# Determinants of Dental Caries in Infants

Jodie Christensen

BSc(Dent) Thesis

Supervisor: Dr. Robert Schroth

ABSTRACT:

**Objectives:** The origins of early childhood caries (ECC) begin prenatally, before teeth arrive. Maternal vitamin D status during pregnancy may affect calcification of the developing dentition, and subsequently predispose children to developmental defects of enamel ECC. This study was conducted in order to determine whether a relationship exists between prenatal maternal vitamin D status (via a cord blood sample) and caries prevalence in offspring. Factors predisposing children to ECC were also explored.

**Methods:** A prospective cohort of expectant mothers was selected from a high-risk urban population seeking prenatal care in Winnipeg, Canada. Participants were recruited into one of two groups; an intervention group and control group. The intervention group received two doses of 50,000 IU of vitamin D, one in the second trimester and one in the third trimester. A prenatal questionnaire was completed at the first visit. Cord blood was taken at birth and analysed for 25(OH)D. Participants returned at the time of their child's first birthday, where a follow up questionnaire and dental exam of the child were completed. The dental examiner was blinded to the vitamin D cord level. A p value $\leq 0.05$ was significant.

**Results:** 283 women were recruited (mean age 23.4 ± 5.6 years); 141 women were in the supplementation group, while 142 served as controls. Cord blood was drawn from 107 women in the intervention group and 109 controls. The mean 25(OH)D level was 49.6 ± 24.3 nmol/L. 175 women returned for the infant follow-up visit. The mean age of the children was 19.7 ± 8.1 months and 52% were male. Overall, 26.3% of children had ECC, and the mean decayed tooth (dt) score was 0.94 ± 2.16 teeth (range 0-16). There was no significant difference in prevalence of children with ECC between the intervention and control group (p=0.21). The 25(OH)D status

also did not significantly impact ECC (p=0.54). However, it was determined that mothers with higher cord 25(OH)D levels had infants with significantly lower dt scores (p=0.0011). Factors associated with ECC included, receiving government assistance (p=0.011), household income below $28 000 (p=0.0024), unemployment (p=0.00019), presence of enamel hypoplasia (p=0.0063) and developmental defects of enamel (p=0.0086), longer duration of being bottle-fed (p=0.0079) and age (p<0.0001).

**Conclusion:** The vitamin D dose used in this study did not significantly increase the cord blood vitamin D status compared to the control group. No relationship was found to exist between the two groups and prevalence of ECC. However, significance was seen in an inverse relationship between 25(OH)D levels and the number of decayed primary teeth. Similarly designed studies, with an altered vitamin D regimen, need to be conducted in order to receive more conclusive results.

INTRODUCTION:

Dental caries is the most common chronic disease affecting children.[1,2] Decay that develops during infancy and the preschool years is referred to as Early Childhood Caries (ECC). It is defined by the presence of 1 or more decayed, missing, or filled teeth within the primary dentition of a child under 6 years.[3] A more aggressive form of ECC, termed Severe Early Childhood Caries (S-ECC), sometimes manifests and usually requires rehabilitative dental surgery performed in hospital under general anesthesia.[3] Children with ECC can often suffer from oral pain, have altered eating patterns, have growth and development issues, and may suffer from poorer nutritional status and well-being.[4] Other impacts of untreated severe caries in young children include altered sleep patterns, and absence from or inability to concentrate in school.[2,5]

ECC is a multi-factorial disease[5,6], influenced by diet, eating frequency, microflora variations, fluoride use,[1] and the social determinants of health.[7] Children from lower socio-economic households are at higher risk for caries often because families are unable to purchase nutritious foods, diets may be high in sugar[2], oral health literacy of parents may be limited, and they may have limited access to dental care.[8]

The role of diet in the development and prevention of dental caries prevention was the focus of much research during the 1920s and 1930s.[9-11] Lady May Mellanby's pioneering studies explored the impact of vitamin D rich diets on caries and tooth resistance.[9] Findings from her 1928 paper concluded that diets rich in vitamin D helped prevent caries initiation, as well as limited or arrested the spread of caries. Conversely, diets low in vitamin D showed no such suppression.[9]

