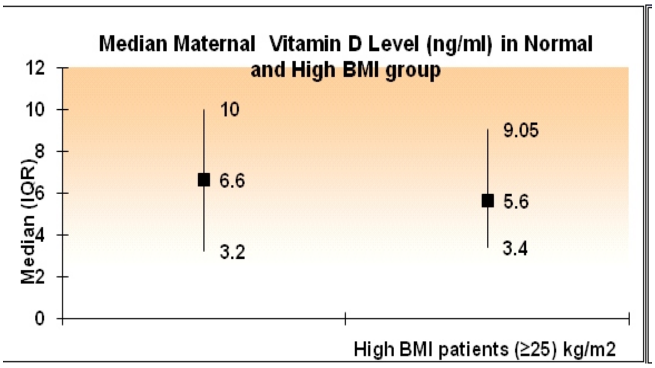

Figure 3: Shows Median Maternal Vitamin D Level in Normal (18.5 - 24.9) kg/m^2 and High BMI (≥ 25)kg/m^2 patients.

In the normal BMI range (18.5-24.9) kg/m^2 95.2% of the neonates born to preeclamptic mothers had severe vitamin D deficiency(<10ng/ml) while 64.7% of the neonates born to normotensive mothers with normal BMI had severely vitamin D deficient status. This difference among the two groups in terms of number of severely vitamin D deficient neonates born to mothers across normal BMI range was statistically significant with p value of 0.033. When the two groups were compared for the number of severely vitamin D deficient neonates born to mothers across higher BMI range (>25 kg/m^2), the difference between the two groups slightly narrowed down with 86.2% of the neonates born to preeclamptic mothers in the study group being severely vitamin D deficient as compared to 68.8% of the neonates born to normotensive mothers in the control group. Here the difference was not statistically significant (p value 0.054). (Table 4; Fig. 4)

Table 4: Showing Distribution of Cord Blood Vitamin D Levels in neonates born to Normal (18.5 - 24.9) kg/m^2 and High BMI(≥25)kg/m^2 mothers

Maternal BMI (kg/m^2)	Cord Blood Vitamin D Levels (ng/ml)	Control Group		Study Group		P Value
		No. of neonates	%	No. of neonates	%	
18.5 - 24.9	<10	22	64.7%	20	95.2%	0.033*
	10 – 20	9	26.5%	1	4.8%	
	>20	3	8.8%	0	0.0%	
	Total	34	100%	21	100%	
≥25	<10	11	68.8%	25	86.2%	0.054*
	10 – 20	2	12.5%	4	13.8%	
	>20	3	18.7%	0	0.0%	
	Total	16	100%	29	100%	

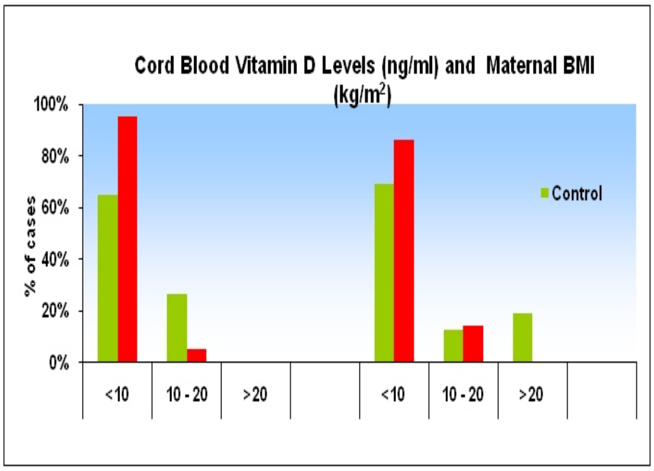

Figure 4. Shows Distribution of Cord Blood Vitamin D Levels in neonates born to Normal (18.5 - 24.9) kg/m^2 and High BMI(≥25)kg/m^2 mothers.

When all the neonates from both the groups were considered as a single cohort then median vitamin D levels were found to be slightly higher in neonates (6ng/ml) born to normal BMI mothers (n=55) as compared to levels (5.8ng/ml) in neonates born to higher BMI mothers (n=45). The difference was not significant with p value of 0.92. (Table5; Fig. 5)

Table 5: Showing Median Cord Blood Vitamin D Levels in neonates born to normal (18.5 - 24.9) kg/m^2 and high BMI (≥25)kg/m^2 mothers.

