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RESEARCH PAPER

Assessment of Vitamin D Status and Response to Vitamin D Supplementation in Obese and Non-obese Children at a Tertiary Care Hospital

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Abstract

Background: Obesity seems to be a critical issue nowadays because of its high prevalence and its adverse effects on health. There is some evidence indicating the relationship between obesity and lower serum 25-hydroxyvitamin D concentration.

Objectives: The objectives of this study were to assess the vitamin D status and estimate the response to vitamin D in obese and non-obese children after vitamin D supplementation.

Methods: This was a Quasi experimental study, done in Paediatric Endocrinology Clinic and Paediatric Outdoor, Bangabandhu Shiekh Mujib Medical University (BSMMU) from August 2018 to February 2019. Vitamin D was measured in 20 obese and 20 non-obese children aged 10-18 years. Hypovitaminosis D was observed in all (100%) obese children and 15 (75%) non-obese children. Four thousand IU was given orally daily in obese and non-obese vitamin D deficient children for 3 months. Serum levels of vitamin D, calcium, inorganic phosphate, Alkaline Phosphatase (ALP) and Parathormone (PTH) also measured before and after vitamin D supplementation.

Results: The mean age was 11.64±1.40 years in obese and11.15±2.40 years in non-obese children, and male female ratio was 1:1.3. Hypovitaminosis D was present in 100% in obese and 75% in non-obese children. Vitamin D deficiency (VDD) was observed in 85% and vitamin D insufficiency (VDI) was in 15% in obese children. In non-obese children VDD was observed in 86.7% and VDI in 13.3% cases. In both the groups serum vitamin D was increased, alkaline phosphatase and parathormone levels were decreased significantly, and serum calcium was increased and serum inorganic phosphatase was decreased but not statistically significant after four thousand IU daily vitamin D supplementation for three months. After vitamin D supplementation, vitamin D status were found normal in 60% obese and 53.3% non-obese children, VDI were in 30% obese/overweight and 26.7% in non-obese children, and VDD were in 10% obese/overweight and 20% in non-obese children.

Conclusion: VDD was observed in both obese and non-obese children. Therapeutic responses were observed with 4000 IU/day vitamin D supplementation for three months in both the groups.

Keywords: Vitamin D, overweight, obese, non-obese, vitamin D deficiency, vitamin D insufficiency

Introduction

Childhood obesity is a major global health crisis. The worldwide prevalence of childhood overweight and obesity rose by nearly 50% over a span of three decades.[1] The prevalence of obesity and overweight among Bangladeshi school children of 6 to 15-years old were reported to be 3.5% and 9.7% respectively. Several studies showed decreased level of vitamin D in obese/overweight children.[2] The inverse association between higher body fat and lower vitamin D levels has been attributed to sequestration of the fat-soluble vitamin within the plentiful adipose tissue. Degradation of vitamin D in adipose tissue causing lower bioavailibity.[3] The effects of vitamin D deficiency (VDD) has been related to the pathogenesis of comorbidities

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such as insulin resistance, type 2 diabetes, hypertension, dyslipidemia, cardiovascular diseases and osteoporosis.[4] Zee Harel's study found that 100% obese children had (VDD) and another study conducted by Aypak in Egypt found 98.2% children had (VDD).[5,6] Limited data is available about (VDD) in obese children and non-obese children in Bangladesh. One study done in Bangladesh showed 42.02% non-obese children aged 5-11years and 46.75% non-obese children aged 12-16 years were vitamin D deficient.[7] Response to treatment with contradictory results have been reported in obese children with (VDD). However, there are insufficient data about the ideal vitamin D regimen to correct 25-Hydroxyvitamin D [25(OH)D] level in healthy children and adolescents. Limited studies in obese children and adults suggest that obese individuals tend to have a poor response to vitamin D supplementation.[8] High dose weekly vitamin D supplementation regimen (50,000 IU once a week for 6-8 weeks) in vitamin D deficient adolescents was found to normalize 25(OH)D levels in only a minority of subjects.[9] A study in preadolescent children also concluded that vitamin D3 supplementation with 400 IU/day for 1 month was not effective in increasing the 25(OH)D levels in majority of the subjects.[8] The objectives of the present study were there for to assess vitamin D status in Bangladeshi obese and non-obese children and to observe responses to vitamin D supplementation among those children.

