Vitamin D Status of Mother During Pregnancy and its Association with Bone Mineral Content in Off Spring

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ABSTRACT

Introduction: Vitamin D is essential for the maintenance of the calcium homeostasis and bone mineralization regulation. In adults and in children, Vitamin D deficiency manifests as rickets and osteomalacia respectively. The individuals with vitamin D deficiency are also associated with significantly increased risk of occurrence of fractures. The low values of vitamin D in the mothers during pregnancy are hypothesized to be associated with the low bone mineral content (BMC) in the off-springs. Hence; we prospectively analyzed the correlation between the maternal 25-hydroxyvitamin D [25(OH) D] concentrations in pregnant women and BMC of their off-springs.

Material and methods: The present cohort study was carried in the department of Gynaecology and obstetrics and Department of orthopeadics of the medical institution and included assessment of pregnant women. Only those subjects were included in the present study in which mother and single ton off spring pair was present and the other had eligible results for results for 25(OH) D concentrations in pregnancy and off spring had undergone dual-energy x-ray absorptiometry (DA) at age 9–10 years. Liquid chromatography tandem mass spectrometry was used for the measurement and assessment of the levels of the serum 25(OH) D levels in mothers and the off-spring. In each trimester of the pregnancy period and overall pregnancy, the mean concentrations of 25(OH) D were calculated. All the results were analyzed by SPSS software.

Results: A total of 4200 mother and off-spring pairs were analyzed in the present study. Mean age of the off-spring at the time of the sample collection and assessment was 9.7 years. In 28 percent of the women, Vitamin D concentration was measured in the first trimester while in women in second and third trimester, the samples were measured in 30 and 42 percent of the cases respectively. For the 25 (OH) D concentrations predicted in the third trimester, we observed that more than 65 percent were sufficient while less than 30 percent were insufficient.

Conclusion: Maternal 25(OH) D concentrations occupy some amount of position in the determination of the bone health of the off-spring.

Keywords: Vitamin D, Off-spring, Pregnancy

INTRODUCTION

For the maintenance of the calcium homeostasis and bone mineralization regulation, Vitamin D is essentially required in the body. Rickets and osteomalacia are the common manifestations of vitamin D deficiency occurring in children and adults respectively. The individuals with vitamin D deficiency are also associated with significantly increased risk of occurrence of fractures.[1,2] Previtamin D3 is formed by the action of ultra-violet B on the human skin resulting in the molecular stability of cholesterol precursor (7-dehydrocholesterol) located in the skin. Vitamin D3 (cholecalciferol) is formed by the conversion from previtamin D3 as a result of chemical rearrangement. This vitamin D3 is taken up into the circulation by action of vitamin D binding protein. Vitamin D may also be derived from the dietary component in the form of Vitamin D2 or vitamin D3 from fatty fishes, egg yolks etc.[3,4] In an off-spring, the low values of vitamin D in the mothers during pregnancy are hypothesized to be associated with the low bone mineral content (BMC). If at any point, this hypothesis proves to be true, this will impose a very big problem for the health care professionals as more than 60 percent of the healthy appearing pregnant females are suffering from the insufficient concentration of 25-hydroxyvitamin D (25[OH] D. Time to time, literature quotes some studies with smaller study groups that have assessed the correlation of maternal vitamin D concentration and the BMC in the off-springs but no single point results haven't been established so far due to wide variations in the results.[5-7] Hence; we prospectively analyzed the correlation between the maternal 25(OH) D concentrations in pregnant women and BMC of their off-springs.

MATERIAL AND METHODS

The present cohort study was carried in the department of Gynaecology and obstetrics and Department of orthopeadics of the medical institution and included assessment of pregnant women of the state population from 2006 to 2013. Ethical approval was taken from the institutional ethical committee and written consent was obtained from all the participants after explaining them in written the entire research protocol. Only those subjects were included in the present study in which mother and single ton off spring pair was present and the other had eligible results for results for 25(OH) D concentrations in pregnancy and off spring had undergone dual-energy x-ray absorptiometry (DA) at age 9–10 years. Blood samples were collected from the mothers as non-fasting samples as a part of the routine antenatal care and were stored in the laboratory at minus twenty degree centigrade during the initial time followed by minus eighty degree centigrade without further freeze–thaw cycles. The storage procedure was followed until the time the samples were used for the assessment of the 25(OH) D levels. No fix time was chosen for the assessment of the samples from the mothers. They could be of any time of pregnancy. Atleast results were used in subjects in whom more than one result was available

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at the time of pregnancy. Date and time of the withdrawal of the blood samples were confirmed from the data records. In case of the off-springs, the samples were withdrawn at the age of nine to ten years. The children were recalled for follow-up for the collection of the samples. Liquid chromatography tandem mass spectrometry was used for the measurement and assessment of the levels of the serum 25(OH) D levels in mothers and the off-spring.[8,9] In each trimester of the pregnancy period and overall pregnancy, the mean concentrations of 25(OH) D were calculated. Since, it is hypothesized that maternal concentration of 25(OH) D during pregnancy affects the BMC, we used the mean differences in total body less head (TBH) and spinal BMC as the main outcome.

