Vitamin D deficiency is associated with metabolic syndrome in Tunisian children with obesity

La carence en vitamine D est associée au syndrome métabolique chez les enfants Tunisiens souffrant d'obésité

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RÉSUMÉ

Introduction: Plusieurs études avaient mis le point sur la carence en vitamine D chez les sujets obèses. Cependant, le statut de la vitamine D chez les enfants Tunisiens obèses et son association avec le risque de syndrome métabolique reste peu étudié.
Objectif: Nous nous sommes proposé d'étudier la prévalence de la carence en vitamine D chez les enfants Tunisiens obèses et de rechercher des corrélations entre la carence en vitamine D et les éléments du syndrome métabolique.
Méthodes: Trente enfants obèses appariés à 30 témoins volontaires de corpulence normale selon l'âge, le genre et le stade pubertaire ont été inclus dans une étude prospective. Les paramètres anthropométriques et la pression artérielle ont été mesurés. Le taux de vitamine D, la glycémie à jeun et le profil lipidique ont été réalisés chez tous les sujets.
Résultats: La carence en vitamine D était plus fréquente chez les enfants obèses (94% vs 80%, p = 0,002). Le niveau de vitamine D était négativement corrélé avec l'IMC (p = 0,001, r = -0,51). Un syndrome métabolique a été diagnostiqué chez six enfants obèses. Les niveaux de vitamine D étaient corrélés négativement avec le tour de taille (p = 0,019, r = -0,13), la tension artérielle systolique (p = 0,04, r = -0,26), le taux de triglycérides (p = 0,025, r = -0,3), l'insuline
(p = 0,01, r = -0,34) et l'indice d'insulino-résistance HOMA-IR (p = 0,035, r = -0,29).
Conclusions: Malgré le climat ensoleillé, le déficit en vitamine D est fréquent en Tunisie. La carence en vitamine D est négativement corrélée à l'IMC et aux éléments du syndrome métabolique

Mots-clés
Vitamine D, Obésité, Insulinorésistance, Enfant

SUMMARY

Background: A negative association between serum vitamin D levels and obesity has been reported by several studies. Data on vitamin D status in Tunisian obese children and its relationship with metabolic syndrome remain rare.
Aim: We aimed to study the prevalence of vitamin D deficiency in Tunisian obese children and to examine the correlation between vitamin D levels and metabolic syndrome.
Methods: Thirty obese children matched to 30 non-overweight volunteer controls by age, gender and pubertal stage were included in a prospective study. Anthropometric parameters and blood pressure were measured. Vitamin D level, fasting glucose and lipid profile were performed in all subjects.
Results: Vitamin D deficiency was more common in obese children (94% vs 80 %, p=0.002). Vitamin D level was negatively correlated with BMI (p= 0.001, r= -0.51). Six obese children were diagnosed with metabolic syndrome. Vitamin D levels were negatively correlated with waist circumference (p=0.019, r=-0.13), systolic Blood pressure (p=0.04, r=-0.26), triglyceride level (p=0.025, r= -0.3), insulin (p=0.01, r=-0.34) and HOMA-IR (p=0.035, r=-0.29).
Conclusions: despite the sunny climate, the deficiency in vitalmine D is common in Tunisia. Vitamin D levels are inversely correlated with BMI and the risk of metabolic syndrome.

Key-words
Keywords: Vitamin D, Obesity, Insulin resistance, Childhood

INTRODUCTION

The prevalence of childhood obesity is increasing steadily all over the world causing a broad range of health problems that previously weren't seen until adulthood. Several Studies have consistently shown that low vitamin D levels are associated with obesity. However, vitamin D status in Tunisian obese children is still unstudied. Moreover, the implication of vitamin D status in the occurrence of the metabolic syndrome (MS) in obese children remains controversial. We aimed to study the prevalence of vitamin D deficiency in Tunisian obese children and to examine the relationship between 25-hydroxyvitamin D (25(OH) D) levels and metabolic syndrome.

