Suboptimal Vitamin D Associated with Dental Caries at an Urban Pediatric Hospital

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Abstract

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Purpose: Inadequate vitamin D levels in children are associated with impaired calcification of hard tissues, including teeth. This study seeks to investigate associations between serum vitamin D levels and dental caries among children who receive care at a major northwest urban hospital.

Study design: This cross-sectional study examined data from Seattle Children's Hospital between 1999 and 2014. Inclusion criteria were children aged 1-6 years with primary dentition, American Society of Anesthesiologists (ASA) health status of I-IV, serum vitamin D levels, and dental data. Vitamin D levels were categorized as optimal (≥ 75 nmol/L) or suboptimal (< 75 nmol/L). Associations between vitamin D and caries were assessed using bivariate and multivariate (modified) Poisson regression models. Multivariate models were adjusted for age, race, ASA classification, season of vitamin D collection, and G-tube feeding status. Critical value was established at 5%.

Results: A total of 824 children were assessed of which 276 (33.5%) met the inclusion criteria. On average, children were 3.4 years old, 50.4% female, 48.9% white, 81.5% ASA III, 36.2% G-tube fed, and 33.3% had tooth decay experience. Children with suboptimal vitamin D levels

were 2 times more likely to have dental caries than children with optimal vitamin D levels (RR 2.16; 95% CI = (1.46,3.19); p=<0.001)

Conclusions: Children with suboptimal levels of vitamin D had an associated increased dental caries risk. Since children seeking care at hospitals are more vulnerable and interventions beyond the realm of the mouth are of relevance, awareness of their vitamin D status should be considered.

Introduction

Vitamin D, a lipid-soluble vitamin, has been at the forefront of current medical research due to its direct effect on the systemic, dental, and bone health of both children and adults.[1] Deficiency of this vitamin leads to impaired calcification of hard tissues like the skeletal framework of the body and mineralized dental tissues.[2, 3] Ameloblasts and odontoblasts, cells that form the building blocks of mineralized dental tissue like enamel and dentin, have been identified as targets for the biologically active form of vitamin D (1,25 –Dihydroxyvitamin D3).[4]

In a systematic review and meta-analysis, Hujoel et al. reported that supplemental vitamin D has been associated with a 47% reduced risk of caries.[5] Further, in an umbrella review of systematic reviews, Theodoratou et al. reported that vitamin D supplementation is probably linked to a decrease in dental caries in children.[6] Proposed biological mechanisms by which vitamin D is linked to dental caries include **1)** Altering the normal tooth development and mineralization process in utero, during the second and third trimester, generating hypoplasia's and consequently increasing the risk for dental caries[7, 8]; **2)** decreasing the activation of antimicrobial proteins (AMP) such as cathelicidins and defensins; relevant elements that help in breaking the membrane integrity of oral bacteria[9, 10]**3)** decreasing the salivary flow and altering its composition by reducing the amount of calcium ions and pH.[11, 12]

While the prevalence of dental caries differs among different populations, tooth decay continues to remain the most common chronic disease in children. It is five times more common than asthma and seven times more common than hay fever.[13] The complex etiology and spectrum of dental caries presentation is worsened in children with underlying systemic conditions due to a host of factors ranging from nutrition, medication use and severity of disease.[14] Children with special health care needs (CSHCN), defined by the Maternal and Child

Health Bureau (MCHB) as "those who have or are at an increased risk for a chronic physical, developmental, behavioral or emotional conditions, and who also require health and related services of a type or amount beyond that required by children generally" are more likely to experience barriers to obtaining dental care.[15, 16] Madden et al. found a high prevalence of vitamin D deficiency and insufficiency in critically ill children.[17] The National Health Interview Survey found that approximately 12% of CSHCN were deficient in at least one aspect of health care, with the greatest unmet need being dental care at approximately 8%.[16, 18]

To the best of our knowledge there has been no previous study looking at the association between vitamin D and dental caries among CSHCN. We hypothesize that suboptimal serum 25(OH) D levels are associated with dental caries.

