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ORIGINAL: Evaluation of Vitamin D Deficiency and Its Relationship with Body Mass Index in Children 1 To 16 Years

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ABSTRACT

Introduction: Body weight gain in children and teenagers is one of the major challenges that cause undesirable health outcomes. Simultaneously with the prevalence of overweight and obesity, children and adolescents are diagnosed with 25-hydroxyvitamin D (25(OH)D) deficiency in different sides of the world. The present study aimed to assess 25(OH)D status among Iranian volunteers aged 1-16 years and find the correlation between 25(OH)D status and body mass index (BMI) subjects.

Material and Methods: The total volunteers included 807 Iranian children aged 1 to 16 referred to the general and endocrinology clinics in Babol city, Mazandaran Province. A trained physician determined anthropometric characteristics. Serum levels of calcium (Ca), phosphate (P), creatinine (Cr), urea, thyroxine (T4), thyroid-stimulating hormone (TSH), and 25(OH)D were assessed in all children.

Results: 25.27% of the children were 25(OH)D deficient, and 59.1% were insufficient. There was no significant difference in serum 25(OH)D level between girls and boys (P=0.13). A significant negative correlation was found in serum 25(OH)D level with weight (P=0.000, r=-0.12), BMI (P=0.000, r=-0.13), and age (P=0.000, r=-0.13).

Conclusion: These data displayed that 25(OH)D insufficiency is highly prevalent among children in the north of Iran. Serum 25(OH)D levels are affected by age and BMI value. Improving vitamin D deficiency helps to maintain the health of children and adolescents during this critical period.

Introduction

Obesity is considered one of the major public health concerns worldwide, and its prevalence in children has reached eightfold since 1975 (1). Based on the world health organization reports, obesity in 2 to 18 years children and teenagers is diagnosed as body mass index (BMI) ≥ 95th percentile, and it has recently become an epidemiologic challenge due to its growing prevalence (2). The four USA, Italy, Mexico, and Greece countries have the highest prevalence of childhood obesity (3, 4).

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Obesity dramatically raises the risk of developing chronic non-communicable diseases and health costs. Today, an important part of public health programs focuses on reducing the prevalence of obesity in different populations of the world (5).

In recent decades, epidemiological studies have indicated that along with the global prevalence of obesity, vitamin D deficiency has attained epidemic levels worldwide (6-8). Vitamin D deficiency or insufficiency is particularly prevalent in children and adolescents in different parts of the world, including the Middle East, Australia, India, South America, and Africa (9, 10). In Iran also, vitamin D deficiency is highly prevalent among children (11). The serum 25-hydroxyvitamin D (25(OH)D) concentration is accepted as the best indicator of vitamin D serum level. Hence, vitamin D deficiency is defined as serum 25(OH)D concentration<20 ng/mL (12). According to this definition, the prevalence of vitamin D deficiency in Iran's central and southern was reported as 30 to 50% in children under 12 years of age (11, 13). Vitamin D is a fat-soluble vitamin responsible for bone mineralization by enhancing kidney absorption of calcium (Ca^{2+}), increasing gastrointestinal absorption of Ca^{2+} and phosphorus (P), and regulating osteoblast activity. Therefore, vitamin D deficiency results in rickets in children and osteomalacia or low bone density in adults. (14, 15). In addition to the traditional role of vitamin D in bone metabolism, its new functional roles have appeared to link vitamin D to different non-communicable diseases. There have been a growing number of evidence on the correlation between vitamin D deficiency and anthropometric characteristics. However, some studies have revealed that vitamin D deficiency in children is related to increasing age and obesity (16). There are restricted data on the correlation of BMI and vitamin D status in Iranian children. The current study was administered to fill the available gap in knowledge on vitamin D in children and adolescents living in the north of Iran. The association of vitamin D status with its various biochemical factors and BMI was assessed over a broad range of ages.

Methods

Subjects' enrollment

To conduct this retrospective study, 807 Iranian children aged 1-16 years were selected among those referred to general and endocrine clinics of children in Babol city, Mazandaran Province, Amir Kala. Exclusion criteria were included bone or Ca^{2+} metabolism disorders, chronic granulomatous disease, endocrine diseases causing obesity such as Cushing syndrome, vitamin D supplements, or certain medications usage such as anticonvulsants. The Ethics Committee of Babol University of Medical Sciences approved the current project. The consent form was signed by the parents of all participants in the project.

