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Comparison of Vitamin D Deficiency and Secondary Hyperparathyroidism in Obese and Non-obese Children and Adolescents

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Abstract: Obesity subjects individuals into metabolic and endocrine disorders. Thus obesity may increase the risk of vitamin D deficiency. This text aims at studying the prevalence of vitamin D deficiency and secondary hyperparathyroidism in obese children. In a non-randomized case control study on 52 obese children (body mass index (BMI)>95th percentile) aged 4 to 16 years undertaken at the outpatient endocrine clinic of the Children Hospital at Tabriz University between 2009-2011. This study was conducted to compare the prevalence of vitamin D deficiency and secondary hyperparathyroidism in obese children compared with 57 non obese (BMI<85th percentile). 109 children including 52 (50.5%) boys and 57 (49.5%) girls were studied. Most of case (76.9%) and control (42.1%) groups suffered from degrees of vitamin D deficiency. There was meaningful statistical difference between two groups considering to vitamin D deficiency and parathyroid hormone ($p = 0.001$). A negative relations was found between iPTH and vit D level ($p<0.001$, $r = -0.2$), BMI and 25-OH vit D ($p<0.001$, $r = -0.2$). A positive relation was observed between parathyroid hormone and BMI ($p = 0.009$, $r = 0.1$). Obese children are at high risk at vitamin D deficiency and secondary hyperparathyroidism. BMI appears to be an important risk factor for vitamin D deficiency.

Key words: Vitamin D, obesity, hyperparathyroidism, children

INTRODUCTION

Obesity is one of the most important problems encountered by the children. Considering national statistic of the United States, prevalence of overweight and obesity in children and adolescents has significantly increased during the last decades to about 250 million or 7 percent of the world population suffer from obesity and two or three times of them have overweight (Yanovski and Yanovski, 2003). One of these studies revealed that prevalence of overweight was two times in 6-11 years old children and three times in 12-17 years old ones (Speiser *et al*., 2005). Overweight and obesity prevalence increased from 8.7 to 13.5% in boys and 11.8 to 18.6% in girls of developing countries from 1998 to 2004 (Bovet *et al*., 2006). Periodical studies provide information about significant increase of adolescents' obesity and overweight in their school years. So, obesity epidemic is a global problem (Gordon *et al*., 2004; Janssen *et al*., 2005). In recent years, Prevalence of obesity and overweight has significantly increased in our country (Jazayeri, 2005). Imposing of prevailing and treating charges which arises from diseases related to obesity to the care and health systems has significantly increased within the last 20 years and led to considerable growth in economical charges (Wang and Dietz, 2002).

Obesity in childhood is accompanied with complications such as obstructive sleep apnea, asthma, orthopedic problems, hyperandrogenism and cardiovascular diseases. Such complications can threat children health and increase load of disease on country care and health system. (El-Helaly *et al*., 2009; Afridi *et al*., 2003). Also, obesity is closely related to the increase of risk of suffering from impaired glucose tolerance and insulin resistance in children and adolescents (Ghergherechi and Tabrizi, 2010) and is accompanied with disorder in nutrition biochemical condition through increase in body mass index (Need *et al*., 2005). Bioavailability of vitamin D through dermal resources and diet decreases among the obese and is probably destroyed by fat contexts (Wortsman *et al*., 2000).

Twenty five (OH) D serum concentrations is the best marker of whole body vitamin D condition (Moradzadeh *et al*., 2008; Norman, 1998). In fact, low 25 (HD) D serums and the resulted hyperparathyroidism

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are regarded as obesity endocrine disorders (Kamycheva *et al*., 2004). It has been demonstrated that obese children and adults have low 25 (HD) D serum and Intact Higher Levels of Parathyroid Hormone (iPTH) (Parikh *et al*., 2004; Alsayed *et al*., 2007). Therefore, obesity increases risk of vitamin D deficiency. This study aims at comparing biochemical markers of vitamin D deficiency in obese and non-obese children.