Methods

Study Population:

This cross-sectional study examined data on children aged 1-6 years, who were seen at Seattle Children's Hospital (SCH) between 1999 and 2014. Seattle Children's hospital is a 250 bed children's hospital and is the largest pediatric referral center for the Pacific Northwest. It also serves as the pediatric academic medical center for the states of Washington, Alaska, Idaho, and Montana – the largest region of any children's hospital in the country. Data collection involved collaboration with the Seattle Children's Research Institute (SCRI), which forms the research division of SCH. In accordance with the study design and variables determined a priori, SCRI sent de-identified patient information. The target population was all children who had received a vitamin D measurement and had dental exam data within 6 months. The age range of 6 years and younger was chosen, as the study goal was to limit the examination to the primary dentition. This study was approved by the Seattle Children's Hospital Institutional review board (IRB) (IRB# 14692).

Variables:

Demographic variables: Demographic data for children 6 years and under was collected from their medical records in CIS (Clinical Information System). Demographic variables included in the analysis were age, gender, race/ethnicity and general health status. Age was measured in years; Race was categorized as White, Black, Asian, Native Hawaiian/Pacific Islander, Multiple and Other/Missing. The American Society of Anesthesiologists' physical status classification was used to report general health status (ASA I, II, III or IV).

Dental Variables/dmft data: The dental examination data was collected from the electronic medical record. Dental caries presence (Y/N), and mean decay, missing, filled teeth (dmft) was assessed by accessing the dental exam records. For individuals that had had multiple dental exams, the first dental exam at SCH was used to record the dmft data. Children that had erupted permanent teeth (permanent 1st molars or incisors- given the age of 6 years) were excluded from the study. Since there is evidence that it takes an average of 12-24 months for incipient lesions to develop into clinical cavitation in the primary dentition, it was decided that the dental exam and the vitamin D date of collection should be within +/- 6 months of each other to more accurately predict an association[19]

Serum Vitamin D-25 (OH) levels: Serum 25-hydroxyvitamin D (25(OH) D) measurements were taken from the laboratory values section of the patient's health records. These were reported in ng/mL and then converted to nmol/L for purposes of standardization and reporting. Vitamin D deficiency was defined using the Institute of Medicine 2011 report as serum 25(OH) D levels less than 30nmol/L.[20] Vitamin D inadequacy was defined as levels between 30 nmol/L and 49 nmol/L.[20]

Optimal vitamin D was defined as 75 nmol/L or higher and suboptimal vitamin D was defined as levels less than 75 nmol/L. This measure of vitamin D was used since there is a growing body of evidence that reports the cutoff for adequacy set forth by the Institute of Medicine at 50 nmol/L protects only against the more severe conditions like Osteomalacia or rickets and hence a 25(OH) D concentration of 75 nmol/L or more was the more desirable cut-off.[21-23]

Gastrostomy-tube (G-tube) status: Since individuals that are G-tube fed have limited to no oral intake, G-tube use was considered to be a confounding factor in determining an association

between vitamin D deficiency and dental caries. Therefore, G-tube use (Y/N) was extracted from the patient's medical record and included as a potential confounder in adjusted regression models.

Season of Vitamin D collection: Season of vitamin D collection was determined from the date the vitamin D sample was obtained. As per the study published by Schroth et al, in 2014, two seasons were identified: Winter: November-April, and Summer: May-October[24].

Data Analysis

Descriptive statistics (means, standard deviations (SD), counts, and percentages) were calculated for all variables by caries experience. Adjusted and unadjusted relative risks (RR) from modified Poisson regression examined the association between vitamin D and dental caries experience[25]. Due to the cross-sectional nature of this study, it was determined that mean dmft was the most appropriate estimate of dmft. Hence, adjusted and unadjusted slopes from linear regression were used to examine the association between Vitamin D and mean dmft. The multivariable regression models were adjusted for age, gender, race/ethnicity, G-tube status and ASA status. Data analysis was performed using Stata Version 12.1 (Stata-Corp, College Station, Texas). The statistical significance level was set to $p < 0.05$