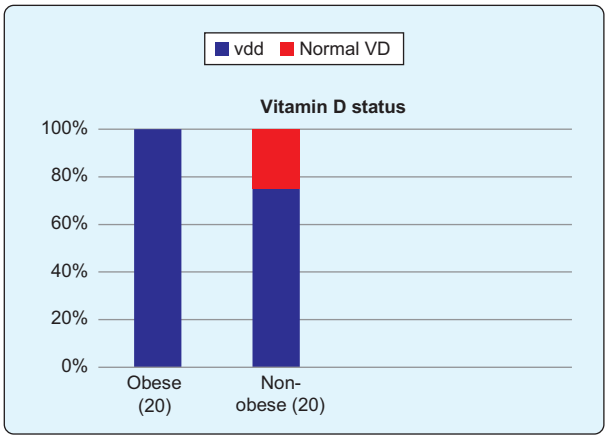
Materials and methods

This Quasi experimental study was done in Paediatric Endocrinology Clinic, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU). Twenty obese children aged 10 to 18 years, and age and sex matched twenty non-obese children were included in this study. Informed consent was obtained from each participant and their parents, and confirmed the participants compliance. Children who were taking systemic steroid, children suffering from genetic diseases (Prader-Willi Syndrome, Bardet-Biedl Syndrome), endocrine diseases (Hypothyroidism, Cushing Syndrome, Hypothalamic disorder), neurological diseases (Epilepsy getting Sodium valproate), having known liver or renal diseases and those who were treated with vitamin D and/or calcium within 1 year were excluded from study. Data were collected from patients and/or guardian by predesigned questionnaire. Obese and non-obese children were defined as BMI the 95th percentile and 5th to <85th percentile for age and sex according to CDC Chart respectively. VDD was defined as a serum 25(OH)D concentration of <20ng/ml, VDI as 20-<30ng/ml and vitamin D sufficiency as ≥30 ng/mL. At first blood samples of VDD/VDI were confirmed in 20 obese and 15 non-obese children and 4000IU vitamin D/day were supplemented orally for 3 months. Second blood samples were collected after 3 months of vitamin D supplementation. Serum vitamin D, calcium, inorganic phosphate, alkaline phosphatase (ALP) and parathormone (PTH) were measured in both the samples. Collected blood samples were send to Biochemistry Department of BSMMU immediately and serum was separated in micro centrifuged tubes and analyses were done immediately. Serum 25(OH)D level was measured by 5P02 ARCHITECT 25 OH Vitamin D reagent kit, PTH was determined by chemiluminescent immunoassay by using intact PTH test kit with the machine SIEMENS (Immulite 2000 System). Serum calcium was measured by CA method with the reagent Glycine buffer ocpc/8-Quinolinol, serum inorganic phosphate was measured by PHOS method by autoanalyzer (Black man Coulter auto analyzer, USA) and serum alkaline phosphatase (ALP) was measured by Trans-phosphorylation method by using the reagent P-nitrophenyl phosphate. These investigations were done by using the machine SIEMENS (Dimension RxL Max System) in the Department of Biochemistry, BSMMU. The data were analyzed by SPSS-20. Continuous variables were expressed as mean ± standard deviation and were evaluated by the unpaired Student's t test. Similarly, categorical variables were expressed as percentage of the total and were evaluated by the chi-square d (÷2) test to measure the level of significance (p value <0.05 was considered significant).