METHODS

We performed a case-control study between Marsh 2017 and June 2018. We prospectively included 30 children with obesity defined as a Body Mass Index (BMI) at or above the 95th percentile for children of the same age (3). At the same time, age-gender and Tanner stage-matched healthy controls were recruited from the department of pediatrics. Exclusion criteria for both patients and healthy volunteer controls were steroid treatment during the preceding 12 months, syndromic obesity, subjects with known vitamin D deficiency or neurological conditions reducing physical activity and sunlight exposure. A written informed consent was obtained from at least 1 parent for each subject. A clinical history was taken and participants underwent a physical examination, including a detailed assessment of pubertal development based on Tanner stages, anthropometric parameters (height, weight), waist circumference (WC) and blood pressure. BMI was calculated by dividing a person's weight in kilograms by the square of height in meters. Blood samples were collected after an overnight fast for measurement of blood glucose (FBG), blood insulin, total cholesterol (TC), high-density lipoprotein cholesterol (HDLC), triglycerides (TG) and serum 25(OH)D using an autoanalyzer (Cobas 6000 Roche).Insulin resistance was based on the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) using FBG and F fasting blood insulin. The diagnosis of MS was based on criteria of the National Cholesterol Education Program Adult Treatment panel III modified by Cook et al (4). It was made if at least three of the five following conditions were present: waist circumference over 90th percentile for children of the same age and sex, blood pressure ≥ 90th percentile for age and height, fasting triglyceride (TG) level ≥1.1g/L, fasting high-density lipoprotein (HDL) cholesterol level less than 0.4 g/Land fasting blood sugar over 1.1 g/L. The Endocrine Society guidelines were used to categorize included children as vitamin D deficient (<20 ng/mL), insufficient (20-29 ng/mL), or sufficient (≥30 ng/mL) (5). All analyses were performed using SPSS software version 21.0. We compared categorical variables with chi-square test or Fisher's exact test and continuous variables with the student t test. Spearman's correlation was used to find the association between 25(OH) D and other parameters. A two-tailed p< 0.05 was considered statistically significant for all the tests.

Ethics approval and consent to participate: Written informed consent was obtained from all parents of the patients

RESULTS

A total of 60 children were included in the study;30 obese children and 30 healthy controls.The median age was 104.43±28.64 months (range 58-151 months) in patients and 106.13±30.68 months (range 48- 156 months) in controls. The clinical findings are shown in table1.

Table 1: Clinical data of the group of obese children and the group of healthy controls

	Patients (n=30)	Controls (n=30)	p
Age (months)	104.43 ± 28	106.13 ± 30	_
Gender, male/female (n(%))	11 (37)/19 (63)	11 (37)/19 (63)	_
Pubertal/ pre-pubertal (n)	7/23	7/23	_
Weight (Kg)	56 ± 14	41 ± 10.3	$<10^{-3}$
Height (cm)	132.17 ± 15.3	134.4 ± 14.9	$<10^{-3}$
BMI (kg/ m^2)	31.65 ± 2.27	22.3 ± 1.6	$<10^{-3}$
Waist circumference (cm)	85.1 ± 11.5	71.6 ± 7.1	$<10^{-3}$
Systolic blood pressure (mm Hg)	11.68 ± 0.7	11 ± 0.6	0.006
Diastolic blood pressure (mm Hg)	7.46 ± 0.5	6.95 ± 0.7	0.002

The two groups were comparable in relation to confounding factors such as age, gender and pubertal stage. Median 25(OH) D levels were 17.2±5.9 and 25.08±7.37ng/mL respectively in obese and normal weight

children (p=0.001). Of all children, 38.3 % were diagnosed with vitamin D insufficiency and 48.3 % with vitamin D deficiency. Twenty three cases and 6 controls were vitamin D deficient. Five patients and 18 controls had insufficient levels and only 2 cases and 6 control subjects had sufficient levels. Thereby, vitamin D insufficiency/deficiency was more common in obese children (94% versus 80 %; p=0.002). The average FBG level was significantly higher in obese children (5.18±1.9 versus 4.29±0.9 mmol/L; p= 0.049). Median serum cholesterol was 3.95±1.03 g/L in cases and 3.42±0.58 g/L in controls (p=0.58). Serum TG level was higher in cases group (1.46±0.7g/L versus 1.11±0.48g/L; p=0.045). Median HDLC levels were 1.01±0.4 and 1.21±0.41 g/L respectively in the two groups (p=0.1). There was no significant difference between the two groups regarding insulin levels (37.11 ± 39.3 versus 20.7 ± 19.7; p=0.083). Similarly, median HOMA-IR rates were comparable in both groups (7.87 ± 9.40 versus 6.15 ± 8.60; p= 0.53). For MS criteria, abdominal obesity was constant in patients and was found in three control subjects (p=0.001). Two children in each group had hyperglycemia. Nine obese children were diagnosed with high blood pressure. Hypertriglyceridemia was found in 18 and 12 children respectively in the obese group and the control group (p= 0.053). Serum HDLC levels were above 0.4 g /L in all children included in both groups. Six obese children were diagnosed with MS which was absent in healthy children. 25 (OH) D levels were negatively correlated with BMI (p= 0.001, r= -0.51), waist circumference, (p=0.019, r=-0.13), SBP (p=0.04, r=-0.26), TG level (p=0.025, r= -0.3), insulin (p=0.01, r=-0.34) and HOMA-IR (p=0.035, r=-0.29), but not with FBG (p=0.85, r=0.025), and HDLC (p=0.8, r= 0.035).