	Normal BMI mothers (18.5 - 24.9) kg/m^2 (n=55)		High BMI mothers (≥25)kg/m^2 (n=45)		P Value
	Median	IQR	Median	IQR	
Cord Blood Vitamin DLevel (ng/ml)	6	3.2 - 9.7	5.8	3.75 - 7.9	0.92

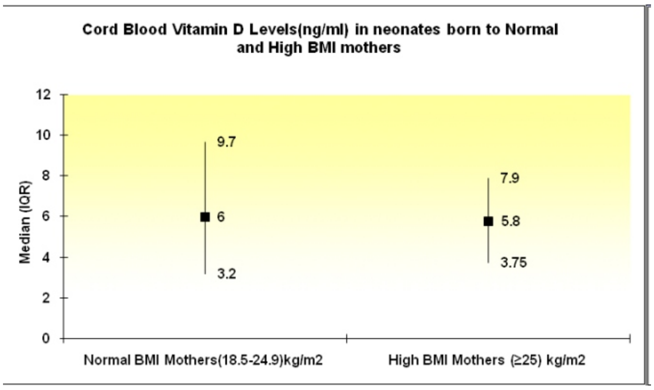

Figure 5: Shows Median Cord Blood Vitamin D Levels in neonates born to normal (18.5 - 24.9) kg/m^2 and high BMI (≥25)kg/m^2 mothers.

DISCUSSION

When all the 100 patients were being considered, median vitamin D levels were found to be higher (6.6ng/ml) in normal BMI patients (n=55) as compared to levels (5.6ng/ml) in patients with higher BMI (n=45). These results are in line with various studies which report consistently low levels of vitamin D in patients with higher BMI whereas some studies have reported this association to be fallacious (Powe et al 2010 [3]) in view of VDBP which also decrease in obese patients, thus maintaining similar concentration of 'Free vitamin D' in them when compared to their normal BMI counterparts. The literature in tune with the above discussion is as follows.

Obesity is associated with alterations in the vitamin D levels. Various studies by Compston et al (1981)[4], Buffington et al(1993)[5], Bell et al(1985)[6], Liel Y et al (1988)[7]reported an inverse correlation between 25 (OH) D and body fat and consistently low levels of 25-hydroxyvitamin D 25(OH) D in morbidly obese patients.

Lumb *et al*[1] in 1971 hypothesized that vitamin D after absorption is sequestered and stored in tissues like fat and muscle and then released slowly into the circulation in which it is used biologically and also reported that total body fat (TBF) is another variable that influences serum calcidiol levels. Serum 25(OH) D levels are more strongly correlated with %TBF, compared with body weight or BMI, indicating that it is adiposity, not simply body mass, that influences the serum level of 25(OH) D. This relationship seems to be related to differences in volume of distribution of 25(OH) D in fat mass. The mechanism of variations in serum 25(OH) D levels in both non-obese and obese individuals appears to be related to availability of adipose tissue leading to excessive storage of the precursor in the fat tissue. The low levels of 25(OH) D in obesity have been attributed to multiple factors like decreased exposure to sunlight because of limited mobility, negative feedback from elevated 1,25-hydroxyvitaminD and PTH levels on hepatic synthesis of 25(OH) D and excessive storage of vitamin D in the adipose tissue. Liel Y et al (1988)[7] had suggested that serum 25(OH) D increases appropriately in response to UV radiation in obese individuals, implying that low vitamin D levels do not result from impaired dermal production and delivery. A study by Worstman *et al*(2000)[2] stated that the subcutaneous fat, which is known to store vitamin D3, sequestered more of the synthesized vitamin D3 in the obese than in the non-obese subjects. Scragg *et al.* (1995)[8] in their cross sectional study had reported no correlation between serum vitamin D levels and BMI, indicating that increasing adiposity causes relative resistance to standard doses of vitamin D. Arunabh et al (2003)[9] reported that percentage body fat is independently associated with serum levels of 25(OH) D in healthy women besides other well-known factors such as dietary vitamin D intake, season, age, and race. Although the impact of body fat is relatively small, it is statistically significant and may influence the way we assess vitamin D nutrition and recommend suppleme - ntation in healthy women. Individuals with higher percentage body fat may require higher vitamin D intake to attain optimal 25(OH) D levels, compared with lean individuals; therefore, body fat should be taken into consideration when assessing vitamin D requirements.