Results

Five thousand five-hundred and twenty-four children who were seen at SCH between the years of 1999 and 2014 were screened. Eight hundred and twenty-four of these children had "Vitamin D" and "Dental Exam Data" in their records. Data was collected on 561 study participants that met the inclusion criteria (Figure 1). After excluding patients that did not have vitamin D data in the ± 6 month range, 276 children with a mean age of 3.4 years (SD: ± 1.47) were included in the study (Table 1). The majority of the patients were male (49.6%) and Caucasians (48.9%). More than three-quarters of the patients were ASA III (81.5%) and 36.2% had a G-tube in place for nutritional intake. Genetic conditions were the most commonly noted primary diagnosis (30.4%), followed by neurologic (18.4%), cancer (16.3%) and organ system disorders (14.4%). Patients that had conditions which could not be listed into any of the above mentioned groups, like infections, autoimmune diseases, and behavioral conditions like autism were grouped under the 'Other' category for ease of analysis. Almost half of the children (49.2%) had suboptimal vitamin D levels, while 12.7% of the patients had insufficient vitamin D levels and 2.9% had deficient vitamin D levels. More than half of the patients (52.2%) had a vitamin D serum level collected between the months of May to October. The overall prevalence of dental caries in the population was 33.3% (n = 92). The mean number of decayed teeth in the patient pool was 1.97 ± 3.9 and the overall dmft in the population was found to be 2.1 ± 4.

Vitamin D deficiency (<30 nmol/L) or insufficiency (<50 nmol/L) was not associated with caries experience (RR: 1.52, 95%CI (0.74, 3.11) P=0.25; RR: 0.69, 95%CI (0.46, 1.03) P=0.07) or overall dmft (Slope: 0.91, 95%CI (-1.91, 3.73) P=0.53; Slope -0.68, 95%CI (-2.10-0.74,) P=0.34), and this did not change after adjusting for potential confounders (RR: 2.06, 95%CI (0.86, 4.92) P=0.10; RR: 0.66, 95%CI (0.43, 1.00) P=0.05) (Slope: 1.84, 95%CI (-1.29, 4.97) P=0.25; Slope -1.05, 95%CI (-2.51-0.40,) P=0.15). Children with suboptimal vitamin D

levels were found to be two times more likely to develop caries (RR=2.13, 95%CI (1.47-3.07); P=<0.001), and their dmft score was 1.68 higher, compared to the optimal group (Slope: 1.68, 95%CI (0.76-2.61), p=<0.001). After adjusting for age, race, ASA status, G-tube status and season of vitamin D collection, suboptimal vitamin D levels (<75 nmol/L) were still associated with an increased risk of dental caries, compared with optimal vitamin D levels. (RR: 2.16, 95%CI (1.46-3.19), p=<0.001). The adjusted multivariable linear regression model indicated that children having suboptimal vitamin D levels had an overall dmft index that was 1.89 higher than children with optimal vitamin D levels (Slope: 1.89, 95 %CI: 0.93-2.9, p = <0.001) (Table 2,3).The multivariable analysis also showed that children with suboptimal vitamin D that had a G-tube, had 1.02 lesser dmft compared to children without a G-tube (Slope: -1.02, 95%CI (-2.0--0.01), p=0.05)

Discussion

This is the first, and the largest study (patient data over a period of sixteen years: 1999-2014) to the best of our knowledge that explored the association between having suboptimal levels of vitamin D and its impact on the dental caries experience of children receiving care at an urban hospital. Dental caries is a serious public health problem worldwide [26]. While the prevalence of tooth decay differs among different populations, it continues to remain one of the most common chronic diseases in children and has significant co-morbidities associated with it [27]. The majority of the patients (81.5%) included in this study had an ASA III status, which may be due to the fact that they were seen in the largest tertiary and quaternary care hospital in the Pacific Northwest. Although our inclusion criteria was patients with an ASA class of I-IV, there were no patients in our study that had an ASA classification of I or IV. Genetic conditions were the most frequently reported primary diagnosis in 30.4% of the population followed by Neurologic (18.4%) and Cancer (16.3%). Given the overall medical conditions of these patients, it is relevant to assess their oral health and underlying vitamin D status.

It has been known since the early 1900's that vitamin D deficiency is associated with dental caries and that supplemental vitamin D is protective against tooth decay. [28]. A historical placebo controlled trial in 425 children showed that increasing vitamin D supplements was associated with a reduction in the incidence of caries[29]. More recent studies have continued to solidify this claim. In a recent review, Grant et al. reported that serum vitamin D levels above 30-40ng/mL (75-100 nmol/L) may significantly reduce the risk of dental caries.[30]. Because of its complexity, dental caries is a disease that goes beyond an unbalanced oral environment to encompass the entire body; hence searching for preventive efforts beyond the oral cavity should be investigated.

