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Vitamin D Abnormalities: More Common in US Children with T1D than in Healthy Children

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Abstract

Background: Pediatric patients with type 1 diabetes (T1D) have increased risk for low bone mineral density, which may be due in part to low 25-hydroxyvitamin D levels. Vitamin D levels are influenced by sunlight exposure and thus display geographical variation. We hypothesize that the prevalence of 25-hydroxyvitamin D deficiency (<20 ng/mL) and insufficiency (20 - 29 ng/mL) in children with T1D living in the United States is higher than in healthy children and that diabetes duration, HbA1c, and insulin dose/kg are inversely associated with 25-hydroxyvitamin D levels. Methods: Medical records of patients with T1D being followed in Tennessee were reviewed for demographics, medical information, and 25-hydroxyvitamin D levels during the previous 2 years. Control subjects were obtained from a de-identified database of healthy pediatric subjects living in a similar geographical area. Chi squared tests and multivariable linear regression were performed. Results: Children and adolescents with T1D (n = 276; median age 14 years) have a significantly higher percentage of vitamin D deficiency and insufficiency compared with healthy pediatric controls (n = 100; median age 11.2 years) (68% versus 44%; p < 0.001). The median 25-hydroxyvitamin D level is 24 ng/mL versus 31 ng/mL, respectively. After adjusting for age, race, gender, UV light exposure, BMI, and multivitamin supplementation, children and adolescents with T1D have a serum 25-hydroxyvitamin D level 6.7 ng/mL lower than the control population [CI (4.11, 9.21), p < 0.0001]. Within the T1D population, there is no clear association between diabetes duration, HbA1c, or insulin dose/kg and 25-hydroxyvitamin D levels. Conclusions: There is an increased prevalence of 25-hydroxyvitamin D deficiency and insufficiency in US. children with T1D compared with geographically similar children without diabetes. Further research is needed to determine whether decreased serum 25-hydroxyvitamin D can be alleviated via dietary or behavioral modifications in this population.

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Keywords

Vitamin D Deficiency, Vitamin D Insufficiency, 25-Hydroxyvitamin D, Diabetes Mellitus Type 1, Pediatric

1. Introduction

Adults living with type 1 diabetes mellitus (T1D) have decreased bone mineral density and are more likely to have osteoporosis compared with healthy controls [1]. This is significant for overall health as low bone mineral density is associated with an increased risk of fragility fractures, non-cause specific mortality, and cardiovascular mortality [2]. The decreased bone mineral density associated with T1D may be due to a variety of factors, including earlier age at onset of diabetes [3] and coexisting conditions such as celiac disease [4] or thyroid disease [5]. Similarly, low serum 25-hydroxyvitamin D levels are associated with poor bone mineral density, and patients with T1D may have low 25-hydroxyvitamin D levels, which may be most significant in patients with poor diabetes control [6].

The majority of bone mineral density is accrued during childhood and adolescence, and failure to achieve adequate peak bone mass during childhood may lead to bone abnormalities and increased fracture risk during adulthood [7]. As many as 70% of healthy children in the United States have vitamin D abnormalities, and many may therefore not achieve adequate peak bone mass [8]. This risk may be even more pronounced in children with T1D, as there have been several recent studies reporting the high prevalence of vitamin D abnormalities in such children [9]-[11]. Additionally, low levels of serum 25-hydroxyvitamin D has recently been correlated with non-skeletal effects in children and adolescents with T1D. It has been reported that 25-hydroxyvitamin D deficiency is associated with a significantly higher insulin requirement [12] and an increased prevalence of retinopathy [13].

To better understand possible disparities, several recent studies have offered a comparison between subjects with T1D and control subjects without T1D, with mixed results. A study in Qatari youth with age-matched controls reported increased 25-hydroxyvitamin D deficiency/insufficiency with T1D [14]; however this population may not be generalizable to US children due to a much higher overall prevalence of vitamin D deficiency/insufficiency reported amongst the Qatari (90.6% in subjects with T1D compared to 85.3% in control subjects). In Australia, Greer *et al.* also reported a significant difference between groups [15]. In contrast, it has been reported in Denmark that no difference was detected between children with newly diagnosed T1D and their healthy siblings [16].

