Sex Differences in Vitamin D Deficiency and Anthropometric Measurements in School-age Children from Rural Areas in Israel

Eias Kassem MD[1,2], Sigal Eilat-Adar PhD[3], Mahmood Sindiani Med[3], and Sigal Ben-Zaken PhD[3]

[1]Department of Pediatrics, Hillel Yaffe Medical Center, Hadera, Israel
[2]Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, Israel
[3]Genetics and Molecular Biology Laboratory, Zinman College of Physical Education and Sports Sciences at Wingate Institute, Netanya, Israel

ABSTRACT **Background:** Vitamin D is essential for skeletal health. Because peak bone mass accrual occurs during childhood and adolescence, vitamin D insufficiency during this period of life could cause adverse health outcomes.

Objectives: To explore the potential sex differences in anthropometric indicators and vitamin D status among primary school-age children.

Methods: A modified food-frequency intake questionnaire was completed by 116 pre-pubertal children (52 girls, 64 boys). Body measurements were recorded and blood was drawn to assess vitamin D status. All children were of Arab-Israeli origin and lived in villages or rural areas in the north-east area of Israel.

Results: Prevalence of obesity was higher among girls (34%) compared to boys (21.9%, $P = 0.018$). All the children were vitamin D insufficient, and 80% were deficient. Plasma vitamin D was significantly higher among boys (12.4 ng/ml) compared to girls (9.1 ng/ml, $P < 0.01$). A significant negative correlation was found between vitamin D status and weight percentile for girls ($r = -0.43$, $P < 0.05$) but not for boys. There was a trend toward a statistically significant inverse correlation between vitamin D status and body fat percent in the girls ($r = -0.37$, $P = 0.07$). Sex frameworks are important for the understanding of the determinants of health and the development of effective health promotion programs.

Conclusions: Pre-pubertal girls in Arab villages should be provided with tailor-made nutrition and physical activity programs for promoting health.

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KEY WORDS: food-frequency questionnaire, pre-pubertal age, vitamin D deficiency

Vitamin D plays a part in many functions in the metabolism of the human body and its deficiency and insufficiency could cause adverse health outcomes [1]. Since adequate vitamin D is essential for skeletal health [2] and peak bone mass accrual occurs during childhood and adolescence, identifying and treating vitamin D deficiency during this period may be particularly important. Vitamin D deficiency and insufficiency among children and adolescents was reported in some studies [3], however only a few of them addressed the sex differences.

Vitamin D is produced by activation of cholesterol by sunlight in a multi-phase mechanism [1]. The biologically active form, 1,25 di-hydroxyvitamin D [1,25(OH)2D] regulates more than 200 different genes, directly or indirectly, by binding them to vitamin D nuclear hormone receptors (VDR). VDR are found ubiquitously in the nucleus of all tissues and cells of the immune system, and can respond to the activated 1,25(OH)2D for gene expression at virtually any site in the body. Having these various endocrine and paracrine functions may explain why vitamin D has widespread effects on various disease processes. Therefore, it is possibly more accurate to call vitamin D a steroid hormone rather than a vitamin.

The incidence of obesity is increasing throughout the world. Over 340 million children and adolescents aged 5–19 years were identified as overweight or obese in 2016 [4]. Obesity is a multifactorial trait that results from numerous factors and is considered to be a risk factor for morbidity and mortality. Obesity is also associated with vitamin D deficiency [1]. 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 [5]. It is also suggested that excess body fat may disrupt hormonal pathways important for skeletal health [6]. For example, leptin, an adipocyte-derived hormone that binds to osteoblasts, appears to activate a pathway that inhibits renal synthesis of the active form of vitamin D. However, low dietary vitamin D intake and limited sun exposure may serve as confounders to these mechanisms [5].

The etiology of overweight and obesity in girls and boys may be different due to biology as well as to society and culture [7]. Boys and girls differ in body composition, patterns of weight gain, and hormone biology, and may be influenced by certain social, ethnic, genetic, and environmental factors [8]. Sex differences in the prevalence of childhood obesity have been observed in many countries. Some studies reported a higher prevalence of overweight and obesity among girls compared to boys [9], whereas others have reported the opposite [10]. Sex differences were also attributed to behavioral determinants, such as eating high calorie fast food, increasing portion size, and taking into consideration the low cost of high calorie food, together with a decrease in physical activity due to increased time spent watching television and using computers and other electronic devices [11]. In comparing ethnicity differences among adults, the prevalence of current obesity was 52% in Arab women compared to 31% in Jewish women ($P < 0.001$) and 25% in Arab men compared to 23% in Jewish men ($P = 0.6$).