There has been an ongoing dialogue about the correct dietary requirements and supplementation of vitamin D. The Institute of Medicine published a report in 2011 on the dietary requirements of Vitamin D and found that levels of 50 nmol/L were needed to meet the needs of at least 97.5% of the population.[20] There is a growing body of evidence that reports the cutoff for adequacy set forth by the Institute of Medicine at 50 nmol/L protects only against the more severe conditions like Osteomalacia or Rickets and that a 25(OH)D concentration of 75 nmol/L or more was the more desirable to cut-off. [21-23] Vieth et al. reported that serum 25(OH)D levels over 70 nmol/L had health benefits that included improved tooth attachment, decreased colorectal cancer, decreased levels of depression and overall well-being [23]. The difference in the specification of cut-points for serum 25(OH)D levels reflect the different views on current evidence and may have ramifications for the prevalence of optimal vitamin D levels.

This study's findings on suboptimal levels of vitamin D and dental caries were comparable to what has been previously reported in the literature. In a national cross-sectional study of Canadian school-aged children, Schroth et al. reported that Vitamin D concentrations (≥75 nmol/L) were associated with a 39% lower odds for dental caries and overall caries experience in young school-aged children [21]. On exploring the association between prenatal vitamin D and dental caries in infants, Schroth et al. reported that infants whose mothers had optimal prenatal 25(OH)D concentrations(≥ 75 nmol/L), had significantly lower decayed teeth[24]. This study did not find any association between having deficient or inadequate levels of vitamin D and overall caries experience.

Other variables that were found to be associated with caries in this population were Asian race and Other/Multiple race. This is consistent with what has been reported in the literature as far as vitamin D deficiency in children and can be biologically explained based on the fact that

pigmentation reduces vitamin D production in the skin.[31-33]In addition, there has been some research that shows Asians have altered vitamin D metabolism caused by increased 25(OH) D, 24 hydroxylase activity that makes them genetically prone to vitamin D deficiency [34].

There are certain limitations in this study that need to be acknowledged. More than a third (36.2%) of the patients were G-tube fed. G-tube usage was considered to be a confounding factor in examining the vitamin D deficiency and the dental caries experience of these children and was adjusted for in the final model. The median vitamin D value for children that had a G-tube is higher than those that did not (Figure 3). This could be due to the fact that a lot of these chronically ill children have frequent medical exams and are being treated for multiple existing co-morbidities and tend to receive adequate supplementation through the G-tube, and hence their lab values tend to be more regulated and scrutinized. Also, most of the common enteral feeding formulas contain vitamin D, in addition to other nutrients as a form of supplementation. An additional limitation is that the dental exam data that was recorded was completed by a diverse number of providers. There were some providers who were more detailed and reported prior caries experience, filled teeth and other dental findings more consistently as compared to others. This limitation may have led to the dmft scores in this study being underestimated. Finally, it is important to highlight that our study is not establishing causation but determining an association between having suboptimal levels of vitamin D and the dental caries experience of CSHCN. There is a need of well-designed prospective clinical trials to establish the minimum 25(OH) D levels needed to ensure optimum dental health in this susceptible population.

In summary, the results from this study indicate that CSHCN with suboptimal vitamin D levels were found to be at a two times higher risk of developing caries. This finding highlights the importance of reconsidering the cut-offs for optimal vitamin D levels in children who are not

healthy. Vitamin D insufficiency is a common problem in pediatric medicine especially in those who have chronic illnesses, are malnourished, are geographically limited to the amount of sun exposure, those with darker skin, or are on chronic medications.[35] The unmet dental needs of this vulnerable cohort add an additional layer of complexity in caring for them. Ensuring optimal levels of vitamin D can be an effective public health measure of relevance to the dental and medical community that can help avoid adverse health outcomes throughout life, as well as reduce the burden of a preventable disease like dental caries.