As serum 25-hydroxyvitamin D levels are reflective of dietary intake as well as sun exposure, geographical distribution of 25-hydryoxyvitamin D abnormalities varies significantly; even within North America, results have varied. A study performed in Florida reported no significant difference between T1D and control groups [17]; however, this study included children, adolescents, and adults, thus preventing accurate comparison. In contrast, a more recent study evaluating Canadian adolescents and teenagers reported 32.8% of individuals with established T1D have 25-hydroxyvitamin D deficiency, compared to only 11.8% of the similar-aged healthy Canadian population [18]. Given these conflicting results within North American populations, additional clarification is needed to better understand the relationship between T1D and 25-hydroxyvitamin D in this region.

Therefore, we explored whether pediatric subjects with T1D differ from a control population of pediatric subjects living in middle Tennessee, within the United States. We hypothesize that the prevalence of 25-hydroxyvitamin D deficiency/insufficiency in children with T1D is higher than in healthy children and that diabetes duration, HbA1c, and insulin dose/kg is inversely associated with 25-hydroxyvitamin D levels.

2. Methods

2.1. Study Design

The inclusion criteria for this cross-sectional study were patients who were less than 21 years of age diagnosed with T1D who receive care at Monroe Carell Jr. Children's Hospital at Vanderbilt University Medical Center. Only patients of diabetes providers who screen all patients' serum 25-hydroxyvitamin D levels were included, to

alleviate bias. No patients were excluded from this study. Data was collected from the medical record, and the following characteristics were obtained for each patient within the past 2 years: height, weight, age, gender, race/ethnicity, date of diabetes diagnosis, and the presence of additional diagnoses including: thyroid disease, celiac disease, Turner Syndrome, Trisomy 21, and Addison's disease. All medications were recorded including type of insulin utilized, total insulin dose/kg, method of insulin delivery (injection versus pump) and use of supplementation with vitamin D or multivitamin. Laboratory values included a serum 25-hydroxyvitamin D level and all HbA1c values from the two years prior to 25-hydroxyvitamin D measurement.

The control population data was collected from a de-identified database of 100 healthy pediatric patients who live in similar middle-Tennessee geography, as previously reported [19]. This population included individuals between the ages of 1 - 21 years who live in similar middle-Tennessee geography and who were having bloodwork obtained at an outpatient clinic at Vanderbilt Children's Hospital. Control subjects were excluded if they had the following diagnoses: osteopenia, osteoporosis, osteogenesis imperfecta, previously diagnosed vitamin D insufficiency/deficiency, more than two bone fractures during the prior year, chronic or current glucocorticoid use, thyrotoxicosis, gastrointestinal disease such as celiac disease causing possible malabsorption, diabetes mellitus, history of or current treatment for malignancy, or were of non-weight bearing status. No patient approached about the study declined to participate. This dataset contains age, gender, race/ethnicity, height, weight, use of vitamin supplementation, and a single serum 25-hydroxyvitamin D level for each patient.

All data were stored in a secured, de-identified password-protected REDcap database [20]. The study was approved by the Institutional Review Board.

2.2. Anthropometric Evaluation

Body mass index was calculated based on the formula: weight (kg)/height (m^2). BMI Z-scores were calculated using age and gender-standardized growth population norms based on the Centers for Disease Control and Prevention's Year 2000 Growth Charts.

2.3. Laboratory Evaluation

The vitamin D measurement utilized for both groups was 25-hydroxyvitamin D, which is the standard indicator of vitamin D status, and levels were measured via liquid chromatography/ tandem mass spectrometry (Mayo Medical Laboratories, Rochester, MN). The total 25-hydroxyvitamin D concentrations were calculated by summing the measured values of 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3. Intra- and inter-assay coefficients of variation have previously been reported to be <7% [21]. The criteria used to determine 25-hydroxyvitamin D deficiency, insufficiency, and sufficiency were 25-hydroxyvitamin D levels of <20 ng/mL, 20 - 29 ng/mL, and ≥30 ng/mL respectively [22]. HbA1c was measured by point-of-care immunoassay using the DCA Vantage Analyzer (Siemens Healthcare Diagnostics, Deerfield, IL, USA).