Anthropometric measurement

The anthropometric characteristics of children, including weight and height, were determined by a trained physician. All subjects were weighed to the nearest 0·1 kg using a standard scale (Seca, Germany). The height of volunteers was measured with a wall-mounted stadiometer with a scale accurate to the nearest 0·5 cm. During anthropometric measurements, the children wore only light clothing and no shoes. BMI value was estimated as body weight/ body height^2 (kg/m^2).

Biochemical variables

A 10 ml fasting blood sample was obtained from all participants, centrifuged, and then separated serums were stored at −20°C until further biochemical analysis. The serum level of 25(OH)D was measured by the Electro-Chemi-Luminescence kit (Roche). Based on current Endocrine Society clinical practice guidelines, vitamin D deficiency and insufficiency were defined as serum 25(OH)D <20 ng/mL and 21<25(OH)D<29 ng/mL (17). The serum concentration of thyroxine (T4) and thyroid-stimulating hormone (TSH) were determined by enzyme-linked immunosorbent assay (ELISA).

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Normal ranges for TSH and T4 were 0.25-4.3 mIU/L and 5-12 µg/dL, respectively. Serum $Ca2^{+}$, P, urea, and creatinine (Cr) were measured by commercial kits using an auto-analyzer (Biosystems SA, Spain). Normal values for serum corrected Ca^{2+} was 8.5–10.5 mg/dL, for P was 3.7–5.4 mg/dL for children <16 years old, for urea 5-20 mg/dL, and for Cr was 0.8 to 1.15 mg/dL, respectively.

Statistical analysis

Statistical analyses were performed by IBM SPSS Statistics software, version 18.0. All variables are reported as mean ± standard deviation (SD). Kolmogorov–Smirnov (KS) test was employed to evaluate the normality of data distribution. Mann–Whitney test, Student's t-test, and ANOVA were utilized for the comparison of parameters. The correlations between variables were determined using Pearson's test. A P-value less than 0·05 was set as significant.

Results

In this retrospective study, the medical records of 807 children and adolescents between 1 and 16 years of age were reviewed. The anthropometric and biochemical characteristics of the study population are given in ***Table 1***. The results were expressed as mean ± SD in four groups separated by age. The results presented in ***Table 1*** show that serum Cr, P, 25(OH)D, height, weight, and BMI are significantly different between the four groups (P <0.05). There was no meaningful variation in the serum concentration of urea, T4, TSH, and Ca^{2+} among the desired groups (P>0.05; ***Table 1***).

Table 2 presents the results as mean ± SD and based on gender separation. 376 of the participants were girls, and 432 of them were boys. There was no notable diversity in the amount of 25(OH)D, T4, and P among the two groups (P> 0.05), but a significant difference was observed in other biochemical values, urea, Cr, Ca, height, weight, and BMI, between boy and girl groups.

BMI values in three groups separated by 25(OH)D amounts were demonstrated in ***Figure 1***. Adequate 25(OH)D was >30 ng/mL, insufficient 25(OH)D was between 10 to 30 ng/mL, and deficient 25(OH)D was <10 ng/mL. There was a significant difference between the three groups in terms of BMI (P <0.05). ***Figure 2*** shows the correlation between 25(OH)D and BMI in 807 children and adolescents between 1 and 16 years of age.

In ***Table3***, a significant negative correlation was found in serum 25(OH)D level with weight (P=0.000, r=-0.12), BMI (P=0.000, r=-0.13), and age (P=0.000, r=-0.13) respectively.

Table 1. Comparison of anthropometric characteristics and laboratory parameters in four groups, separated by age

	GroupI (1-4years) (n=94)	GroupII (5-8years) (n=335)	GroupIII (9-12years) (n=270)	GroupIV (13-16years) (n=108)	P-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Urea (mg/dL)	23.55±7.89	22.83±6.02	23.51±7.11	26.34±8.21	0.24
Cr (mg/dL)	0.51±0.09	0.54±0.09	0.62±0.08	0.72±0.16	0.00
T4 (µg/dL)	9.57±5.52	8.87±1.61	8.69±5.56	7.79±0.98	0.14
TSH (mIU/L)	2.52±1.34	2.61±1.3	2.7±1.19	2.33±0.99	0.17
Ca (mg/dL)	9.89±0.39	9.83±0.38	9.6±0.37	9.79±0.37	0.115
P (mg/dL)	5.32±0.52	5.13±0.56	4.95±0.72	4.62±0.72	0.000
25(OH)D (ng/mL)	22.26±10.56	19.96±12.6	19.78±12.42	15.86±7.85	0.001
Length (cm)	91.82±9.47	118.3±12.73	138.35±10.10	152.61±12.41	0.000
Weight (kg)	13.44±4.05	25.27±14.34	38.60±13.95	52.14±17.49	0.000
BMI (kg/m^2)	13.44±4.05	25.27±14.34	38.6±13.95	52.14±17.49	0.000

