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Vitamin D status in children and adolescents with type 1 diabetes in a sun-rich environment

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Abstract

Background: **Vitamin D has been associated with a variety of autoimmunity conditions including type 1 diabetes (T1D). Studies have indicated an increased prevalence of vitamin D deficiency in children with T1D.**

Objective: **The aim of our study was to examine vitamin D levels in a sample of children with type 1 diabetes in a primarily Hispanic population living in a sun-rich location.**

Materials and Methods: **Results were obtained from a retrospective chart review in children (N = 350) diagnosed with T1D who had serum 25-hydroxyvitamin D [25(OH)D] level data available from a clinical visit (2008-2012). Vitamin D deficiency was defined as 25(OH)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 (64%) of our population was Hispanic [23.4% Non-Hispanic White (NHW), 12.6% Non-Hispanic Black (NHB)]. Mean age was 12.3 years (range 0.08-19.2 years). Mean BMI percentile for age was 66.1%, 19.3% were overweight and 12.7% obese. Mean 25(OH)D level was 72.9 nmol/L. Half of the sample was vitamin D insufficient (50.8%) and 11.7% were vitamin D deficient. Increasing age and BMI percentile were associated with lower 25(OH)D levels. Vitamin D was significantly lower among NHB compared to Hispanic and NHW.**

Conclusions: **Despite a sun-rich environment, there was a high prevalence of vitamin D insufficiency in children with T1D, particularly among NHB subjects. Consistent with previous studies, hypovitaminosis D was inversely proportional to age and BMI. Compared to national data, children residing in a sun-rich environment may have a decreased the risk of hypovitaminosis but the prevalence remains unexpectedly high.**

Introduction

Historically, vitamin D deficiency in children has been associated with rickets; however, increasing evidence suggests its association with a variety of non-skeletal conditions. Vitamin D insufficiency is associated with increased risk of several autoimmune conditions including type 1 diabetes, asthma, and multiple sclerosis[1]. The active form of vitamin D (1,25-dihydrovitamin D) directly affects immune response through differentiation and function of T- and B-cells, dendritic cells, and macrophages[2]. In addition, the role of immunity has been increasingly recognized not only for T1D but also for T2D[3], and Vitamin D action has been recognized to include important immunomodulatory effects, including a decrease of Th1 and Th17 levels and increased regulatory cell activity[4]. For these reasons, high dose Vitamin D treatment has been recently proposed to treat subjects with T1D in combination with high dose Omega 3 fatty acids[5,6]. Evidence suggests that vitamin D may directly impact pancreatic β-cells survival though its effects on systemic inflammation[7]. Population studies indicate vitamin D supplementation during pregnancy and childhood may decrease the risk of developing type 1 diabetes[1]. Additionally, geographic and seasonal variation in the incidence of type 1 diabetes suggests an association with sun exposure[8]. Studies regarding vitamin D status in children and adolescents with type 1 diabetes are limited and primarily outside of the United States. Therefore, the aim of our study was to examine vitamin D levels in a sample of children with type 1 diabetes in a primarily Hispanic population living in a sun-rich location.

Patients and Methods

Patients

A retrospective medical chart review identified children and adolescents (N=350) with a diagnosis of type 1 diabetes who were seen at the pediatric diabetes clinic at University of Miami Miller School of Medicine (Miami, FL, USA, 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 (UMA) 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 markers. Multiple regression analysis estimated the vitamin D means for different groups by age, gender, race and duration of diabetes. Seasons were defined based on the date of spring and fall equinox, summer and winter solstice dates for the respective study years.

