Original article

Relationship Between Vitamin-D and Obesity in Pediatric Outpatients, at King Khalid General Hospital, Majmaah, Saudi Arabia

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Abstract:

Background: In many countries, overweight and obesity are becoming a serious threat to the health of the population. Several studies have found a strong independent relationship between vitamin D levels and several metabolic complications of obesity. However, it is still not known if vitamin D deficiency is directly responsible in the pathogenesis of these complications or just a secondary consequence of obesity. With an increasing number of research studies, it is evident that improvement of Vitamin D status could lead to good health outcomes especially related to obesity. **Aims:** This study sought to find any possible association between body mass index (BMI) and serum level of vitamin D in 6-13 year-old children attending the outpatient department (OPD) at King Khaled Hospital, Majmaah, KSA. **Settings and Design:** This cross-sectional observational study was done on 86 children who were 6 to 13 years old attending the OPD from March 2016 to February 2017. **Materials and Methods:** Anthropometric indices (weight, height and waist circumference) were assessed by using identical instruments. The hematological profile of all study participants was also evaluated for biochemical parameters such as fasting blood sugar, insulin, total cholesterol (LDL, HDL, triglycerides). **Results:** This study revealed a high prevalence (83.7%) of vitamin D deficiency and insufficiency, with 50 (58.1%) children with vitamin D levels in the deficiency range (<20 nmol/L), 22 (25.6%) in the insufficiency range (20-30 nmol/L), and only 14 (16.3%) with adequate, or sufficient, vitamin D levels (>30 nmol/L). There were significant differences in vitamin D deficiency between male and female children; with females more deficient in Vitamin D than males. Vitamin D levels and BMI status were not significant between the vitamin D level and BMI; although there was significant inverse correlation between waist circumference and vitamin D levels. **Conclusion:** Vitamin D deficiency is common in children, and is more prevalent in females as compared to males. There was a significant relationship between waist circumference and vitamin D. More exposure to sunlight and prescription Vitamin D pediatric supplements and/or food fortification is recommended.

Keywords: Obesity, BMI, vitamin D. Pediatrics.

الملخص:

خلفية: في كثير من البلدان، أصبحت زيادة الوزن والبدانة تهديدا خطيرا لصحة الانسان. وقد وجدت العديد من الدراسات وجود علاقة مستقلة قوية بين مستويات فيتامين (د) وعدد من مضاعفات التمثيل الغذائي للبدانة. ومع ذلك، فإنه لا يزال غير معروف ما إذا كان نقص فيتامين (د) هو المسؤول مباشرة في التسبب في هذه المضاعفات أو مجرد نتيجة ثانوية من السمنة.

أوضحت عدد من الدراسات البحثية أن تحسين حالة فيتامين (د) يمكن أن يؤدي إلى نتائج صحية جيدة تتعلق بالبدانة.

الأهداف: هدفت هذه الدراسة إلى العثور على أي ارتباط ممكن بين مؤشر كتلة الجسم ومستوى فيتامين (د) في أمصال الأطفال الذين تتراوح أعمارهم ما بين ٦-١٣ عاما، والذين يعاودون قسم العيادات الخارجية في مستشفى الملك خالد، المجمعة، المملكة العربية السعودية. وقد تم إجراء هذه الدراسة الرصدية المستعرضة على ٨٦ طفلا تتراوح أعمارهم بين ٦ و١٣ عاما في الفترة الزمنية من مارس ٢٠١٦ إلى فبراير ٢٠١٧.

المواد والطرق: تم تقييم المؤشرات الأنثروبومترية (الوزن والطول ومحيط الخصر) باستخدام صكوك مماثلة. تم تقييم الشخصية الدموية لجميع المشاركين في الدراسة بالإضافة الي موسمات الكيمياء الحيوية مثل تركيز سكر الدم عند الصيام، الأنسولين، الكوليسترول الكلي (الدهون منخفضة الكثافة، الدهون مرتفعة الكثافة، الدهون الثلاثية).

النتائج: كشفت هذه الدراسة ان ٧٢ (٨٣,٧٪) من الاطفال يعانون نقص وعدم كفاية فيتامين (د) وهذا يعتبر معدل انتشار مرتفع. مع وجود ٥٠ (٥٨,١٪) من الأطفال يعانون نقص مستويات فيتامين (د) في نطاق اقل من (٢٠ نانو مول / لتر)، بينما ٢٢ (٢٥,٦٪) يعانون من عوز وقصور مستوي فيتامين (د) (٢٠-٣٠ نانو مول / لتر)، وفقط ١٤ (١٦,٣٪) كانوا ضمن المستوي الكافي والطبيعي لفيتامين (د) (أكثر من ٣٠ نانو مول / لتر). وكان هناك نقص معنوية في مستويات فيتامين (د) للأطفال الإناث عند مقارنتهم بالذكور. بينما كانت العلاقة بين مستويات فيتامين (د) وحالة مؤشر كتلة الجسم غير معنوية. على الرغم من وجود علاقة عكسية كبيرة بين محيط الخصر ومستويات فيتامين (د).