Results

In this study for serum vitamin D measurement, 20 obese and 20 non-obese children aged 10 -18 years were included. The mean age was 11.64±1.40 years

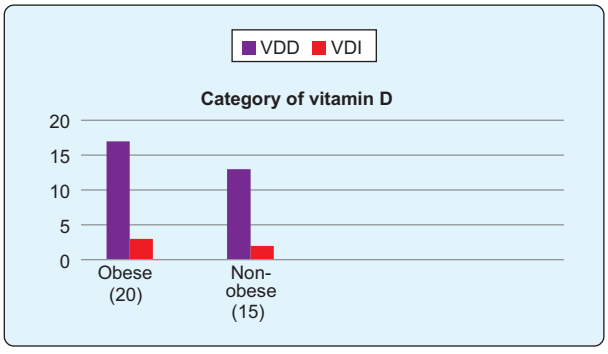
and 12.15±2.40 years in obese and non-obese children respectively, female and male ratio was 1: 1.4, and 75% percent obese and 60% non-obese children were from urban area. Mean weight of obese children was 68.5±75 kg and non-obese children was 44.3±61.54 kg, mean height was 149.05±11.36 cm in obese children and 143.47±12.92 cm in non-obese children and, BMI was 29.61±4.12 kg/m^2 in obese and 16.45±2.27 kg/m^2 in non-obese children. Hypovitaminosis D was observed in 20 (100%) obese children and 15(75%) non-obese children (Figure 1).



Value expressed in number and percentage.

Figure 1: Vitamin D status in obese (n=20) and non-obese children (n=20)

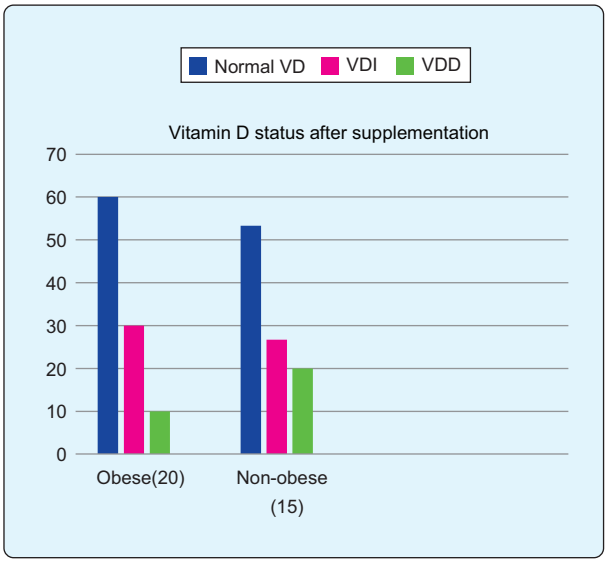
Among 20 obese children, 17(85%) were vitamin D deficient and 3 (15%) were vitamin D insufficient and among 15 non-obese children, 13 (86.7%) were vitamin D deficient, and 2(13.3%) were vitamin D insufficient (Figure 2).



Value expressed in number

Figure 2: Category of vitamin D in obese and overweight children

Table 1 shows that after supplementation, Vitamin D was increased from 13.15± 4.81 ng/ml to 29.53±9.2 ng/ml (p=0.001), ALP was decreased from 239.5±100.9IU/L to 169.75±58.78IU/L (p=0.01) and PTH was decreased 65.74±18.19 pg/ml to 43.75±12.81pg/ml (p=0.0001) in obese children. In non-obese children, vitamin D was increased from 14.63±4.95 ng/ml to 33.16± 9.20 ng/ml (p=0.0001), ALP was decreased from 225.6±96.9 IU/L to 166.67±53.01 IU/L (p=0.04) and PTH was decreased from 72.66±21.29 pg/ml to 37.45±17.92 pg/ml (p= 0.0001) after vitamin D Supplementation. Serum calcium and inorganic phosphate were not changed significantly in both obese and non-obese children. Table 2 shows that serum vitamin D was low but ALP and PTH were high in obese than non-obese group before and after vitamin D supplementation. Serum calcium and inorganic phosphate were not significantly different between the two groups. At the end of vitamin D supplementation period, vitamin D were found to be normal in 60% obese and 53.3% in non-obese children, VDI were in 30% obese and 26.7% in non-obese children, and VDD were in 10% obese and 20% in non-obese children (Figure 3).