STATISTICAL ANALYSIS

All the results were analyzed by SPSS software. Multivariate regression curve and chi-square test were used for the assessment of level of significance.

RESULTS

In the present study a total of 4200 mother and off-spring pair were analyzed. Mean age of the off-spring at the time of the sample collection and assessment was 9.7 years. In 28 percent of the women, Vitamin D concentration was measured in the first trimester while in women in second and third trimester, the samples were measured in 30 and 42 percent of the cases respectively. Table 1 shows the multivariate correlation between third trimester maternal 25(OH) D concentration and BMC of the off-spring. Lowest value of the mean 25(OH) D concentration was observed in the first trimester while the highest concentration was observed in the third trimester. Figure 1 shows maternal estimated exposure to ultra-violet B in the third trimester of the pregnancy and the BMC of the off-spring. Table 2 highlights the p-value for the maternal estimated exposure to ultra-violet B in the third trimester of the pregnancy and the BMC of the off-spring. For the 25 (OH) D concentrations predicted in the third trimester, we observed that more than 65 percent were sufficient while less than 30 percent were insufficient. Positive association was observed in context of exposure to ultraviolet B in the third trimester and TBH BMC.

DISCUSSION

In post-natal life, importance of Vitamin D for the physiologic functioning of the muscle is a well proven fact. Isolation of vitamin D receptor (VR) in the skeletal muscles is also proved along with positive correlation of polymorphisms in the VDR and strength if muscles.[10-12] Proximal myopathy is associated with severe vitamin D deficiency. Improvement of proximal myopathy is also seen in persons who were administered with vitamin D supplementation. Reduced physical performance

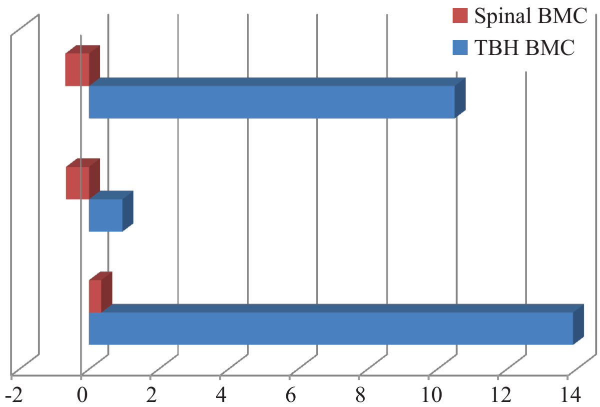

Figure-1: Maternal estimated exposure to ultra-violet B in the third trimester of the pregnancy and the BMC of the off-spring

Parameter		Model 1		Model 2		Model 3		Model 4	
		Mean difference in BMC per 25(OH)D category	p-value	Mean difference in BMC per 25(OH)D category	p-value	Mean difference in BMC per 25(OH)D category	p-value	Mean difference in BMC per 25(OH)D category	p-value
TBH BMC	Sufficient	0	0.5	0	0.5	0	0.4	0	0.5
	Insufficient	-0.8		-2.0		1.1		-2.5	
	Deficient	-9.8		-11.5		1.1		-12.5	
Spine BMC	Sufficient	0	0.4	0	0.4	0	0.6	0	0.6
	Insufficient	-0.2		-0.4		-0.2		-0.4	
	Deficient	-0.9		-0.9		-0.4		-0.9	

BMC: bone-mineral content, 25(OH)D=25–hydroxyvitamin-D, TBLH: Total body less head, Model 1: Adjusted for maternal age and off spring mean age and sex, Model 2: Model 1 along with adjusted maternal education, smoking in pregnancy, and body-mass index before pregnancy, Model 3: Model 2 along with potential mediation by off spring 25(OH) D concentrations, Model 4: Linear trend testing across the 25(OH) D categories

Table-1: Multivariate correlation between third trimester maternal 25(OH) D concentration and BMC of the off-spring

Parameter	Unadjusted eUVB		eUVB adjusted for the off-spring's age		eUVB adjusted for the off-spring's age and the maternal 25(OH) D concentration	
	Mean difference	p-value	Mean difference	p-value	Mean difference	p-value
TBH BMC	13.9	0.02*	0.96	0.4	10.5	0.8
Spinal BMC	0.35	0.5	-0.66	0.03*	-0.68	0.03*