2.4. UV Index

Ambient ultraviolet (UV) light was examined by using the reported UV index for Nashville, TN. Records of the UV index for Nashville were obtained from the National Oceanic and Atmospheric Administration (NOAA) Climate Prediction Center (CPC) website [23]. Reported UV indices issued for the 30 days preceding serum 25-hydroxyvitamin D measurement were averaged, and this value is referred to as the UV30.

2.5. Statistical Methods

Descriptive statistics were provided for both subject groups. A contingency table was created with a corresponding Chi-square test of association to compare the prevalence of 25-hydroxyvitamin D insufficiency and deficiency among T1D and normal controls. The alpha-value employed was 0.05. Multiple linear regression was performed to regress 25-hydroxyvitamin D levels on groups, adjusting for race, age, gender, UV index, BMI Z-score, and multivitamin supplementation. A similar multiple linear regression model was used to assess the association of the covariates with the 25-hydroxyvitamin D levels within the T1D patient group. Restricted cubic splines were initially considered for all continuous variables (age, UV index, BMI Z-score, HbA1c values, duration of diabetes and insulin dose/kg) to allow for non-linear associations with 25-hydroxyvitamin D levels, but the splines were reduced to linear coefficients if there was not strong evidence of non-linearity.

3. Results

A total of 276 subjects with T1D and 100 healthy pediatric subjects without T1D were evaluated in this study. Of the patients with T1D, there were 268 with established T1D, while 8 were considered new-onset (less than 90 days from diagnosis). T1D patients were analyzed collectively. Participant characteristics are presented in **Table 1**. Subjects with T1D were more likely than subjects without T1D to be older (median of 14 vs. 11.2 years, $p < 0.001$), Caucasian (85% vs. 67%, $p < 0.001$), and to have a lower UV30 (5.7 vs. 6.8, $p = 0.021$). Subjects with T1D were less likely to report regular supplementation with a multivitamin compared to those without T1D (11% vs. 28%, $p < 0.001$).

Within the T1D group, the median length of time since diagnosis was 4.9 years (IQR: 2.8, 9.2 years). The median HbA1c during the 2 years prior to the time of 25-hydroxyvitamin D measurement and the median HbA1c value at the time of 25-hydroxyvitamin D measurement were the same [8.6% (IQR 7.9%, 9.4%) vs. 8.6% (IQR: 7.9%, 9.8%), respectively]; 48% of subjects used injections while the remaining 52% used an insulin pump for delivery. Additional diagnosis included: thyroid disease (n = 39), celiac disease (n = 17), Addison's disease (n = 3), Turner syndrome (n = 2), and Trisomy 21 (n = 1).

The T1D population had a significantly lower 25-hydroxyvitamin D level than the control population, 24 ng/mL versus 31 ng/mL ($p < 0.001$, **Table 2**) univariately. The T1D subjects also had significantly higher percentages of 25-hydroxyvitamin D deficiency and insufficiency compared to healthy controls. In the T1D group, 32% were 25-hydroxyvitamin D deficient, 36% insufficient and 33% sufficient. In the control group, 14% were deficient, 30% insufficient, and 56% sufficient ($p < 0.001$, **Table 2**, **Figure 1**).

Table 1. Subject characteristics.

	TID (n = 276)	Control (n = 100)	p Value
Age (years)	14 [11, 16]	11.2 [7.1, 14]	<0.001
Gender (% female)	45	35	0.092
Race/Ethnicity (% Caucasian, non-Hispanic) (% African American) (% Other)	 85 10 5	 67 20 13	<0.001
BMI z-score	0.7 [−0.008, 1.4]	0.5 [−0.5, 1.6]	0.44
UV30*	5.7 [2.0, 7.8]	6.8 [3.0, 9.1]	0.021
Regular supplementation with multivitamin (%)	11	28	<0.001
Duration of T1D (years)	4.9 [2.8, 9.2]	-	
HbA1c at time of 25-hydroxyvitamin D measurement (%, mmol/mol)	8.6 [7.9, 9.8] 70 [63, 84]	-	
Two year average HbA1c (%, mmol/mol)	8.6 [7.9, 9.4] 70 [63, 79]	-	
Insulin pump use (%)	52	-	
Total insulin dose (unit/kg/day)	0.94 [0.74, 1.16]	-	

Results shown as median and [IQR] interquartile range. *UV30: A measurement of the average UV index (amount of UV light) in the patient's geographic location during the 30 days prior to the serum 25-hydroxyvitamin D evaluation.