All variables are presented as mean ±SD. * P-value refers to the comparison of each value between age categories. BMI: Body mass index; Ca: Calcium; P: phosphorus; Cr: creatinine; T4: thyroxine; TSH: Thyroid-stimulating hormone; 25(OH)D: 25-hydroxyvitamin D.

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Table 2. Comparison of studied factors based on gender separation

	Mean ±SD		P-value
	Female (n=376)	Male (n=432)	
T4 (µg/dL)	8.98±5.28	8.94±3.52	0.9
TSH (mIU/L)	2.7±1.3	2.53±1.23	0.04
Urea (mg/dL)	24.73±7.29	23.18±7.18	0.003
Cr (mg/dL)	0.6±0.12	0.59±0.1	0.07
Ca (mg/dL)	9.79±0.37	9.84±0.38	0.02
P (mg/dL)	5.03±0.65	5.02±0.67	0.93
25(OH)D (ng/mL)	20.29±11.61	19.03±12.09	0.13
Length (cm)	128.3±22.31	125±19.53	0.02
Weight (kg)	33.58±20.19	30.53±15.50	0.01
BMI (kg/m^2)	33.58±20.19	30.53±15.50	0.01

All results are displayed as mean ±SD. *P-value refers to the comparison of each value between gender groups. BMI: Body mass index; Ca: Calcium; P: phosphorus; Cr: creatinine; T4: thyroxine; TSH: Thyroid-stimulating hormone; 25(OH)D: 25-hydroxyvitamin D.

Table 3. Correlation of serum vitamin D levels with age, weight, height, BMI, and biochemical parameters

		Ca	P	Urea	Cr	T4	TSH	Age	Weight	BMI
25(OH)D	Pearson Correlation	.018	-.002	.043	.006	.051	.046	-.131**	-.135**	-.135**
	Sig. (2-tailed)	.615	.956	.233	.863	8.15	.206	.000	.000	.000

**P-value <0·01 was set as significant. BMI: Body mass index; Ca: Calcium; P: phosphorus; Cr: creatinine; T4: thyroxine; TSH: Thyroid-stimulating hormone; 25(OH)D: 25-hydroxyvitamin D.

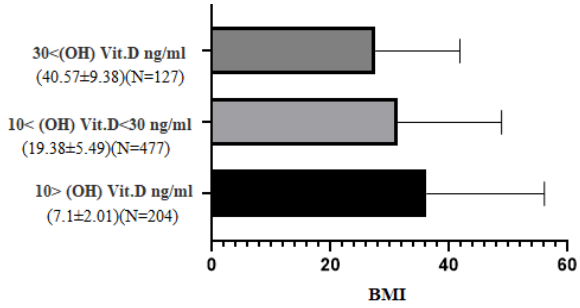

Figure 1. Comparison of BMI in three groups based on the amount of vitamin D. All variables are shown as mean ±SD. P-value <0.05 was set as significant. BMI: Body mass index; 25(OH)D: 25-hydroxyvitamin D.

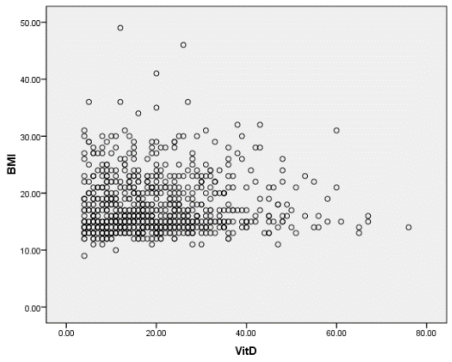

Figure 2. Correlation between vitamin D and BMI in 807 children and adolescents between 1 to 16 years (r = -0.13 and P=0.000).

Discussion

Based on this large population-based retrospective study, we found a remarkably high prevalence of vitamin D insufficiency in Iranian children aged 1-16 years in Babol city, a northern part of Iran. There was an inverse correlation between 25(OH)D concentration and age, weight, height, and BMI values.