Rosenstreich et al (1971)[10] in their study reported that body adipose tissue can accumulate about 10-12% of supplemented dose of vitamin D. Persons with high BMI usually have a high content of body fat, acting as a reservoir for lipid-soluble vitamin D resulting in its increased sequestration and low availability and as a consequence, low serum 25(OH)D levels. Also the release of vitamin D from the fat is proportional to the concentration of the vitamin in the adipose tissue which is an extremely slow process acting as a protective mechanism against the toxic effects of active forms of vitamin D and maintaining an optimal level of vitamin D in the blood. On the other hand, Florez Het al (2007)[11] reported that obese persons may be expected to produce more vitamin D in the skin, since they have up to 20% larger body surface area than normal weight persons, but the same amount of provitamin D (7-dehydrocholesterol) per unit body surface area .

In addition, 25(OH)D levels are more likely to be associated with body mass index at the time of measurement rather than pre-pregnancy body mass index because lower circulating 25(OH)D levels in obese subjects are likely due to the deposition of vitamin D in adipose tissue. It is unclear whether the deficit in circulating 25(OH)D levels in the obese has physiologic consequences. However, because women who gain more weight in pregnancy are at greater risk for preeclampsia ,adjustment for pre-pregnancy body mass index may be an inadequate method to account for the potential confounding effect of adiposity, while adjustment for body mass index at the time of 25(OH)D measurement may be more likely to account for this.

Past studies examining vitamin D levels in association with hypertension have not concurrently measured levels of vitamin D binding protein or calculated free vitamin D levels. Powe et al(2010)[3] did not find alteration in VDBP levels in preeclampsia, but found that, like total 25(OH)D, VDBP levels were lower in black subjects and decreased with increasing adiposity. Consequently, calculated free 25(OH)D levels were not lower among black or obese women, who have been previously reported to have vitamin D deficiency. These associations with VDBP have not been previously reported in pregnant or non-pregnant populations. If their results are generalized to the non-pregnant population, reexamination of vitamin D deficiency in the context of VDBP levels is compelling, as such analysis may reveal that some individuals otherwise considered "vitamin D deficient" have normal free 25(OH)D levels due to a concomitant decrease in VDBP. However, the free hormone hypothesis with regards to 25(OH)D has not yet been proven or disproven in a pregnant or non-pregnant population and requires further study.

Exactly parallel results, to what were observed in case of association between maternal vitamin D levels & BMI, were found when we tried to assess the relation between cord blood vitamin D and maternal BMI. Here also while the number of neonates born to severely vitamin D deficient mothers of the study group decreased by around 9% on moving from normal maternal BMI to higher maternal BMI ranges. On the contrary in the control group, number of neonates born to severely vitamin D deficient mothers increased by 4% on moving from normal maternal BMI to higher maternal BMI values. Thus, no uniform trend could be elicited in terms of number of severely vitamin D deficient neonates and their relation to maternal BMI, although, when all the neonates from both the groups were considered as a single cohort then median vitamin D levels were found to be slightly higher in neonates (6ng/ml) born to normal BMI mothers (n=55) as compared to levels (5.8ng/ml) in neonates born to higher BMI mothers (n=45). The cord blood differences between neonates born to obese and normal-weight women were consistent with the findings of Bodnar *et al (2007)*[12] in which neonates born to obese women had lower cord blood 25-OH D levels compared with neonates born to normal-weight women. Variance in cord blood 25-OH D levels was closely associated with four factors: maternal 25-OHD level, the presence of maternal obesity, maternal age and neonatal adiposity.

The only source of vitamin D in the newborn is through maternal placental transfer of the nutrient hormone, 25(OH) D. Obese pregnant women are not transferring their25(OH) D to their neonates as effectively as lean women, despite having equivalent 25(OH) D themselves. It is consistent with the theory of reduced bioavailability of vitamin D in obesity by Wortsman J et al (2000)[2] which states that obese women may need larger amounts of vitamin D supplementation to provide their neonates with sufficient levels of vitamin D.

CONCLUSION

Vitamin D levels are related to maternal body mass index. Individuals with higher percentage body fat may require higher vitamin D intake to attain optimal 25(OH) D levels, compared with lean individuals and thereby may prevent pregnancy complications like Pre eclampsia.

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