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Vitamin D status in children and adolescents with type 2 diabetes in a sun-rich environment

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Abstract

Background: **In obese children, hypovitaminosis D has been found to be associated with common risk factors for type 2 diabetes including abnormal fasting insulin, glucose and hemoglobin A1c. Adult type 2 diabetics have a lower vitamin D levels but this has not been documented in children/adolescents who reside in a sun-rich environment.**

Objective: **The purpose of this study was to estimate the prevalence of vitamin D insufficiency/deficiency in children with type 2 diabetes in a sun-rich environment.**

Materials and Methods: **Children (N = 48) diagnosed with type 2 diabetes who had serum 25-hydroxyvitamin D level data available from a clinical visit (2008-2012). Results were obtained from a retrospective chart review. Vitamin D deficiency was defined as 25-hydroxyvitamin D level ≤ 50 nmol/L and insufficiency ≤ 75 nmol/L. Obesity was defined as body mass index (BMI) >95% and overweight as BMI >85- <95% for age and sex.**

Results: **The majority of the population was non-Hispanic black (73%), followed by 22% Hispanic, and 4% non-Hispanic white. Mean age was 15.0 years (range 8.7-18.5 years). Forty subjects (83%) were obese (mean BMI 96.1%). Mean 25-hydroxyviatmin D level was 47.4 nmol/L. The majority (97%) were vitamin D insufficient and 62% were vitamin D deficient. Correlation with BMI z-score was not significant. Vitamin D status did not vary by race.**

Conclusions: **Vitamin D deficiency is extremely common in a sun-rich environment among adolescents with type 2 diabetes, independent of BMI or race. Type 2 diabetes may be an added risk for vitamin D deficiency among obese, multiethnic children/adolescents even in a sun-rich environment.**

Introduction

More than half of children and adolescents in the United States have vitamin D insufficiency, also known as hypovitaminosis D[1]. Hypovitaminosis D in children has been increasingly associated with a variety of nonskeletal conditions such as multiple sclerosis, wheezing illnesses, type 1 diabetes, and cardiovascular disease[1-3]. In children and adolescents, low vitamin D levels have been associated with risk factors for type 2 diabetes including abnormal insulin sensitivity, fasting glucose, fasting insulin levels, and hemoglobin A1c[4-6]. Several studies have documented a high prevalence of vitamin D deficiency among adult subjects with type 2 diabetes[7]. However, there are no studies to date that show a difference in vitamin D status in children with type 2 diabetes including among multiethnic children. We sought to determine the vitamin D status in a clinical sample of multiethnic children with type 2 diabetes who reside in a sun-rich environment.

Patients and Methods

Ethics Statement

This study was approved by and in accordance with the Ethical Standards of the University of Miami Institutional Review Board.

Patients

A retrospective medical chart review identified children and adolescents (N=48) with a diagnosis of type 2 diabetes who were seen at the pediatric diabetes clinic at University of Miami Miller School of Medicine (Miami, FL, latitude 25°, urban population) between July 2008 and April 2012. Additionally, each subject had to have the following clinical data available for analysis inclusion: a serum 25-hydroxyvitamin D level [25(OH)D], hemoglobin A1c (HbA1c), low- and high- density lipoprotein (LDL and HDL), triglycerides, urinary microalbumin and body mass index (BMI). Vitamin D deficiency was defined as 25(OH)D level ≤ 50 nmol/L and vitamin D insufficiency was defined as 25(OH)D level ≤ 75 nmol/L. Obesity was defined as BMI > 95% for age and sex. Overweight was defined as BMI > 85-<95% and normal weight was defined as BMI < 85% for age and sex. Seasons were defined based on the date of the spring and fall equinox and summer and winter solstice dates for the respective study years.

Statistical Analysis

Chi-square and Fisher's exact test were conducted to assess the associations between categorical variables and correlation analysis used for the relationship between vitamin D and other cardiometabolic markers. Multiple regression analysis estimated the vitamin D means for different groups by age, gender, race and duration of diabetes.

Results

The majority of our population were 1 non-Hispanic black (NHB) (73%), followed by 22% Hispanic, 4% non-Hispanic white (NHW), and 6% other/unknown and 2 female (60%). Mean age was 15.0 years (range 8.7-18.5 years). The majority of the sample were older adolescents (60% were over 15 years of age). Vitamin D status did not differ significantly by gender or age. Mean 25(OH)D level was 47.4 nmol/L (range 22.5-82.4 nmol/L). Ninety-seven percent of the sample (N=47) had vitamin D insufficiency. Sixty-two percent (N=30) had vitamin D deficiency. Vitamin D did not vary significantly by race (Figure 1) or BMI.