Table 2. Serum 25-hydroxyvitamin D status: Pediatric TID patients compared with healthy pediatric control patients.

	TID N = 276	Control N = 100	p Value
Serum 25-hydroxyvitamin D (ng/mL)	24 [19, 32]	31 [25, 37]	<0.001
Deficient (<20 ng/mL)	32%	14%	<0.001
Insufficient (20 - 29 ng/mL)	36%	30%	
Sufficient (≥30 ng/mL)	33%	56%	

Results shown as median and [IQR] interquartile range.

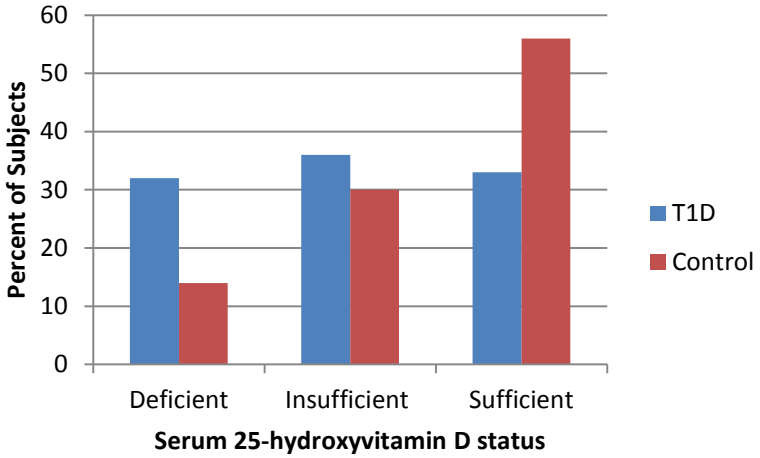

Figure 1. Descriptive chart showing serum 25-hydroxyvitamin D status between children and adolescents with T1D (n = 276) versus pediatric control population (n = 100). Categorization based on Endocrine Society Clinical Practice Guidelines: Deficient is defined as 25-hydroxyvitamin D level < 20 ng/mL; insufficient as 20 - 29 ng/ mL; sufficient as ≥30 ng/ mL.

In the multivariable linear model adjusting for covariates, the 25-hydroxyvitamin D levels for T1D patients were on average 6.67 ng/mL lower than those of normal controls, with a 95% confidence interval of (4.13, 9.22) and p value of <0.001 (**Table 3**). Caucasian race and UV30 were positively associated with 25-hydroxyvitamin D levels ($p < 0.001$ and $p = 0.0006$, respectively). There were significant linear and non-linear associations of 25-hydroxyvitamin D with both age [$p = 0.002$ and $p = 0.002$ (CI −0.14, 0.00), **Figure 2**] and BMI Z-score [$p = 0.005$ and $p = 0.002$ (CI −5.99, −1.62), **Figure 3**]. No significant association between 25-hydroxyvitamin D levels and gender or reported multivitamin/vitamin D supplementation was detected.

For the subset analysis of T1D subjects, none of the continuous explanatory variables showed evidence of non-linear associations with 25-hydroxyvitamin D level and hence were modeled with linear coefficients. After adjusting for other variables in the model, Caucasians had elevated 25-hydroxyvitamin D levels compared to African Americans and other races ($p = 0.001$) (**Table 4**). No statistically significant association was found between serum 25-hydroxyvitamin D levels and gender, body mass index, UV30, duration of diabetes, HbA1c value, use of injection versus pump, total insulin dose/kg, or supplementation with a multivitamin.

An additional subset analysis was performed comparing patients with T1D and additional comorbid autoimmune diagnoses and those with only T1D. The median 25-hydroxyvitamin D level in patients with T1D and other autoimmune diagnoses (hypothyroidism, n = 39; celiac disease, n = 17; and Addison's disease, n = 3) was 24.0 ng/mL (20.0, 32.0) and the median 25-hydroxyvitamin D level in patients with T1D but without other autoimmune diagnoses (n = 224) was 23.0 ng/mL (18.8, 33.0), $p = 0.73$. Of the 52 patients with additional autoimmune diagnoses, four had both hypothyroidism and celiac disease and all three patients who had Addison's disease also had hypothyroidism. No patients had both Addison's disease and celiac disease.