Value expressed in number and percentage.

Figure 3: Vitamin D status in obese and non-obese children after vitamin D supplementation (n=35)

Table 1: Laboratory parameters in serum of obese and non-obese vitamin D deficient children before and after vitamin D supplementation (n=35)

Serum Parameters(mean±SD)	Obese (n=20)			Non-obese (n=15)		
	Before	after	P value	Before	after	P value
Vitamin D (ng/mL)	13.15± 4.81	29.53± 9.20	0.001	14.63±4.95	33.16±7.67	0.0001
S. calcium (mg/dL)	9.69±0.65	9.75±0.35	0.69	9,39±0.57	9.67±0.39	0.13
Inorganic phosphate (mg/dL)	5.11±0.74	4.74±0.54	0.05	4.81±2.05	4.14±2.12	0.86
Alkaline phosphatase (IU/L)	239.5±100.91	169.75±58.78	0.01	225.6±96.9	166.67±53.01	0.04
Parathormone (pg/mL)	65.74±18.19	43.75±12.81	0.0001	72.66±21.29	37.45±17.92	0.0001

Results are expressed as mean ± SD; *p* value was obtained by Paired t -test;
Pd™ 0.05: Significant, P>0.05: Not significant

Table 2: Comparison of laboratory parameters in serum before and after vitamin D supplementation between obese and non-obese vitamin D deficient/insufficient children.

Serum Parameters(mean±SD)	Before vitamin D supplementation (n=35)			After vitamin D supplementation (n=35)		
	Obese (n-20)	Non-obese (n=15)	P value	Obese (n-20)	Non-obese (n-15)	P value
Vitamin D (ng/ml)	13.15± 4.81	14.63±4.95	0.28	29.53± 9.20	33.16±7.67	0.06
S. calcium (mg/dl)	9.69±0.65	9,39±0.57	0.95	9.75±0.35	9.67±0.39	0.77
Inorganic phosphate (mg/dl)	5.15±0.74	4.81±2.05	0.06	4.74±0.54	4.14±2.12	0.06
Alkaline phosphatase (IU/L)	239.5±100.91	225.6±96.9	0.69	169.75±58.78	166.67±53.01	0.05
Parathormone (pg/ml)	65.74±18.19	72.66±21.29	0.11	43.75±12.81	37.45±17.92	0.91

Results are expressed as mean ± SD; *p* value was obtained by Paired t-test;
Pd™ 0.05: Significant, P>0.05: Not significant

Discussion

Vitamin D deficiency is a major health issue in the world, causing rickets in young children and osteomalacia in adults.[10] According to recent studies, VDD is related to obesity and adipose tissue which could be a target organ of vitamin D, and the vitamin D receptor (VDR) was recently found in adipose tissue.[11] The mean ages of our respondents were 11.64±1.40 years in obese and 12.15±2.40 years in non-obese children. These were similar to an Indian study by Khadgawat which reported the mean age of obese population as 13 ± 3 years.[12] In this study mean BMI was 29.61±4.12 kg/m² in obese children and 16.45±2.27 kg/m² kg/m² in non-obese children. In another two studies, the mean BMI was 24.39 ± 3.24 kg/m² and 27.36 ± 4.22 kg/m² in obese, and 13.45 kg/m2 and 16.30 ± 1.01 kg/m² in non-obese children which were similar to our study.[13,14] Obesity has become an epidemiologic problem recently because of its increasing prevalence as reported by World Health Organization (WHO).[15] There were evidence indicating the association between obesity and lower serum vitamin D.[16] In our study VDD and VDI were observed in 100% in obese and 75% in non-obese children. In obese group, 85% had VDD and 15% had VDI and 86.7% non-obese children had VDD and 13.3% had VDI. Gupta et. al showed that 80% obese children had VDD, 20% had VDI and none of them had sufficient vitamin D levels. They also observed that 10% non-obese children had VDD, 35% had VDI and 55% had sufficient vitamin D.[13] A study done in Italy among 444 obese and 113 non-obese children found that 81.1% of the obese and 71.7% of the non-obese children were suffering from hypovitaminosis D.[17]