The majority of subjects (83%) were obese and only 3 patients were normal weight. Mean BMI percentile for age and sex was 96.1% (range 51-99.9%). Mean BMI for the sample was 36.2 kg/m2 (range 16.2-61.9 kg/m^2) and BMI z-score was 2.16 (range 0.02-3.06). Children with vitamin D deficiency had a slightly higher BMI (37.3 kg/m^2) compared to those with vitamin D insufficiency (36.3 kg/m^2) (NS) (Table 1).

Seasonal variation indicated lower 25(OH)D levels in winter and spring. The winter and spring seasons included 20 patients whose mean 25(OH) D was 43.0 nmol/L (Figure 2). The remaining 28 patients tested during the summer and fall seasons had a mean 25(OH)D level of 50.7 nmol/L. There was no significant association between 25(OH)D levels and duration of diabetes, HbA1c, LDL, HDL, triglycerides, or urinary microalbumin (Table 2).

Discussion

Our results show that Vitamin D deficiency is extremely common in a sun-rich environment among adolescents with type 2 diabetes, independent of BMI or race. We found no association between Vi-

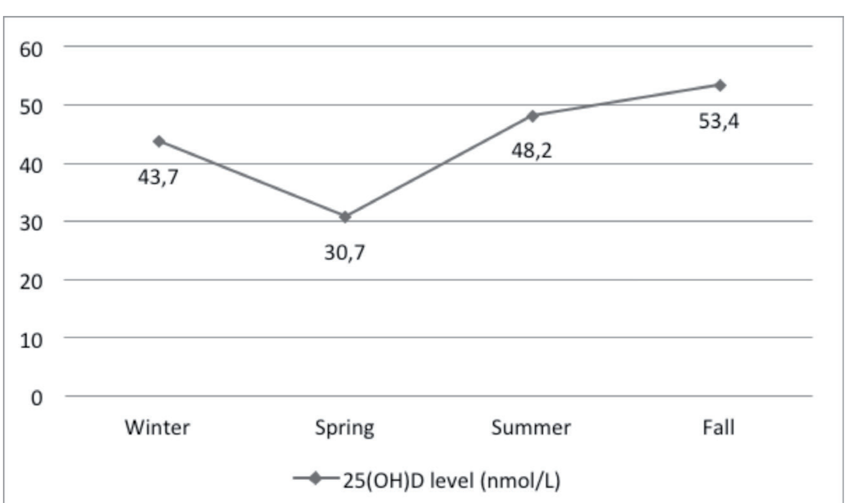

Figure 1. Mean 25-hydroxyvitamin D levels by Ethnic Group (%). 25-hydroxyvitamin D (25(OH)D); Non-Hispanic Black (NHB); Non-Hispanic White (NHW).

Table 1. Vitamin D status in normal, overweight and obese subjects.

Vitamin D status	Body Mass Index Percentile Group			
	Normal weight N (%)	Overweight N (%)	Obese N (%)	*p*-value
25(OH)D ≤ 50 nmol/L	1 (3%)	4 (13%)	25 (83%)	0.42
25(OH)D ≤ 75 nmol/L	3 (6%)	5 (11%)	39 (83%)	0.90

Vitamin D insufficiency [25(OH)D ≤ 50 nmol/L] and deficiency [25(OH)D ≤ 75 nmol/L] in normal weight (BMI ≤ 85%), overweight (BMI 85-95%) and obese (BMI ≥ 95%) subjects. Body mass index (BMI). 25-hydroxyvitamin D [25(OH)D].

tamin D levels and several other cardiometabolic disease risk factors. These findings suggest that type 2 diabetes may be an added risk for vitamin D deficiency among obese, multiethnic children/ adolescents.