الاستنتاج: نقص فيتامين (د) شائع لدى الأطفال، وهو أكثر انتشارا في الإناث مقارنة بالذكور. كانت هناك علاقة كبيرة بين محيط الخصر وفيتامين (د). يوصى بزيادة التعرض لأشعة الشمس وتناول الأطفال لوصفات طبية تحتوي على مكملات غذائية غنية بفيتامين (د).

الكلمات الرئيسية: السمنة، مؤشر كتلة الجسم، فيتامين (د)، الأطفال.

Background:

Childhood obesity affects both developed and developing countries of all socioeconomic groups, irrespective of age, sex or ethnicity. As per data from the International Obesity Task Force, at least 155 million school-age children worldwide are overweight or obese. [1] The traditional Middle Eastern diet, characterized by high-fiber content and low in fatty acids, cholesterol and sodium, has changed to a "westernized" diet with high intake of energy-dense foods rich in fat, cholesterol, free sugars, and sodium. and low in dietary fiber. [2] As such the Middle Eastern populations are at great risk of vitamin D deficiency due to a diet low in vitamin D and low sunshine exposure. Obesity is also a risk factor for vitamin D deficiency since vitamin D is sequestered in body fat. [1] Vitamin D deficiency is pandemic, and has been implicated in a wide variety of disease states.[3)] Vitamin D deficiency is estimated to affect approximately 30-50% of people worldwide.[4] Middle Eastern populations are known to be at risk of vitamin D deficiency due to a diet low in vitamin D and limited exposure to sunshine.[5] It is established fact that vitamin D plays a significant role in the absorption of calcium and phosphorous. Recently, the focus has been on growing evidence of an association between vitamin D insufficiency and various chronic diseases, mainly cardiovascular disease. In the recent past, it was found that impaired glucose homeostasis is also associated with vitamin D deficiency and more common in overweight and obese children. [6,7] While the relationship between vitamin D status and obesity is well documented, there is confusion as to whether vitamin D deficiency has a direct effect on obesity or results as a consequence of obesity. [8.9] This confusion is perpetuated by mixed results seen not only in human but also animal studies investigating the effectiveness of vitamin D supplementation to reduce body weight and adiposity [10-12]. Therefore, this study was designed to determine the possible relationship between body mass index (BMI) and serum level of vitamin D in 6-13-year-old children attending the outpatient department (OPD) at King Khaled Hospital, Majmaah, Saudi Arabia. The current study is believed to be the first to examine the relationship between vitamin D and obesity among 6-13-year-old children.

Hypothesis:

Vitamin D will be lower in underweight and overweight/obese children. In overweight children, excess body fat may cause increased Vitamin D sequestration and result in low Vitamin D availability and, as a consequence, low serum 25(OH)D levels. BMI and waist circumference will show an inverse association with vitamin D that is Low serum 25(OH)D levels are associated to higher BMI.

Methods:

Ethical Principles

Ethics committee approval was provided by the Majmaah University Scientific Committee. Self-designed questionnaires were completed after receiving a written informed consent from parents/guardians of participants. Addi-

tionally, verbal consent was received from all children who participated in the study.

Participants

Included in this study were 86 children (48 female and 38 male), aged 6-13 years, visiting the OPD of King Khaled Hospital. This was a cross-sectional study having quantitative variables. Exclusion criteria for both obese and normal wieght children were 1) use of an anticonvulsant or systemic glucocorticoid, 2) use of a vitamin D supplement more than 400 IU/d, 3) hepatic disease, 4) renal disease, or malabsorptive disorder, 5) disorder of bone or calcium metabolism (including known vitamin D deficiency) and 6) obesity due to a genetic disorder.

Anthropometric parameters

Height was calculated on all respondents using a fixed stadiometer with a vertical backboard and a moveable headboard. [13] Participant's weight was taken with a digital scale. [13] BMI was calculated using the universal formula (weight in kilograms divided by height in meters squared). Waist circumference was measured in centimeters on all participants using a measuring tape using the standard World Health Organization (WHO) protocol midpoint between last floating rib and top of the iliac crest in midaxillary line. [14] To reduce subjective error, all measurements were taken by one individual.