APPENDIX:

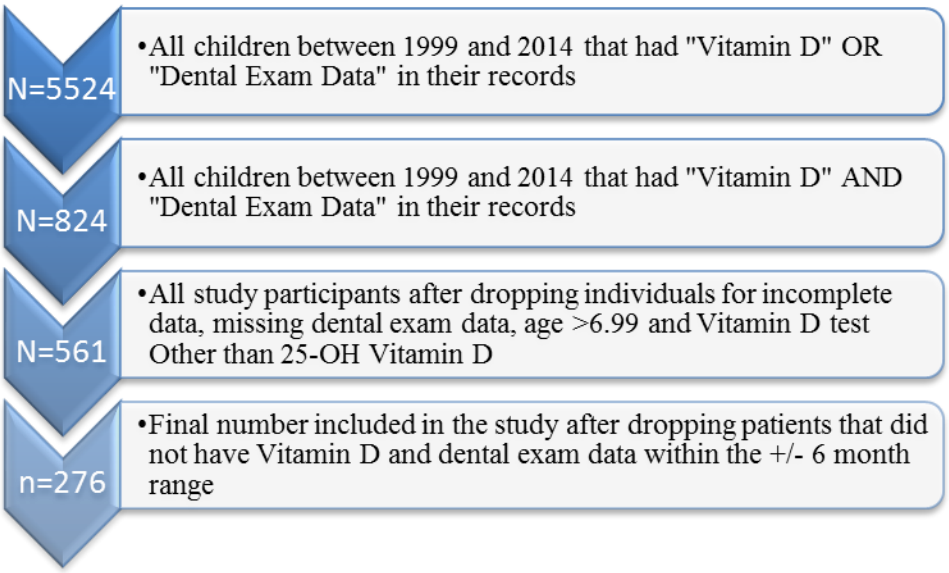

Figure 1: Flow chart showing the initial number of patients that were enrolled (N=5524) and the final number eligible for inclusion in the study (n=276).

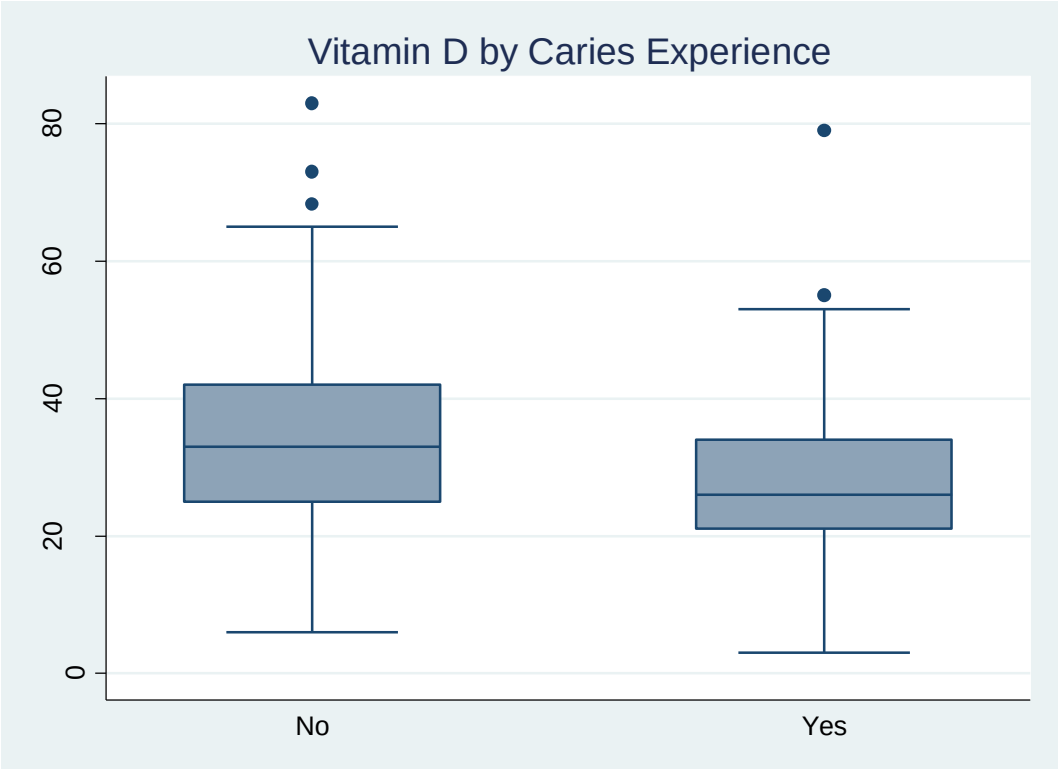

Figure 2: Vitamin D levels by Caries Experience (Y/N)