Although the median reported body mass index (BMI) did not differ significantly between Arabs and Jews at age 18 years [4], in an analysis of 94,239 Israeli children 2–18 years old, the Jewish population showed a higher rate of overweight and obesity compared to the Arab population for all age groups The prevalence of obesity was higher in males compared to females (11.5% vs. 9.5%, respectively, $P < 0.0001$). However, the prevalence of obesity was especially high in the north-east area of Israel [12].

Understanding sex differences in child and adolescent overweight and obesity as well as associated predictors, will enable the development and implementation of policy and intervention policies. Accordingly, the purpose of the current study was to investigate potential sex differences in anthropometric indicators and vitamin D status among Arab Israeli primary school children.

PATIENTS AND METHODS

STUDY POPULATION

We recruited 116 pre-pubertal (Tanner stage 1–2) Israeli Arab children (52 girls, 64 boys), aged 6 to 12 for this study. They completed a modified food frequency questionnaire on their milk and dairy product intake, their body measures were recorded, and blood was drawn for vitamin D status assessment. All children were of Arab-Israeli origin.

The study was approved by the institutional review board of the Hillel Yaffe Medical Center, Hadera, Israel, according to the Declaration of Helsinki. A signed written informed consent was obtained from all participants and their parents.

VITAMIN D STATUS

Serum 25(OH)D was measured by chemiluminescent immunoassay (ARUP Laboratories, Salt Lake City, UT, USA). The intra-assay coefficient of variation was 6% at 30.8 nmol/L and 4% at90.5 nmol/L, and the inter-assay coefficient of variation was8% at 31.0 nmol/L and 6% at 90.5 nmol/L. Vitamin D status was classified as deficiency (serum 25(OH)D ≤ 20 ng/ml), insufficiency (serum 25(OH)D > 20 to < 30 ng/ml), and sufficiency (serum 25(OH)D ≥ 30 ng/ml).

ANTHROPOMETRIC MEASURES

Standard, calibrated scales and stadiometers was used to determine height and weight, and BMI was calculated. Overweight and obesity were defined as percentiles for age using the standards from the U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. Overweight was defined as BMI above the 85th percentile for age and obesity was defined as BMI above the 95th percentile for age. The physical maturity of the study participants was assessed by a validated self-administered questionnaire that has been widely used as a non-invasive indicator of pubertal status.

FOOD INTAKE

A self-administered non-quantitative food frequency questionnaire (FFQ), which was developed previously for the Israeli population, was used to assess daily frequency of dairy product intake. The list of dairy products was adjusted to the study population, using local foods. The questionnaire was translated to Arabic and then re-translated into Hebrew [13].

STATISTICAL ANALYSIS

Data are presented as average ± standard deviation for continuous variables and number (percent) for categorical variables. The *t*-test was used to compare continuous variables and chi-square for categorical variables. Correlations between vitamin D and anthropometric measures were implemented using Pearson's correlation for normal distribution. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 20.5 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

Participant anthropometric measures are presented in Table 1. Overall, BMI percentile, mean body fat, and weight percentile were significantly higher among girls compared to boys. The prevalence of obesity was 34.0% in girls compared to 21.9% in boys ($P = 0.018$).

The participant vitamin D status is presented in Table 2. All children were vitamin D insufficient (below 25 ng/ml), and 80% were deficient. Plasma vitamin D was significantly ($P < 0.01$) higher among boys (12.4 ng/ml) compared to girls (9.1 ng/ml).

A significant negative correlation was found between vitamin D status and weight percentile among girls ($r = -0.43$, $P < 0.05$) for girls but not for boys. There was a trend towards a statistically significant inverse correlation between vitamin D status and body fat percent in girls, ($r = -0.37$, $P = 0.07$).

Serum calcium and creatinine were higher in boys within normal levels, which has no clinical significance. Phosphorus, magnesium, uric acid, alkaline phosphatase, and albumin did not differ between the sexes.

Reported frequency of dairy product intake did not differ by gender and was not associated with vitamin D status or anthropometric measures.

Table 1. Participant anthropometric measures, by sex

	Girls (n=50)	Boys (n=64)	Total	*P* value
Age in years, mean ± SD	9.3 ± 2.3	9.3 ± 2.3	9.4 ± 2.6	NS
Mean body mass index percentile (%)	71.8 (27.7)	59.0 (29.3)	65.0 (29.3)	0.009
Mean body fat (%)	22.7 (6.1)	12.3 (5.5)	16.9 (5.7)	0.025
Overweight, %	34.0	21.9	33.3	0.018
Obesity, %	14.0	3.1	13.7	0.018
Height percentile (%)	60.5 (32.7)	49.4 (36.6)	54.2 (35.3)	NS
Weight percentile (%)	71.0 (29.6)	57.1 (32.1)	63.2 (31.2)	0.019