DISCUSSION

In the present study, vitamin D insufficiency/deficiency was significantly more common in obese children as compared to normal-weight subjects. 25 (OH) D levels were negatively correlated with WC, SBP, TG level, insulin and HOMA-IR. According to the World Health Organization (WHO) report in 2016 (6), the prevalence of obesity increased from 4% in 1975 to 18% in 2016. The number of children under 5 years of age with obesity has increased by nearly 50%. In addition, this alarming increase in the prevalence of obesity, which has been previously described as a problem of developed and industrialized countries, is gradually becoming a serious health problem around the world that also affects low and middle-income country (7). The MS, as defined above, is the most common and serious complication of obesity with a prevalence ranging from 15 to 54% (8, 9-13). In our study, six obese children (20%) were diagnosed with MS. The impact of obesity on the prevalence of MS is widely reported. However, there are several definitions of MS in children making comparison between populations difficult. Vitamin D deficiency is reported by several studies in proportions ranging from 19 to 95% (14-16). Similarly, suboptimal vitamin D levels were found in 87% of the children included in this study. Our results are in agreement with earlier studies that showed the association between low 25 (OH) D levels and childhood obesity (14-16). The physiological mechanisms of this association remain unknown. Vitamin D sequestration in fat cells has been suggested. On the other hand, because vitamin D receptors are present in adipose tissue, vitamin D is probably implicated in regulation of fat cells (17) and might contribute to the increase of fat mass in vitamin D deficiency. To our knowledge, the correlation between vitamin D status and MS parameters remains poorly studied. In a recent study including a sample of 2492 children, Carolyn and Yan (18) found a negative correlation between vitamin D and central adiposity. Using the same ES suboptimal criteria of serum 25(OH) D, WC was 2 to 3 times greater in vitamin D deficient Chilean children as compared to non-deficient subjects (19).While a significant higher risk for cardiovascular disease and MS has been proved in adults; this association is still controversial in children. In the American cross-sectional population-based study (18), low serum 25(OH) D was associated with higher SBP and lower HDL-C. Experimental evidence suggests that vitamin D regulates the rennin-angiotensin system to lower blood pressure (20). Moreover, in a recent study of Atabek et al (14), low vitamin D level was the best predictor of carotid intima media thickness. Thereby, this condition could worsen the atherosclerotic process and MS in obese children. In other studies, no associations between vitamin D deficiency and MS parameters have been found (21, 22). Hence, further studies are needed to better investigate the implications of vitamin D status in MS in children. The major strength of this study was its prospective character comparing two groups of children of the same age, sex, pubertal stage, and the same ethnicity. We evaluated the associations between vitamin

D status and both obesity and MS. Our findings could have important therapeutic implications since vitamin D-deficient-patients will be supplemented. Limitations of this study include the single measurement of 25 (OH) D levels in a single center and the small sample size.

CONCLUSIONS

This study demonstrates that the majority of children in our country had inadequate vitamin D status. Vitamin D levels were negatively correlated with BMI and could increase the risk of occurrence of MS. Pediatricians should be aware of the high prevalence of vitamin D insufficiency/deficiency in obese children. Thus 25 (OH) should be performed in obese children. In case of deficiency, regular follow-up will be mandatory. Finally, Vitamin D supplementation should be considered to reduce cardiovascular risk.

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