Biochemical parameters

Fasting venous blood sample was examined for fasting plasma glucose and lipid profile by auto analyzer with standard kits. Plasma insulin was measured by radioimmunoassay (RIA), specific for human insulin and less than 0.2% cross-reactivity with human proinsulin and no cross reactivity with c-peptide or insulin-like growth factor. Vitamin D levels were determined by a chemiluminescence assay using the LIAISON 25-hydroxy vitamin D TOTAL assay (DiaSorin, Ltd.). The lower and upper detection limits are 10 nmol/L and 375 nmol/L, respectively. [15] In-house testing estimated the assay coefficient of variation within runs as 3.2% to 8.5% and between runs as 6.9% to 12.7%.[15] For quality control purposes, 10% of samples were run in duplicate. Vitamin D levels less than 20 nmol/L were grouped as a deficiency, levels between 20-30 nmol\L were grouped as inadequate and those ≥30 nmol\L were considered as sufficient. [16]

Classification of BMI

Pediatric BMI is age and sex specific and uses growth curves for diagnosis. [17] WHO growth curves are based on optimal growth conditions.[14] Children whose BMI is <5% is categorized under, those having BMI between 5% to 84.99% as normal weight, and those having BMI from 85 % to <95% as overweight and ≥95% as obese using the Centers for Disease Control and Prevention growth curves from the year 2000.[18]

Statistical Analysis

Data were described as mean ± standard deviation and percentage. Independent student's t-test was done to compare the two groups. A P-value of ≤0.05 was considered as statistically significant. Statistical Package for

Social Sciences (SPSS) 20.0 and MS Excel were used for the data analysis. SAS (Statistical Analysis Systems) software was used that considers bootstrap weights. To take account of the multiplicity of analysis, a conservative alpha level of <0.001 was defined as the threshold of statistical significance. To find the significance of study parameters on the categorical scale between two or more groups Chi-square/Fisher Exact test was used.

Results:

Baseline characteristics of both male and female children are represented in Table 1. The levels of vitamin D in females and males were 16.07 ±6.71 and 19.63±7.26 nmol/L, respectively. This difference was statistically significant (p = 0.014). Significant difference was also found in waist circumference, insulin level, total cholesterol and LDL between males and females.

Table 1. Baseline characteristics of study subjects by sex

Parameters	Female (n = 48) Mean±SD	Male (n = 38) Mean±SD	P value
Vitamin D	16.07±6.71	19.63±7.26	0.042*
BMI (kg/m2)	23.63±12.82	19.78±7.80	0.314
WC (cm)	59.47±13.82	59.25±13.60	0.028*
FBS (mmol/L)	5.21±0.95	5.06±0.82	0.429
Insulin	45.37±31.51	120.27±51.83	0.008*
Cholesterol	165.32±21.48	184.78±34.80	0.049*
HDL (mmol/L)	52.06±11.08	50.75±13.27	0.803
LDL (mmol/L)	135.87±36.99	121.02±27.58	0.037*
TG (mmol/L)	108.06±44.99	131.46±50.81	0.748
SBP (mm Hg)	110.08±6.50	114.16±8.04	0.624
DBP (mm Hg)	74.67±6.61	78.32±12.96	0.913

Abbreviations: BMI, body mass index; WC, Waist circumference; FBS, Fasting blood sugar; HDL-C, high-density lipoprotein-cholesterol; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Prevalence and intensity of vitamin D deficiency

Vitamin D Status*	Number	Percent (%)
Deficiency	50	58.1
Insufficiency	22	25.6
Sufficiency	14	16.3
Total	**86**	**100**

*Level of <20 nmol/L was considered as deficiency, 20-30 nmol/L as insufficiency, and ≥30 ng /mL as sufficiency.[16]

In the selected sample of 86 children, most (83.7%) of them showed lack in the level of vitamin D . Vitamin D deficiency was observed in more than half of children (58.1%) and it was insufficient in one quarter of children (25.6%) (Table 2).

Table 3: Body mass indices categories*

Body Mass Index (kg/m2)	Total N (%)	Male = 38 N (%)	Female = 48 N (%)
<5% (underweight)	**8 (9.3)**	**4 (10.5)**	**4 (8.3)**
5% to 84.99% (normal weight)	**52 (60.5)**	**24 (63.2)**	**28 (58.3)**
85% to <95% (overweight)	**20 (23.3)**	**8 (21.1)**	**12 (25.0)**
≥95% (obese)	**6 (7.0)**	**2 (5.3%)**	**4 (8.3)**

*As per Centers for Disease Control and Prevention growth curves from the year 2000. The majority of children (60.5%) had normal weight, one quarter (23.3%) were categorized as overweight; whereas a small percentage of children were underweight (9.3%) or obese (7%). BMI was not significantly correlated with vitamin D (r = -0.114, p = 0.674) (Table 3).