Several cross-sectional studies have been performed to appraise the prevalence of Vit D deficiency in Iran's south and central parts. In a study, Neyestani and his colleagues reported an 86% prevalence of Vit D deficiency among schoolchildren aged 9–12 years in Tehran (18). In another study conducted in children aged 7–12 years, Rabbani et al. showed that 53.6% of children and adolescent girls had serum 25(OH)D <20 ng/ml in Tehran (19). Also, a high prevalence of Vit D deficiency (25(OH)D <20 ng/ml) in Isfahan children aged 6–7 years was observed in the Ardestani et al. study (20). Saki and her co-workers, in a cross-sectional study, illustrated that 25(OH)D deficiency is highly common among children in the south of Iran, which is related to increasing age (13).

The present study assessed 25(OH)D status in children aged 1–16 years in Babol city, in the

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north of Iran, and shows a high prevalence of vitamin D insufficiency with age. The findings of the present study were in line with previous studies in other parts of Iran. The results of our study and other investigations showed that Iranian children suffer from vitamin D deficiency. Given the importance of vitamin D in children's growth and health, a proper program is needed to improve vitamin D deficiency.

Many well-documented factors influence the serum concentration of 25(OH)D in humans, including exposure to sunlight, diet, gastrointestinal, and renal disorders. Besides, lower 25(OH)D status concentrations have been related to older age, higher BMI, female gender, black ethnicity, and winter season (21-23). Our data exhibited an inverse association between serum concentration of 25(OH)D status and children's age. Some evidence in Korea and Europe has also revealed that younger adolescents had higher serum levels of 25(OH)D status than older ones (17, 24, 25). Commonly, elderly persons are subject to 25(OH)D status deficiency due to several risk factors, like diminished production of 25(OH)D status in the skin, reduced sunlight exposure, decreased intestinal absorption, and declined hydroxylation in the kidney (26-29). In addition to age, BMI is also an important factor influencing 25(OH)D status. Many reports have demonstrated a negative association between BMI and serum 25(OH)D status. Brock et al. demonstrated that BMI >30 kg/m^2 is one of the essential factors that influence 25(OH)D status (30). Our study showed that BMI had an inverse association with serum 25(OH)D concentration, and 25(OH)D insufficiency is more prevalent among overweight and obese subjects. Another remarkable result was the negative correlation between BMI and serum 25(OH)D concentration (P=0.000, r=-0.13), which was similar to data reported by other previous studies (31). In a study of obese and non-obese American children, subjects were treated with 200 IU/day of vitamin D3 for 30 days. K Rajakumar et al. showed that vitamin D3 oral treatment was more impressive in non-obese people (32). Motlaghzadeh et al. illustrated a high frequency of vitamin D deficiency between obese Iranian children. They observed an inadequate therapeutic response to vitamin D3 in obese children (33). According to this information, it can conclude that the inadequate therapeutic response to oral administration of vitamin D3 in obese children probably is linked to higher fat stores as well as distinct metabolism of 25(OH)D in obese persons. Based on the information provided in reliable sources, 25(OH)D may be arrested in fat stores and alleviated its bioavailability (34). Because subjects with normal weight have fat tissue less than that of overweight subjects, they might reveal higher 25(OH)D availability. This information is in agreement with the results shown in the present study. Leptin released from excess body fat is one of the important factors influencing decreased 25(OH)D levels through inhibiting 25(OH)D activation in kidneys (35).

One of the limitations of this study is that diverse vitamin D–related genetic factors and signaling pathways were not evaluated so that these are probable relevant factors.

Conclusion

Altogether, this study supports an inverse correlation between obesity and vitamin D status in children and teenagers. The therapeutic strategies should be advanced to hamper vitamin D deficiency during this important period, although further investigations are required to assign the pathophysiology of the reduction in serum 25(OH)D level observed during obesity. Finally, recent conception from genetic analyses displays urgent use of personalized nutrition for vitamin D deficiency, whereby certain vitamin D receptor (VDR) profiles may engage in designing a response to vitamin D supplementation in the future.

Ethical standards statement

The current study was exerted in the general and endocrine clinics of children in Babol city, Mazandaran Province, Amir Kala

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Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to governmental policy and privacy.

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Conflicts of interest

The authors have stated that no conflict of interest occurs.

Authors' contributions

All authors have intellectually committed to the study design and process. The final manuscript was revised and accepted by all authors.

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