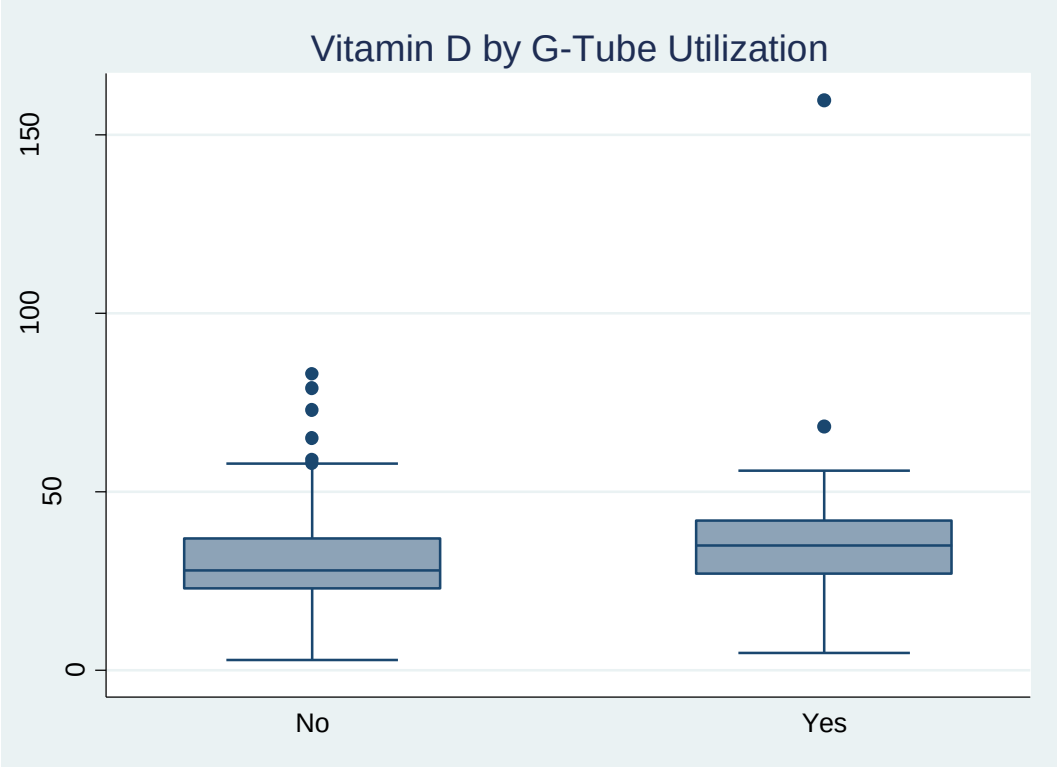

Figure 3: Vitamin D levels by G-tube utilization (Y/N)

Table 1: Characteristics of study participants by dental caries prevalence

	Caries Experience		
	No N = 184	**Yes N = 92**	**Total N = 276**
	N (%)	**N (%)**	**N (%)**
Age			
< 1	4 (2.2)	2 (2.2)	6 (2.2)
1-3	86 (46.7)	28 (30.4)	114 (41.3)
>3-6	94(51.1)	62 (67.4)	156 (56.5)
Sex			
Male	86 (46.7)	51 (55.4)	137 (49.6)
Female	98 (53.3)	41 (44.6)	139 (50.4)
Race/Ethnicity			
White	94 (51.1)	41 (44.6)	135 (48.9)
Asian	13 (7.1)	14 (15.2)	27 (9.8)
Black	15 (8.1)	5 (5.4)	20 (7.3)
Other/Multiple	45 (24.5)	27 (29.4)	72 (26.1)
Missing	17 (9.2)	5 (5.4)	22 (7.9)
Season of Vitamin D collection			
May to October	102 (55.4)	42 (45.6)	144 (52.2)
November to April	82 (44.6)	50 (54.4)	132 (47.8)
Vitamin D status (serum 25[OH]D Concentrations [nmol/L]			
Deficient (<30 nmol/L)			
No	180 (97.8)	88 (95.7)	268 (97.1)
Yes	4 (2.2)	4 (4.3)	8 (2.9)
Insufficient (< 50 nmol/L)			
No	165 (89.7)	76 (82.6)	241 (87.3)
Yes	19 (10.3)	16 (17.4)	35 (12.7)
Suboptimal (<75 nmol/L)			
No	110 (59.8)	30 (32.6)	140 (50.7)
Yes	74 (40.2)	62 (67.4)	136 (49.3)
ASA status			
ASA II	23 (12.5)	26 (28.3)	49 (17.8)
ASA III	160 (87.0)	65 (70.6)	225 (81.5)
ASA IV	1 (0.5)	1 (1.1)	2 (0.7)
G tube Fed			
No	102 (55.4)	74 (80.4)	176 (63.8)
Yes	82 (44.6)	18 (19.6)	100 (36.2)
Primary Diagnosis			
Genetic	59 (32.0)	25(27.2)	84 (30.4)
Other	28 (15.2)	28 (30.4)	56 (20.2)
Neurologic	36 (19.6)	15 (16.3)	51 (18.4)
Cancer	32 (17.4)	13 (14.1)	45 (16.3)
Organ System	29 (15.8)	11 (12.0)	40 (14.4)
Dental caries	**(Mean ± sd)**	**(Mean ± sd)**	**(Mean ± sd)**
Decayed teeth (d)	0	5.92 ± 4.66	1.97 ± 3.87