MATERIALS AND METHODS

Some 4-16 years old obese children and adolescents referred to endocrine clinic of Tabriz Pediatrics Educational and Therapeutic Hospital included in a case control study as the case group after initial examinations, height measuring by centimeter (without shoes) through, use of wall-mounted height testing instrument with the scale of 0.1 cm, weight by kilogram and approximate scale of 0.1 km through use of Sega scale, body mass index was calculated in accordance with the formula of height^2 (m)/weight (kg). They were included in the case group if their body mass index was over than 95% for their age and gender. In the control group, the condition required for entering the study was body mass index less than 85% for age and gender. Understudy individuals and those of the control group were excluded from the study in case of suffering from each of the chronic renal and liver diseases, malabsorption, enteritis and using anticonvulsion and glucocorticoids. Blood samples were taken and sent to the reference laboratory to measure serum levels of 25 (OH) D, iPTH, calcium, phosphor and alkaline phosphatase. Hitachi 911 made in Japan was used to samples measuring of laboratory factors. Serum 25 (OH) D was measured using Nichols Advantage 25 (OH) D chemiluminescent assay (Nichols Institute, San Clemente, CA). PTH was measured using IMMULITE Intact PTH chemiluminescent assay (Diagnostic Products, Los Angeles, CA), PTH over than 58 mL pg^{-1} has been considered as hyperparathyroidism. American Academy of Pediatrics (AAP) defines sever vitamin D deficiency among infants and children as (OH) 25 serum level less than 11 ng mm^{-1}. This study considers 20 D<30 ng dL^{-1} as vitamin D insufficiency, vit D <20 ng dL^{-1} as vitamin D deficiency and less than 10 mg dL^{-1} as sever deficiency. The study conditions explained to the understudy individuals beforehand and they or their guardians consent was obtained for participating in the study. The present study conducted under supervision of Ethic Committee of Tabriz University of Medical Sciences.

Statistical analysis: Central statistical descriptive and distribution indices were used for statistical analysis. Chi-square statistical tests were used to study qualitative variables, respectively. Normal distribution measured by One-Sample Kolmogorov-Smirnov test. Nonparametric tests (Mann-Whitney U) were used to study two case and control groups. Spearman statistical test has been used to study relation of quantitative variables. All statistical analyses were conducted through use of SPSS 16 statistical software. Significance level was set at $p \leq 0.05$.

RESULTS

This study compared 109 children including 52 obese children of the case group with age average of 8.9±7.2 and body mass index over than 95 with 57 children of the control group with the age average of 86.2±24.9 month and body mass index of less than 85%. There was no statistically meaningful difference between the groups considering age and gender and both of them were the same. Average of the measured vitamin D was 44.2±11.2 ng mL^{-1} in the control group. It was equal to 32.7±29.6 ng mL^{-1} in the case group with children of body mass index over than 95%. A statistically meaningful difference was observed between two groups considering average of vitamin D ($p = 0.01$). The measured parathyroid hormone was 60.54±50.6 and 68.53±41.3 pg mL^{-1} for control and case groups, respectively. It is observed that parathyroid hormone is meaningfully increased in obese children than the non-obese ones ($p = 0.03$). In other measured laboratory factors no statistically meaningful difference was observed among obese and non-obese children except phosphor serum level, as seen in Table 1. Prevalence of hyperthyroidism was seen in 24 cases (46.2%) of obese children and 19 cases (33.3%) of non-obese ones. 76.9% of the case group children and 42.1% of the control group suffered from vitamin D deficiency such that sever deficiency of vitamin D was observed in 23 (44.2%) of obese children, average deficiency in 17 (32.7%) and insufficiency in 11 (21.2%) cases. In contrast, sever and average deficiency were observed just in 10 (17.5%) and 14 (24.6%) non-obese children, respectively. Considering insufficient level of vitamin D, most of the obese children (22 cases, 38.6%) were in this level and, in fact, suffered less from deficiency and sever deficiency of vitamin D.