Vitamin D deficiency in children is primarily associated with rickets. However, there is growing evidence that vitamin D deficiency may also be associated with many other conditions including type 1 diabetes, multiple sclerosis, and multiple types of cancer [2, 3]. Several studies in adults [8] and children indicate that low vitamin D levels are associated with increased risk of type 2 diabetes. In children, vitamin D levels have been inversely associated with fasting glucose and insulin and homeostasis model assessment of insulin resistance (HOMA-IR) independent of BMI [1, 6, 9]. In adult type 2 diabetics reports have shown that up to 98% have vitamin D insufficiency [10] and 60.8% have vitamin D deficiency [11]. Additionally, adult type 2 diabetics have lower mean 25(OH)D levels compared to non-diabetic adults (49.1 nmol/L v. 60.1 nmol/L, respectively). Although this study was conducted in Italy, a similar mean 25(OH)D level was found among American adult type 2 diabetics (50.4 nmol/L) [12]. We found a similarly high prevalence of vitamin D insufficiency (97%) and vitamin D deficiency (62%) among children with type 2 diabetes. We also found similar mean 25(OH)D level (47.4 nmol/L) compared to adult type 2 diabetics. Children and adolescents with type 2 diabetes have a high prevalence of hypovitaminosis D, despite residing in a sun-rich environment.

There is accumulating evidence that vitamin D plays a role in glucose homeostasis and is inversely associated with risk of developing type 2 diabetes[8]. Specifically, Vitamin D has a direct effect on pancreatic β-cell function[13,14]. Pancreatic β-cells have vitamin D receptors and express 1-α-hydroxylase enzyme activity. In turn, 1,25-dihydrovitamin D directly increases insulin synthesis and secretion[8,15]. Data from the National Health and Nutrition Examination Survey indicated an inverse association between serum 25(OH)D levels and

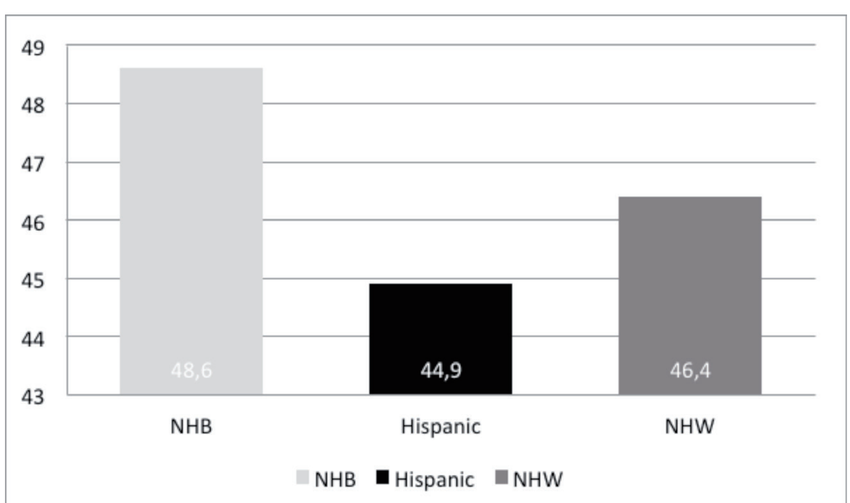

Figure 2. Mean Distribution of Vitamin D (nmol/L) by Season. 25-hydroxyvitamin D [25(OH)D]

Table 2. Vitamin D status based on duration of diabetes, glycemic control, cholesterol panel and urinary microalbumin.

Characteristic	Mean (range)	25(OH)D ≤ 50 nmol/L (deficient)	25(OH)D ≤ 75 nmol/L (insufficient)	*p*-value
HbA1c (%)	7.4 (5.2-12.7)	7.5 (5.2-12.7)	7.4 (5.2-12.7)	0.570
LDL (mg/dl)	100.6 (33-155)	101.4 (33-155)	100.7 (33-155)	0.915
HDL (mg/dl)	47.8 (29-87)	47.6 (29-74)	47.8 (29-87)	0.579
Triglycerides (mg/dl)	135.3 (43-1191)	161 (43-1191)	135.3 (43-1191)	0.949
Urinary microalbumin	34.8 (0.2-822)	47.3 (0.2-822)	34.8 (0.2-822)	0.979

25-hydroxyvitamin D [25(OH)D], Hemoglobin A1c (HbA1c), Low- Density lipoprotein cholesterol (LDL), High-Density lipoprotein cholesterol (HDL). Years (yrs). Month (m)

the prevalence of type 2 diabetes and measures of insulin resistance[8]. Meta-analysis of observational studies in adults indicates the risk of type 2 diabetes decreased by 13% with increased vitamin D supplementation [>500 international units (IU) per day compared to <200 IU per day][7]. In the same analysis, adult subjects with 25(OH)D levels >25 nmol/L had a 43% lower risk of developing type 2 diabetes compare to those with 25(OH)D < 14 nmol/L. In children 25(OH)D level inversely correlates with HOMA-IR, 2-hour glucose, fasting glucose and fasting insulin; independent of BMI[5,6,16,17]. In obese, non-diabetic adolescents fasting glucose improved after treatment with vitamin D[5].