Results

The majority (64%) of our population was Hispanic, followed by 23.4% non-Hispanic white (NHW) and 12.6% non-Hispanic black (NHB). Half of our sample was female. Mean age was 12.3 years, range 0.08-19.2 years. Mean BMI percentile for age was 66.1% (range 0.3-99.6%). Mean 25(OH)D level was 72.9 nmol/L (range 16.5-134.8 nmol/L). Half of the sample was vitamin D insufficient (50.8%) and 11.7% were vitamin D deficient. Increasing age (Figure 1) and BMI percentile (Table 1) were

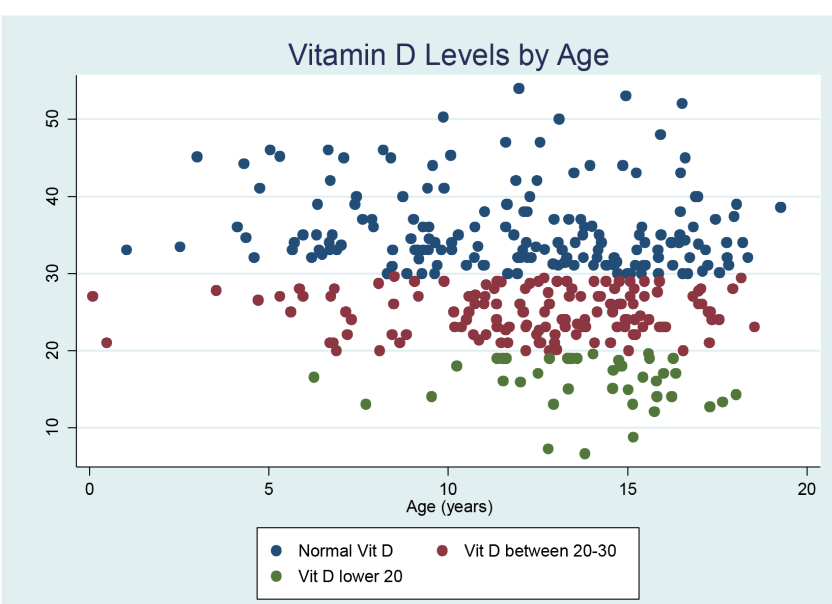

Figure 1. Mean 25-hydroxyvitamin D levels according to age.

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	28 (11.9%)	7 (10.4%)	6 (13.6%)	0.0275
25(OH)D ≤ 75 nmol/L	106 (45.1%)	42 (62.7%)	27 (61.4%)	0.0123

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).

associated with lower 25(OH)D levels (p=0.0024 and p=0.0193, respectively). Vitamin D was significantly lower among NHB compared to Hispanic (p=0.0007) and NHW (p=0.0031) subjects. There was no significant difference in 25(OH)D levels or prevalence of vitamin D insufficiency or deficiency by gender, hemoglobin A1c, duration of diabetes or cardiometabolic risk factors (LDL, HDL, TG, UMA) (Table 2). Samples taken during winter were lower compared to other seasons, average in Winter 27 nmol/L vs in Summer 30 nmol/L and 29 nmol/L in Spring and Fall.

Discussion

Our results indicate a high prevalence of vitamin D insufficiency and deficiency among children and adolescents with type 1 diabetes in a sun-rich environment. Increasing age and BMI were inversely associated with hypovitaminosis D. Vitamin D levels were lower in NHBs compared to Hispanics and NHWs. However, gender, duration of diabetes, hemoglobin A1c and cardiometabolic risk factors were not associated with hypovitaminosis D. Despite a year round sun-rich environment, vitamin D levels showed seasonal variation.

Several studies have indicated that subjects with type 1 diabetes have a lower 25(OH)D level compared to controls[9-11]. Most studies are from outside the United States and some show conflicting results. In Sweden, 25(OH)D levels were significantly lower in type 1 diabetics compared to control subjects (82.4 nmol/L v. 96.6 nmol/L, respectively, p<0.0001)[9]. In Italy, after resolution of acidosis, new onset diabetics also had significantly lower 25(OH)D and 1,25-dihydroxyvitamin D levels compared to controls (p<0.01 and p<0.03, respectively)[12]. In the UV rich environment of Australia, the prevalence of vitamin D deficiency was 43% among adolescents with type 1 diabetes compared to control 19% (mean 25[OH]D level 54.7 nmol/L v. 64.4 nmol/L, respectively, p=0.002)[10]. From a study in northern Florida (Gainesville, FL, USA, latitude 29°) vitamin D insufficiency was equally prevalent among type 1 diabetics and control subjects[13]. Their results showed that subjects (n=110) with type 1 diabetes for ≥ 5 months had a 68.5% prevalence of vitamin D insufficiency and mean 25(OH)D level of 57.9 nmol/L (p=0.46). Their subjects were older (mean age 16.0 years) compared to our population. Evaluation of National Health and Nutrition Examina-