There was a positive statistical relationship between parathyroid hormone level and weight based on BMI

Table 1: Laboratory measured values between case and control groups

Variables	Case group (n = 52)	Control group (n = 57)	p-value
Calcium (mg dL^{-1})	9.8±4	11.13±1.1	0.70
Phosphore (mg dL^{-1})	4.27±0.7	4.5±0.6	0.04
Alkaline phosphatase (mg dL^{-1})	419.1±216.9	431.0±186.3	0.20

Values are as Mean±SD

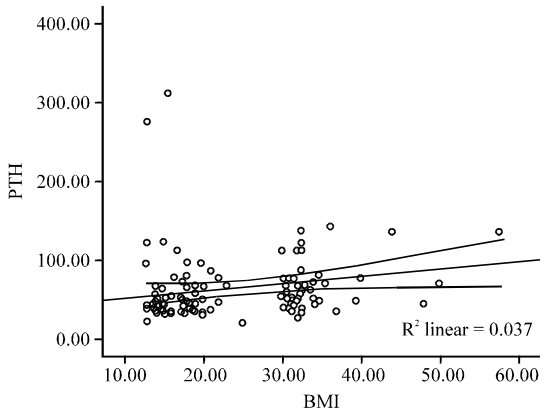

Fig. 1: Positive correlation between BMI and PTH

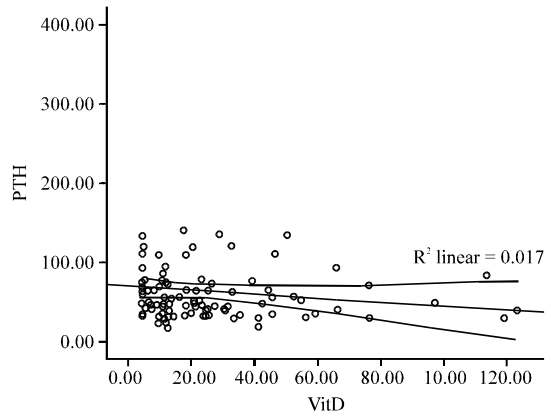

Fig. 2: Significant correlation between vitamin D and PTH

($p = 0.009$, $r = 0.1$). Figure 1 demonstrates that weight gain by children lead to creation of a positive relation between parathyroid hormone level and prevalence of hyperthyroidism. Also, a statistically meaningful relation between parathyroid hormone and vitamin D has been proved in this study, as seen in Fig. 2 ($p<0.001$, $r = -0.2$). According to the Fig. 3, vitamin D level had statistically negative meaningful relation with the children weight based on BMI such that increase of children' weight lead to decrease of vitamin D level and, as a result, its deficiency ($p<0.001$, $r = -0.2$).

DISCUSSION

Obesity is an important health and therapeutic problem in the developing and developed countries. It has significantly increased during the last two decades (Esmaeily *et al*., 2009; Gholamreza and Mohsen, 2007). Obesity subjects individuals into metabolic and endocrine disorders (Afridi *et al*., 2003; Smotkin-Tangorra *et al*., 2007). Accompanying of obesity with diabetes mellitus, coronary vessels diseases, hyperlipidemia and osteoarthritis is well known. Vitamin D deposited in body fat resources after synthesis through skin or having foodstuffs. McCarty and Thomas (2003) suggest that physiologically increase of parathyroid hormone in response to D hypovitaminase condition lead to increase of intercellular calcium in adiposities which result in increased lypogenes and weight increase (McCarty and Thomas, 2003).