4. Discussion

As 25-hydroxyvitamin D levels are generally dependent upon both dietary intake and ultraviolet exposure, geographic location has a significant effect on 25-hydroxyvitamin D level. It is therefore imperative to evaluate the prevalence of 25-hydroxyvitamin D deficiency/insufficiency based on regional or local data when available. When sub-populations are considered, it is preferably with comparison to a control population from the same area. We report that children and adolescents with T1D have a significantly higher prevalence of 25-hydroxyvitamin D deficiency and insufficiency compared with a similar-aged population without diabetes living in the United States, in middle Tennessee (68% versus 44%).

This finding refutes the previous US based study performed in Florida, where Bierschenk *et al.* reported no particular association between reduced serum 25-hydroxyvitamin D levels and T1D [17]. Bierschenk reported a median 25-hydroxyvitamin D level of 23.2 ng/mL, consistent with our reported median of 24 ng/mL. The dif-

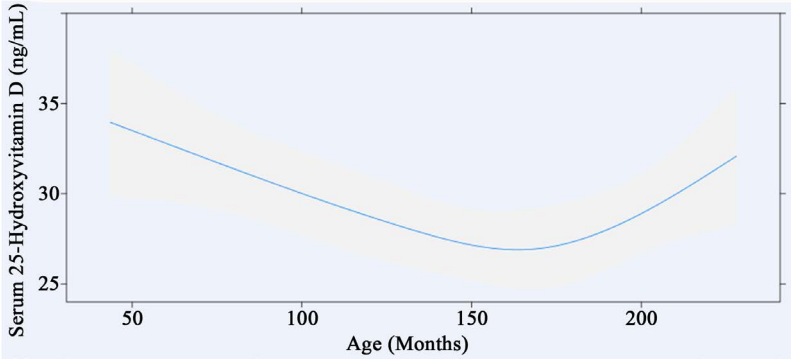

Figure 2. Predicted serum 25-hydroxyvitamin D level by age. Predicted means plot for age: Adjusted to: case = T1D, BMI z-score 0.6533, Caucasian race, male sex, UV30 = 5.648, no reported vitamin D supplement use.

Table 3. All patients: Multivariable analysis of serum 25-hydroxyvitamin D.

	Effect (ng/ml 25-hydroxyvitamin D)	CI	p Value
Group—TID: Control	**−6.67**	**−9.22 to −4.13**	**<0.0001**
Race— African American: Caucasian Other: Caucasian	 **−8.31** **−7.89**	 **−11.33 to −5.28** **−11.85 to −3.92**	**<0.0001**
Age (change from 1st quartile to 3rd quartile)	**−1.60**	**−4.40 to 1.20****	**Slope: 0.002 Non-linear: 0.002**
Gender—Female: Male	−0.70	−2.78 to 1.37	0.51
BMI z-score (change from 1st quartile to 3rd quartile)	**1.52**	**−2.28 to 3.26****	**Slope: 0.005 Non-linear: 0.002**
UV30* (per 1 unit increase)	**0.61**	**0.26 to 0.96**	**0.0006**
Multivitamin Supplementation	1.22	−1.69 to 4.14	0.41

*UV30: A measurement of the average UV index (amount of UV light) in the patient's geographic location during the 30 days prior to the serum 25-hydroxyvitamin D evaluation; **These are significant non-linear associations; see **Figure 2** for predicted means plot for age and **Figure 3** for predicted means plot for BMI z-score.

Table 4. T1D patients: Multivariable analysis of serum 25-hydroxyvitamin D.

	Effect (ng/ml 25-hydroxyvitamin D)	CI	p Value
Race— African American: Caucasian Other: Caucasian	 **−9.14** **−8.83**	 **−14.85 to −3.43** **−16.74 to −0.92**	**0.001**
Age (per 1 month increase)	0.03	−0.01 to 0.08	0.12
Gender—Female: Male	−0.19	−3.34 to 2.96	0.91
BMI z-score (per 1 unit increase)	0.11	−1.51to 1.73	0.89
UV30* (per 1 unit increase)	0.36	−0.17 to 0.89	0.19
Multivitamin Supplementation	0.46	−4.07 to 4.99	0.84
Duration of T1D (per 1 year increase)	−0.36	−0.84 to 0.11	0.14
HbA1c at time of 25-hydroxyvitamin D measurement (per 1% increase)	0.80	−1.31 to 2.92	0.46
Two-year average HbA1c (per 1% increase)	−1.90	−4.21 to 0.41	0.11
Insulin pump use	−2.43	−5.89 to 1.02	0.17
Total insulin dose (per 1 unit/kg/day increase)	−0.76	−6.05 to 4.53	0.78