Olson et.al observed the prevalence of VDD were 92% and 68% in obese and non-obese children respectively.[18] Therefore, a higher prevalence of low serum vitamin D level was observed in the obese group compared with the non-obese. Such a difference can be explained by the storage of vitamin D in fat stores, which is higher in obese Individuals.[19] VDD and excessive fat accumulation have mutually negative effects as a result of excessive metabolic processes, enzymatic disorders against a decreased activity of alpha-hydroxylase, in a fat-infiltrated liver, resulting in accumulation of inactive forms and decreased bioavailability of vitamin D. [20,21] Another reason of

low 25(OH)D concentrations in obese people is possibly due to their sedentary lifestyle, less active physically and decrease in exposure to sunlight which lead to decrease endogenous synthesis of vitamin D.[22] Other hypotheses were that vitamin D metabolism and 25(OH)D synthesis are impaired as a result of hepatic steatosis developing in obesity, and high levels of leptin and IL-6, impaired 25(OH)D synthesis by affecting VDR receptors.[23,24] VDD in obese and non-obese children may be due to many other reasons such as skin pigmentation, physical agents blocking UVR exposure, clothing, latitude, season, air pollution, cloud cover, altitude, sedentary lifestyle and high-rise building.[25-28] It was evident in our study that elevated ALP and PTH levels were observed in both groups similar to observation reported in another study.[29] This is possibly due to hypovitaminosis D.

Significant differences were observed between the obese and non-obese children in PTH and ALP levels after vitamin D supplementation in our study. In a study done in Iran, showed that PTH and ALP were decreased significantly after treatment with vitamin D.[30] In this study, after 4000IU/day vitamin D supplementation for 12 weeks, vitamin D were normal in 60% obese and 53.3% in non-obese children, VDI were in 30% obese and 26.7% in non-obese children and VDD were in 10% obese and 20% in non-obese children.[30] In another study, after the 12 weeks therapy, vitamin D concentrations were normalized in 50.0% of obese adolescents and 89.0% of healthy subjects. In their conclusion, the investigators recommended a dose increase for adolescents with obesity.[31] In another trial conducted in 68 obese adolescents, administration of vitamin D (50,000 IU once weekly for a period of 6-8 weeks) allowed normalization of 25 (OH) D concentrations only in 28%, while a repeated course of the same duration and at the same dose level produced no significant changes in the remaining 72%.[5] Because of the increasing prevalence of obesity worldwide, these findings seem to have become more important than before. Furthermore, we observed that the treatment responses to oral vitamin D were significantly different among the studies. It is also important to note that mean serum vitamin D level change was in obese and non-obese children were not significantly different. Different results were obtained by another group of researchers, who treated Hispanic and African American adolescents with the same dose of vitamin D3 (50,000 IU once a week, for 6 weeks).[4] In another study 18 obese and 18 non-obese adolescents were treated with vitamin D3 (2000 IU/day) orally for 12 weeks and the results revealed that the response to vitamin D supplementation was almost 2-fold lower in the obese group compared with the nonobese one.[32] What could be the reasons for wide variations in reported results on VDD and responses to supplementation. Possibly, ethnic differences leading to genetic variations among various study populations may be responsible, in addition to other apparently known factors.

Conclusion

It was observed that serum Vitamin D levels among our respondents were low in both obese and non-obese children. The responses of obese children to vitamin D supplementation was almost similar to non-obese children. ALP and PTH levels were significantly decreased after vitamin D supplementation in obese and non-obese children. Future studies involving more participants are needed to determine the proper dose of vitamin D therapy in obese and non-obese children in a particular geographical location and ethnic group.

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