Table 2. Participant vitamin D status, by sex

	Girls (n=50)	Boys (n=64)	Total	*P* value
Dairy product intake (%)	25.9 (10.2)	27.9 (11.5)	27.0 (10.9)	NS
Serum vitamin D, ng/ml (%)	9.1 (3.4)	12.4 (3.8)	11.2 (3.9)	< 0.01
Total borderline & deficiency (B&D)	23	42	65	
Borderline, n (%)	2 (8.6)	11 (26.1)	13 (20.0)	0.092
Deficiency, n (%)	21 (91.3)	31 (73.9)	52 (80.0)	0.092
Creatinine, mg/dl	0.46	0.59	0.53	0.01
Calcium, mg/dl	9.71	9.84	9.79	0.06
Phosphor, mg/dl	5.03	5.21	5.13	NS
Magnesium, mg/dl	2.33	2.35	2.34	NS
Uric acid, mg/dl	3.60	3.63	3.62	NS
Alkaline phosphatase, mg/dl	200.45	225.29	211.86	NS
Albumin, mg/dl	4.65	4.67	4.66	NS

DISCUSSION

The current study was conducted to assess levels of vitamin D and the association with obesity among Arab children from rural areas in Israel. A high prevalence of vitamin D deficiency was measured, as supported by previous reports on high vitamin D deficiency among Israeli pediatric populations [3]. In the current study we found a higher prevalence of vitamin D deficiency in girls, while overweight and obesity prevalence among the girls was higher compared with boys. Sex differences in vitamin D deficiency was not observed in other populations, such as in African American children [14], French-Canadian children and adolescents [15], or children in Great Britain [16]. It is possible that the low sun exposure in these countries compared to Israel may explain this difference. The Arab girls in the rural areas in Israel tend to cover their body more than boys, and have lower sun exposure during outside leisure-time activities.

Childhood obesity has been a persistent public health threat, especially in developed countries and low and middle-income countries and particularly in Arab nations [17]. Vitamin D deficiency was associated with obesity in the current study, in accordance with results from other countries [18]. Several cross-sectional studies have shown consistent significant inverse associations between other cardio metabolic parameters and circulating 25(OH)D in children and adults; both may be mediated by obesity [19].

Obese children are more prone to vitamin D deficiency than non-obese children [20], associated with the degree of adiposity. Other known risk factors for vitamin D deficiency include race/ethnicity, with lower levels of vitamin D among people with dark skin [21], lack of sufficient sunlight exposure [22], insufficient physical activity [20], decreased consumption of vitamin D-containing foods such as fish and fortified dairy products, vitamin D malabsorption, and increased vitamin D degradation [21]. Age, sex, and socio-economic status among children were also associated with vitamin D deficiency [2].

In children, vitamin D is essential for skeletal health [2]. Deficiency in children has also been linked to increased cardiovascular risk markers [23], and impaired glucose tolerance [24]. It is therefore essential to assess vitamin D in children.

Obesity and vitamin D deficiency have been classified as epidemics throughout the world. It is unclear whether there is a causal association between obesity and vitamin D deficiency, but the co-morbidity of vitamin D deficiency and obesity is a pronounced health threat, especially among children.

Sex frameworks are not only important to our understanding of the determinants of health, but also for the development of effective health promotion programs. With respect to health in general, integrating sex considerations into interventions may improve their effectiveness [25]. Pre-pubertal girls in Arab villages, especially from the north-east part of Israel, are a high-risk population for developing both obesity and vitamin D deficiency, due to the combination of a number of risk factors: ethnicity, sex, skin color, malnutrition, restricted exposure to sunlight due to traditional long-sleeved clothing, and inadequate physical activity. Therefore, it is recommended that nutrition and physical activity programs be tailored to this subgroup.

LIMITATIONS

While advancing the literature about Vitamin D status among pre-pubertal children and its relation to obesity, several limitations must be acknowledged. First, study population represented children from Arab communities in a rural region in the north-east area of Israel. Future research will benefit from recruiting participants from other communities and other geographical areas. Second, follow-up research will contribute to the understanding of the changes in Vitamin D status-obesity relation through childhood. Third, future research should also include quantifying other factors that may influence vitamin D status such as lifestyle habits (physical activity, exposure to sunlight, closing etc).

CONCLUSIONS

Girls and obese children have more vitamin D deficiency. Obese girls seems to be more prone to have vitamin D deficiency.

Correspondence

Dr. E. Kassem
Dept. of Pediatrics, Hillel Yaffe Medical Center, Hadera 38100, Israel
Fax: (972-4) 774-4186
email: eiask@hy.health.gov.il

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it is not what we do, but also what we do not do, for which we are accountable.
Jean-Baptiste Poquelin, known by his stage name Molière,, actor and playwright (1622–1673), French playwright, actor, and poet