*UV30: A measurement of the average UV index (amount of UV light) in the patient's geographic location during the 30 days prior to the serum 25-hydroxyvitamin D evaluation.

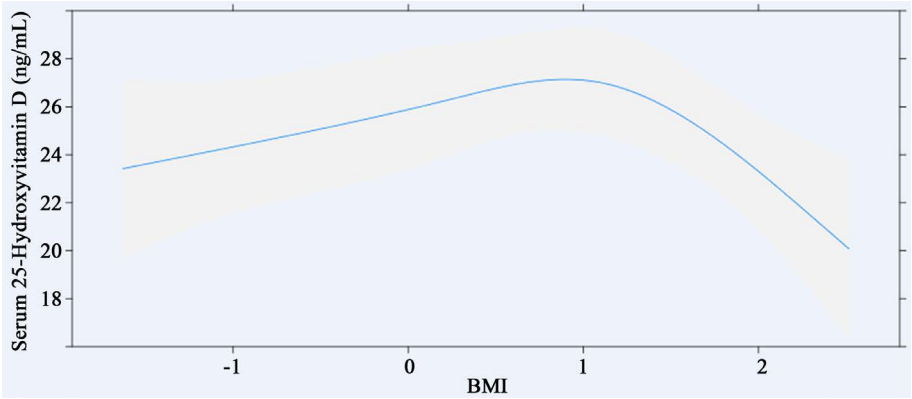

Figure 3. Predicted serum 25-hydroxyvitamin D level for BMI z-score. Predicted means plot for BMI z-score: Adjusted to: case = T1D, 156 months, Caucasian race, male sex, UV30 = 5.648, no reported vitamin D supplement use.

ference was found in healthy controls, with a median of 20.1 ng/mL versus 31 ng/mL, respectively. This discrepancy is likely explained by the age difference in the study reported by Bierschenk; the control population held a median age of 22 years (range 5 - 65.1 years) versus 16 years (range 5.1 - 62.6 years) for patients with established T1D. Our study includes only pediatric patients, allowing a more accurate comparison. Thus, social and recreational habits influenced by age likely explain the different outcomes.

Yeshayahu *et al.* report 25-hydroxyvitamin D deficiency in 32.8% of pediatric patients with T1D living in Canada [18], which is similar to the prevalence in the current study in middle Tennessee (32%). However, the middle Tennessee population with T1D who are sufficient in 25-hydroxyvitamin D is different than the Canadian population: 33% in Tennessee versus 14% in Canada. This disparity was equally true for healthy populations also: 56% versus 35.2%. This is likely due to the significant difference in availability of vitamin D from sunlight between Canada and Tennessee.

In our total group analysis, UV30 was significantly associated with serum 25-hydroxyvitamin D. However, in the multivariable analysis of only patients with T1D, there was no association between UV30 and serum 25-hydroxyvitamin D after adjusting for other covariates. A lack of association between UV30 and 25-hydroxyvitamin D was similarly reported by Greer *et al*. [15]. In this study, it could indicate that children and adolescents with T1D may have decreased time outdoors, as the UV30 is only a measure of ambient UV light and does not necessarily represent any individual's time spent outside or amount of skin exposed to sunlight. Alternatively, the smaller sample size of the subset analysis of T1D subjects resulted in wider 95% confidence intervals, thereby not excluding the possibility of a clinically meaningful association in the population. In the majority of studies of 25-hydroxyvitamin D abnormalities, investigators have typically adjusted for seasonality effects using three-month intervals (e.g. summer, fall, winter, spring). In this study, we have chosen to use UV30 instead of seasons, with the justification that seasons can be viewed as a crude categorization of the ultraviolet index, and hence lose information relative to the UV30.