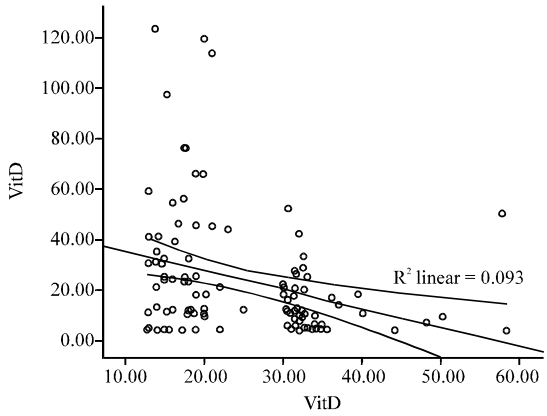

Fig. 3: Negative significant correlation between BMI and vitamin D

Prevalence of vitamin D deficiency has been reported by Gordon *et al*. (2004) studies, 40% had levels lower than optimized one. There was a reverse relation between 25 (OH) D serum and parathyroid hormone level. At this study, one third of individuals suffering from vitamin D deficiency contacted demineralization which states skeleton harmful effects of the condition (Gordon *et al*., 2008). Outila *et al*. (2001) studied effects of vitamin D deficiency on concentration of intact parathyroid hormone (iPTH). This study conducted on 14-16 years old girls (No = 178) out of them 13.5% suffered from vitamin D deficiency. Rajakumar *et al*. (2008) noticed vitamin D deficiency in 57% of understudy obese and 40% of normal individuals which decreased to 24% and 11% after treatment, respectively. In present study, prevalence of vitamin D sever deficiency among children had body mass index higher than 2.44%. The difference between two groups was meaningful and prevalence of vitamin D deficiency among our obese children was more serious than the previous studies. Bell *et al*. (1985) observed that PTH and 1.25 (OH) 2D serum average was meaningfully high and 25-OH D serum average was significantly low in obese persons than the non-obese ones. These results suggest that changes of vitamin D endocrine system in obese individuals are determined

with secondary hyperparathyroidism (Bell *et al*., 1985). In Snijder *et al*. (2005) study, BMI and waist size were significantly related with lower 25-OH D and higher PTH. Also, body fat percent had a strong relationship with these two variables. This study concludes that body total fat is reversely and positively related with 25-OH D and PTH levels, respectively (Snijder *et al*., 2005). Yanoff *et al*. (2006) study revealed that prevalence of D hypovitaminase increases with increase of body mass index. iPTH has a negative relation with 25 (OH) D suggesting that individuals with D hypovitaminase suffer from an important clinical vitamin D deficiency along with secondary hyperparathyroidism. In the study conducted by Alemzadeh *et al*. (2008) prevalence of D hypovitaminase was observed in 74% of 6-17 years old obese children and adolescents with body mass over than 95%. This is while 32% (about one third) of obese children and adolescents definitely suffer from vitamin D deficiency (Alemzadeha *et al*., 2008). Reinehr *et al*. (2007) also confirmed the above-mentioned findings. Similarly, there was a meaningful difference between children with high body mass index and those with normal body mass index at the present study. Also, a meaningful difference was observed in our study between parathyroid hormone levels in obese children than the non-obese ones. Therefore, increase of severity of vitamin D deficiency leads to meaningful increase of hyperparathyroidism. Reinehr *et al*. (2007) observed that obese children have meaningfully higher PTH and lower 25-OH vit D concentrations than the non-obese ones. This is while no meaningful difference was observed considering calcium, phosphate and 1.25-OH vit D. PTH and 25-OH vit D changes had a meaningful relationship with BMI changes but had no relation with insulin sensitivity changes (Reinehr *et al*., 2007). This study concludes that PTH and 25-OH vit D changes are regarded as the result of obesity rather than its cause. In this research, contrary to the above-mentioned one, the only statistical difference resulted from phosphor level between two groups and no difference was observed in other laboratory factors.

CONCLUSION

Obese children are at high risk considering vitamin D deficiency and secondary hyperthyroidism. It seems that BMI may be an important risk factor for vitamin D deficiency. Considering the above cases, it is recommended that obese children especially those with high body mass index take routinely vitamin D supplementary treatment or routinely screened regarding vitamin D deficiency.

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