Significant inverse correlation was observed between waist circumference (WC) and vitamin D levels showing that as WC increases the level of vitamin D decreases and vice versa (r = -0.519, p = 0.031).

Discussion:

Lack of vitamin D could be a pathological condition for many diseases, mainly cardiovascular disease, cancer and autoimmune diseases. [19-22] In contrast, sufficient vitamin D levels are beneficial to the cardiovascular system. So, a close monitoring vitamin D levels has been suggested to be protective to reduce cardiovascular disease and hypertension.

The present study of 86 children observed a lack of vitamin D 83.7% of cases. Cultural and religious practices and norms are the most common reasons why Middle Eastern. [23,24] Because of these norms and practices, people in many countries such as India, Australia, Brazil and the Middle East have a high prevalence of vitamin D deficiency. [25.26] There are several causes of vitamin D deficiency among women in the Gulf region, such as clothing style, lack of foods rich in vitamin D, lack of vitamin D supplements, multiparity and obesity.[27]

Various methods are available for the measurement of vitamin D including liquid chromatography-tandem mass spectrometry, high performance liquid chromatography, radioimmunoassays (IDS and DIASORIN) and chemiluminescent assays (IDS, Advantage, LIASON). [28] Methods are comparable across laboratories, using liquid chromatography-tandem mass spectrometry as a gold standard. [29] However, a limitation of immunoassays is the inability to distinguish between vitamin D2 and D3.

This study showed deficient vitamin D levels in half of all subjects. In addition, there was a significant difference between vitamin D levels in male and female children. Vitamin D deficiency was more prevalent in females. Insufficient studies show the difference between men and women in terms of vitamin D deficiency. Some studies considered vitamin D deficiency based on gender, but with no actual comparison between both genders in terms of vitamin deficiency and its risk factors. [30] In this study, based on the WHO criteria for classification of obesity in children, the majority of children had normal weight, one quarter of children were categorized as overweight, and a small percentage of children were underweight or obese. Further, this study showed that BMI did not significantly correlate with vitamin D in either group. There is a well-established inverse association between body fat mass and serum 25(OH)D levels in both adults and children.[31] The central dogma surrounding this inverse relationship is that circulating vitamin D, derived from both cutaneous and dietary sources, is sequestered by adipose tissue prior to hepatic hydroxylation and is therefore unavailable to be converted to 25(OH)D.[3,9,32] Porcine studies have demonstrated upwards of 65% of vitamin D is stored in adipose tissue.[32,33] In addition to lower circulating levels of 25(OH) D seen in cases of excess adiposity, Lee et al. noted a similar inverse relationship between BMI and vitamin D status in adults receiving daily vitamin D supplementation.[6] These results were consistent with the findings of Heaney et al., who reported that obese individuals require approximately twice as

much vitamin D to produce the same rise in vitamin D status as lean individuals. The present study found the correlation between WC and vitamin D was significantly inverse.

BMI is used as an indicator of body fat accumulation, but BMI is not ideal because it does not differentiate fat tissue from other tissues, such as muscle mass. A further complexity is that in many studies BMI was calculated from self-reported height and weight. This may have introduced systematic bias. [34,35] Central fat mass, central obesity or abdominal obesity can be measured by WC. [36,37] Distribution of adipose tissue predicts obesity-related health risks, including type 2 diabetes, atherogenic dyslipidemia, hypertension and cardiovascular disease.[38] Abdominal obesity is a component of metabolic syndrome, also called syndrome X.

Conclusion:

The present study supported previous findings from numerous Middle Eastern and international studies that revealed a high prevalence of vitamin D deficiency and insufficiency among Middle Eastern populations. The best predictors of vitamin D status seem to be WC relating to metabolic status. Currently, there is a paucity of well-designed, placebo-controlled clinical trials investigating how improving vitamin D status can impact some of these health outcomes. A large survey on a national scale, especially with good design and appropriate standardized methodology is needed to provide a clear picture of the situation in KSA.

Limitations of the study

A limitation of this study is that vitamin D deficiency and insufficiency was defined only by 25(OH)D levels. Further, there is no consensus defining an optimal status of vitamin D in children. In addition, the sample size was small although the study was conducted for a period of one year; and it was very difficult to get consent from parents for a blood sample. Since this study was conducted in a single center, its findings could not be generalized which is a potential limitation. Additionally, keeping in mind the sedentary lifestyle of children and the cultural influence of society, innovative approaches are required to engage children in outdoor activities.

Competing interests

The authors declare no conflicts of interest.

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