Obesity, commonly seen in subjects with type 2 diabetes, is an independent risk factor for vitamin D deficiency in children and adults[1]. Proposed mechanisms for hypovitaminosis D in obesity include limited sun exposure, decreased bioavailability from cutaneous sources and deposition in adipose tissue[18,19]. Recently, a volumetric dilutional model has been proposed to account for lower vitamin D levels in obese individuals[19]. This model indicated that increased volume of distribution throughout the body, not only in adipose tissue, causes lower vitamin D levels in obese subjects. Volumetric dilution indicated a stronger correlation with 25(OH) D levels in both normal and obese individuals than BMI or fat mass. Thus, a higher intake of vitamin D is necessary to maintain adequate levels in an obese individual. A sedentary lifestyle also contributes due to limited sun exposure, which is more commonly seen in obese children. Children who had more than 4 hours of screen time per day are more likely to be vitamin D deficient[1]. Regardless of the mechanism, hypovitaminosis D is prevalent among obese children and adults.

In our study, obesity was shown to be a common factor in the high prevalence of hypovitaminosis D. Similarly, vitamin D status in a study of 411 obese children in the southern United States (Dallas, TX, USA, latitude 32°) indicated that 92% were vitamin D insufficient and 50% were deficient[16]. Their population was 48.6% Hispanic and 27.3% NHB. Therefore, the increased prevalence in our population may in part be due to a higher percentage of NHBs. The black race is an additional risk factor for hypovitaminosis D[1]. Of the Dallas population, 27% were obese and NHB. Of these subjects 93.9% had vitamin D insufficiency and 64.7% had vitamin D deficiency[16]. Recently, 25(OH)D status was reported among NHB adolescents residing in Agusta, GA, USA (latitude 33°)[20]. They reported mean 25(OH)D level of 46.7 nmol/L among 380 non-obese NHB adolescents (mean BMI percentile 66.1%, mean age 16.2 years). Thus the high prevalence of hypovitaminosis D in our population, despite a more southern location, is likely multifactorial, in which obesity, ethnicity and diabetic status play a role. It is noteworthy that despite a sun-rich environment, the prevalence of vitamin D insufficiency and deficiency are significantly high.

Additionally, in the year-round sub-tropical climate of Miami, FL, a seasonal variation in 25(OH) D levels was still seen in our analysis. This is consistence with studies in non-diabetic adults in Miami, Florida where mean 25(OH)D levels were higher in the summer (66.9 nmol/L) compare to winter (58.2 nmol/L)[21]. Their study population was primarily Hispanic, with only 21% NHBs, and weight status was not reported. Our population also had a seasonal variation, but significantly lower 25(OH)D levels which may be related to age, obesity, ethnicity and presence of diabetes.

Limitations

Our population was primarily NHB. Limited subjects of other races may have obscured potential significance between races. Similarly, because the majority of our population was obese with a limited number of normal weight subjects, we may have diluted any Vitamin D dose-response effect.

Another limitation is that we did not have an obese control population. Obesity is strongly associated to vitamin D deficiency/insufficiency. However, a comparison to a study with a similar ethnic mix of 127 obese children showed only 42% to be vitamin D insufficient and 32 % to be vitamin D deficient)[22]. Thus, their study population showed significantly less affected subjects than our study population of children with type 2 diabetes.

Conclusions

Vitamin D deficiency is extremely common in a sun-rich environment among adolescents with type 2 diabetes, independent of BMI or race. There was no significant association between 25(OH)D levels and age, duration of diabetes or HbA1c. We also did not find a significant correlation between 25(OH)D levels and cardiometabolic risk factors, including LDL, HDL, and triglycerides. Vitamin D levels showed seasonal variation, with lower 25(OH)D levels in winter and spring compared to summer and fall. In our study, the high prevalence of vitamin D insufficiency and deficiency suggests that type 2 diabetes may be an added risk for vitamin D deficiency among obese, multiethnic children/adolescents.

Future studies should help determine why children with type 2 diabetes have an increased risk of vitamin D insufficiency/deficiency and whether treatment with vitamin D improves their diabetes control.

Conflict of Interests:

The Authors declare that they have no conflict of interests.

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