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
Duration of diabetes	5.2 yrs (<1 m-15.4 yrs)	5.7 yrs (<1 m-15.1 yrs)	5.3 yrs (<1 m-15.1 yrs)	0.2178
HbA1c (%)	8.7 (5.4-17.5)	9.1 (6.4-17.1)	8.8 (5.6-17.5)	0.1160
LDL (mg/dl)	88.3 (37.0-273.0)	85.4 (45.0-237.0)	85.9 (37.0-273.0)	0.5097
HDL (mg/dl)	59.8 (28.0-116.0)	60.4 (34.0-100.0)	59.6 (34.0-100.0)	0.6726
Triglycerides (mg/dl)	94.5 (26.0-735.0)	113.8 (39.0-735.0)	90.0 (31.0-735.0)	0.9781
Urinary microalbumin	5.2 (0.1-199.0)	6.9 (0.2-86.7)	7.5 (0.1-199.0)	0.2219

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

tion Survey (2001-2004) data in children and adolescents (1-21 years) indicated that older adolescents were more likely to have vitamin D deficiency[14]. This trend was also demonstrated in a group (n=128) of children and adolescents with type 1 diabetes from Boston, MA, USA (p<0.001)[15]. The prevalence of vitamin D insufficiency was 76% and 15% were deficient. Hypovitaminosis D was most prevalent among children 12-18 years of age. We also found an inverse relationship between 25(OH) D levels and age in our population. Our population may have a higher mean 25(OH)D level and lower prevalence of hypovitaminosis D due to a younger age and more southern location compared to the subjects from Gainesville, FL, USA.

Latitude and exposure to the sun correlate with the incidence of type 1 diabetes (p<0.001 and p<0.05, respectively)[16]. The incidence rate of type 1 diabetes from 51 world regions tended to be higher at higher latitudes in both hemispheres (p<0.0001). Latitude can account for 25% of the variation in the incidence rates of type 1 diabetes. Much of this variation can be accounted for due to UVB irradiance and percent cloud cover. In a separate meta-regression analysis, latitude affected 25(OH) D levels in Caucasians (p=0.02)[17]. Decreased exposure to UVB at higher latitudes may be one factor in the onset of diabetes in a genetically susceptible individual.

Additionally, seasonal variation in the onset of type 1 diabetes suggests an association with vitamin D[8]. Highest rates of new onset type 1 diabetes are reported in the winter and lowest in the summer. In non-diabetic adults residing in Miami, FL, USA, seasonal variation in 25(OH)D levels were seen with mean serum 25(OH)D levels lower in the winter compared to summer (58.2 nmol/L v. 66.9 nmol/L, respectively)[18]. Our results also indicate a seasonal variation with lower levels in the winter compared to the summer (67.2 nmol/L v. 73.0 nmol/L, respectively). Our population has higher mean vitamin D levels compared to the adult population. However, the adult population had a higher portion of NHB subjects, which is a known risk factor for hypovitaminosis D[14].

Limitations

As a retrospective study, we were not able to assess vitamin D intake and sun exposure. We did not have a control group for comparison. However, when compared to a similar non-diabetic ethnic population in a study in Atlanta, Georgia (latitude, 33^{0}N), our study population had a much higher incidence of both Vitamin D insufficiency and deficiency[19].

Conclusions

In Miami, FL despite a sun-rich environment, vitamin D insufficiency is prevalent among a multiethnic population of children with type 1 diabetes. Vitamin D insufficiency was more prevalent among NHBs. Hypovitaminosis D was associated with inversely associated with age and BMI.

Future studies would be useful to determine why children with type 1 diabetes have an increased risk of vitamin D insufficiency/deficiency and whether treatment with vitamin D improves their diabetes control or decreases their insulin requirement.

Conflict of Interests:

The Authors declare that they have no conflict of interests.

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