*: Significant

Table-2: p-value for the maternal estimated exposure to ultra-violet B in the third trimester of the pregnancy and the BMC of the off-spring and muscle functions in patients of young and puberty age is seen in patients with subclinical vitamin D insufficiency.[13] Some amount of data do exist in the literature which show that some correlation do exist between maternal serum 25-hydroxy-vitamin D [25(OH)D] levels in pregnant and offspring body composition in childhood.[14] A positive association has been reported in the literature regarding the association of maternal antenatal serum 25(OH) D levels and bone mass of the off-spring.[15] There is a scarcity of data in the literature which highlights the correlation of the muscle development in the post-natal period and exposure of 25(OH) D in the intra-uterine period.[16] Hence; we prospectively analyzed the correlation between the maternal 25(OH) D concentrations in pregnant women and BMC of their off-springs.

In the present study, we didn't observe any association between the maternal 25(OH) D concentration and the BMC of the off-spring in any trimester of the pregnancy. At mean off-spring age of 9.9 years, no effect of maternal 25 (OH) D concentrations was observed on the bone outcomes. The earlier reported positive correlation observed between the ultra-violet B's ambient exposure of the pregnant women during the third trimester and BMC and BMD of the off-spring at 9.9 years of the age could be fully demonstrated by the age of the off-spring at the time of DA.[17] Moon et al investigated the correlation of maternal plasma n-3 and n-6 PUFA status at 34 week gestation and offspring body composition. They analyzed 12583 non-pregnant females and assessed their off spring body composition by dual-energy x-ray absorptiometry. They observed that maternal plasma n-6 PUFA concentration positively predicted offspring fat mass at 4 yr and 6 yr, but observed no correlation with offspring lean mass at either age. From the result, they concluded that in childhood, offspring adiposity might get influenced by maternal n-6 PUFA status during pregnancy.[18] Lawlor et al prospectively assessed the correlation of Vitamin D status of the mother during pregnancy along with bone mineral content in off spring. They observed that 9.9 years was the mean age of the off-spring. Sufficient 25(OH) D concentrations in pregnancy were observed in more than 65 percent of the individuals. Less than 30 percent pregnant females had insufficient 25(OH) D concentrations. From the results, they concluded that no significant correlation exists between maternal vitamin D status in pregnancy and offspring BMC in late childhood.[19] Zhu et al prospectively analyzed the correlation between maternal vitamin D status and peak bone mass of offspring in Western Australian population. They assessed the 25-hydroxyvitamin D levels from the maternal serum samples which were collected at 18 weeks of gestation. They observed that the mean maternal serum 25-hydroxyvitamin D levels was 57.2 nmol/L. Vitamin D-deficiency was observed in less than 40 percent of the pregnant females in the study population. Positive association was seen in between maternal 25-hydroxyvitamin D concentration, total body BMC and BMD in the off spring. From the results, they concluded that in pregnant women, association of vitamin D deficiency exists with the peak bone mass in their off-spring. This further predisposes the children with higher risk of fracture.[20] Petersen et al prospectively analysed the association between the maternal vitamin D concentrations during the time of pregnancy and offspring forearm fractures during childhood. They assessed over 30000 mother and child pairs and analyzed the correlation of vitamin D status in these women and first-time forearm fractures among offspring. They observed that the off-spring of the women who took more than 10 μg/d of the material in the time period of mid-pregnancy were associated with significantly higher risk of development of fractures. From the result, they concluded that in relation to the forearm fractures of the off-spring, no protective action of material vitamin D levels exists.[21] Skaaby et al investigated the correlation of vitamin D concentration and risk of development of cardiovascular abnormalities. They couldn't observe any correlation between the status of vitamin D concentration and the frequency of occurrence of ischemic heart disease or stroke. From the result, they concluded that an inverse correlation exists in between vitamin D concentration and mortality.[22] Strøm et al assessed the association between the maternal serum vitamin D levels and neuro-developmental outcomes in the off-spring. They analyzed 965 subjects in the study and observed a direct correlation between maternal vitamin D status and offspring depression. From the results, they concluded that no association exists in between the fetal effect of vitamin D concentration and behavioural effect of the off-spring.[23] Harvey et al assessed the correlation between maternal plasma 25 (OH) D statuses and offspring lean mass and muscle strength. They prospectively analyzed UK population and evaluated the maternal vitamin D level. They observed a positive correlation between the maternal serum vitamin D concentration and offspring height-adjusted hand grip strength. Also, a positive correlation was observed in their study between Maternal 25(OH)D level s and offspring percent lean mass. From the results, they concluded that during late pregnancy period, intrauterine exposure to 25(OH)D may affect the offspring muscle development.[24]

CONCLUSION

From the above results, the authors concluded that maternal 25(OH)D concentrations occupy some amount of position in the determination of the bone health of the off-spring. However, future studies are advocated for better exploration of this area of medicine.

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