Missing teeth (m)	-	-*	-*
Filled teeth (f)	0	0.4 ± 1.55	0.14 ± 0.91
Decayed, missing or filled	0	6.35 ±4.60	2.1 ± 4.00

*No patients had missing data

Table 2: Unadjusted and adjusted associations of vitamin D levels and measures of tooth decay

	Any Caries				**dmft**			
Vitamin D	Unadjusted RR 95% CI	p-value	Adjusted RR 95% CI	p-value	Unadjusted Slope 95% CI	p-value	Adjusted Slope 95% CI	p-value
Vitamin D Deficient								
No (≥ 30/ nmol/L)	Reference		Reference		Reference		Reference	
Yes (< 30 nmol/L)	1.52 (0.74 -3.11)	0.25	2.06 (0.86-4.92)	0.10	0.91 (-1.91-3.73)	0.53	1.84 (-1.29-4.97)	0.249
Vitamin D Sufficient								
No (≥ 50 nmol/L)	Reference		Reference		Reference		Reference	
Yes (< 50 nmol/L)	0.69 (0.46-1.03)	0.07	0.66 (0.43-1.00)	0.050	-0.68 (-2.10 – 0.74)	0.34	-1.05 (-2.51-0.40)	0.15
Vitamin D Suboptimal								
No (≥ 75 nmol/L)	Reference		Reference		Reference		Reference	
Yes (<75 nmol/L)	2.13 (1.47-3.07)	<0.001	2.16 (1.46-3.19)	<0.001	1.68 (0.76 -2.61)	<0.001	1.89 (0.93-2.85)	<0.001

Table 3: Adjusted associations with suboptimal vitamin D and tooth decay

	Any Caries		dmft	
	Adjusted RR (95% CI)	**p-value**	**Adjusted Slope (95% CI)**	**p-value**
Vitamin D Suboptimal				
No (≥ 75 nmol/L)	Reference		Reference	
Yes (<75 nmol/L)	2.16 (1.46-3.19)	<0.001	1.89 (0.93 -2.90)	<0.001
Age (years)				
< 1	Reference		Reference	
1-3	0.85 (0.20-3.53)	0.819	1.72 (-1.40-4.84)	0.28
>3-6	1.36 (0.33-5.60)	0.665	2.30 (-0.77 – 5.39)	0.14
Race				
White	Reference		Reference	
Asian	1.94 (1.17-3.21)	0.01	2.26 (0.65-3.88)	0.006
Black	0.78 (0.35-1.74)	0.55	-0.78 (-2.6-1.08)	0.41
Other/Multiple	1.69 (1.18-2.41)	0.004	1.71 (0.60-2.82)	0.003
ASA status*				
ASA 2	Reference		Reference	
ASA 3	0.82 (0.58-1.18)	0.297	-1.48 (-2.75- -0.21)	0.02
G- tube				
No	Reference		Reference	
Yes	0.51 (0.32-0.80)	0.003	-1.02 (-2.0 - -0.01)	0.05
Season of vitamin D collection				
November - April	Reference		Reference	
May - October	0.81 (0.59 – 1.12)	0.21	-0.62 (-1.6-0.32)	0.20

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