Consistent with other studies, we report that serum 25-hydroxyvitamin D levels are higher amongst Caucasian children as compared to African American and non-white children [8] [9] [24]. We found a similar association between BMI z-score and vitamin D status as reported in previous studies; both underweight [22] and overweight [8] [25] [26] status are associated with lower serum 25-hydroxyvitamin D levels. Additionally, our data suggest that vitamin D levels may have a bimodal distribution and are higher in the youngest and oldest children, which has been reported previously [27]. However, this is in contrast to other studies which have reported that vitamin D levels are lowest amongst youngest children and teenagers [8] [9] [24] [28].

We did not find a significant association between supplementation with vitamin D or multivitamin and 25-hydroxyvitamin D levels, in contrast to some studies [8] [29] [30]. This is likely due, in part, to the low number of subjects reporting vitamin D supplementation in both groups as well as the variability of vitamin D dosing between patients. In addition, we were unable to ascertain with certainty the frequency of patient supplementation. A treatment study with varying dosing regimens and careful evaluation of compliance should be performed to better evaluate this possibility. Although the frequency of multivitamin or other vitamin D supplementation was low in both groups, supplementation was significantly lower amongst those with T1D. As patients with

T1D have to adhere to a complex insulin treatment regimen, less concern may be given to other aspects of health perceived by parents as non-essential.

The T1D population had numerous co-morbid conditions, as there were 39 patients with a diagnosis of thyroid disease (14.1%), 17 with celiac disease (6.2%), 3 with Addison's disease (1.1%), 2 with Turner syndrome (0.7%), and 1 with Trisomy 21 (0.4%). It has been well-described that patients with T1D are at increased risk for other such genetic and autoimmune disorders [31]-[33]. Our findings are similar to the recently reported coexistence of each of the aforementioned diagnoses within a population of young adults with T1D as follows: thyroid disease (9.5%), celiac disease (7%), Addison's disease (0.7%), Turner syndrome (3.5%), and Trisomy 21 (0.7%) [34]. Several of these disorders are also associated with decreased bone mineral density due to either disease course or therapy [4] [5] [35] [36], warranting special concern in such patients. An additional multivariable analysis of the subjects with T1D and either thyroid disease, celiac disease, Addison's disease, Turner Syndrome, or Trisomy 21 revealed no significant change in results. Therefore, these additional diagnoses are not associated with lower levels of 25-hydroxyvitamin D in T1D subjects.

The relationship between 25-hydroxyvitamin D and T1D is complex and not fully understood. Vitamin D may be protective against development of T1D, as a recent meta-analysis demonstrated decreased risk for T1D in subjects who received vitamin D supplementation during early life compared with those who did not receive vitamin D supplementation (pooled OR 0.71, $p < 0.001$) [37]. Moreover, it has been suggested that there is a dose-dependent positive correlation between vitamin D supplementation at a young age and decreased risk for T1D [38]. Evaluation of this relationship in US military personnel revealed that non-Hispanic white individuals with 25-hydroxyvitamin D levels of ≥100 nmol/L had a 44% lower risk of developing T1D than those with levels < 75 nmol/L ($p = 0.03$) [39]. Similarly, a recent study reported that 25-hydroxyvitamin D levels are lower in children with pre-T1D as compared to autoantibody-negative children [40]. Thus, there is compelling evidence that low 25-hydroxyvitamin D may reflect the primary immunological disorder. 25-hydroxyvitamin D may have a role in regulation of the immune system including T and B lymphocytes, promoting a more tolerant immunological status [37] [41]. Additionally, 25-hydroxyvitamin D may have direct effects on B-cells, such as improving insulin secretion and improving islet morphology [41] [42].

In conclusion, children and adolescents with T1D have significantly increased prevalence of 25-hydroxyvitamin D deficiency/insufficiency compared to a similarly aged control population in middle-Tennessee, and this is not moderated by control, duration, or insulin management of diabetes. This may increase risk of complications such as diabetic retinopathy, and have a significant impact upon bone health in patients with T1D. These youth may not attain adequate peak bone mass, the effects of which may contribute to increased risk for osteoporosis, fragility fractures, non-cause specific mortality, and cardiovascular mortality as adults [2]. Further research should be pursued to determine whether decreased serum 25-hydroxyvitamin D can be alleviated via dietary or behavioral modifications in this population.

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