The active form of vitamin D, 1,25-dihyroxyvitamin D [1,25(OH)2D] regulates blood calcium by absorbing calcium from the intestines.[5,12] Its role in calcium and phosphorus homeostasis is key for proper formation and maintenance of hard tissues,[12] including the mineralization of teeth.[5] Vitamin D is also required in several cellular pathways including the immune response, cellular differentiation, proliferation and apoptosis.[13] Therefore, vitamin D may offer some protection against cariogenic microorganisms.[14]

Vitamin D is obtained either exogenously through diet and supplements or endogenously via solar radiation.[5] Endogenous production is considerably limited in darker skinned individuals, as additional melanin acts as a natural sunscreen.[15] Populations residing in northern latitudes are also disadvantaged regarding endogenous production, especially during the winter months (i.e. November to March) when sunlight exposure is severely limited.[13,16]

In Canada, milk, margarine and milk alternatives are fortified with vitamin D,[16,17] and are the major sources of dietary vitamin D.[17] Fish, eggs and liver are also high in vitamin D content.[5] Health Canada lists the Daily Recommended Intake (DRI) of vitamin D as 600 IU for individuals aged 1-70, and for pregnant and lactating women.[18] Most can achieve this DRI through daily supplements, including prenatal vitamins which supply 400 IU vitamin D.[12] The Canadian Paediatric Society recommends that infants receive 400 IU daily in the summer and up to 800 IU during the winter months.[19] Clinically, vitamin D status is measured using the dominant form of plasma vitamin D, 25(OH)D. It works well as an indicator as it accounts for both cutaneous and dietary sources.[13,15] Achieving optimal levels of 25(OH)D is especially important for pregnant women as fetal concentrations rely mainly upon maternal concentrations. Optimal concentrations are those that reach or exceed 75 nmol/L.[15] However, the Institute of Medicine

lists the adequate concentration as ≥ 50 nmol/L.[20] Vitamin D inadequacy during pregnancy is linked to infantile rickets, improper bone development, neonatal hypocalcaemia, type 1 diabetes, and asthma.[12,15] It has also been identified as a possible risk factor for ECC.[14]

Early research by Cockburn reported that 400 IU of vitamin D daily during pregnancy was significantly associated with a lower prevalence of enamel defects in offspring.[21] Furthermore, a recent study by Schroth et. al. has reported for the first time that maternal prenatal vitamin D levels may influence the development of ECC.[14] Findings report that mothers of infants with ECC demonstrate lower prenatal 25(OH)D levels than mothers of caries-free infants[14]. It is during the second trimester, where primary tooth calcification in utero begins, where maternal vitamin D status affects the teeth.[5,14]

The purpose of this study was to investigate prenatal and early childhood origins of caries and whether prenatal vitamin D supplementation during pregnancy improved cord 25(OH)D levels and whether there was an impact on caries development in their infants.

METHODS:

A prospective cohort study was undertaken to investigate the influence of high dose vitamin D supplementation administered to pregnant women on cord 25-hydroxyvitamin D (25(OH)D) levels obtained from newborns and infant health outcomes, including infant oral health. This study was approved by the University of Manitoba's Biomedical Research Ethics Board. All participants provided written informed consent.

Participants were recruited from the Women's Hospital Outpatient Department of the Health Sciences Centre, Winnipeg, Canada (latitude 49° 53' N) during one of their prenatal

appointments. This clinic serves a primarily inner-city clientele, including Aboriginal women, those with limited socioeconomic status (SES), and newcomers to Canada. Participants self-selected themselves to one of two groupings. Those in the intervention (i.e. supplementation) group were recruited during their first or second trimester and consented to take two oral doses of 50,000 International Units (IU) of vitamin D in their second and third trimesters. Women not willing to take the vitamin D supplements and those recruited past the window of opportunity to be in the intervention group served as controls.

All participants received standard prenatal care, including use of prenatal vitamins. Those who had known hypercalcemia, kidney disease, inborn errors of metabolism, chronic illness (excluding diabetes), and current involvement in a related clinical study were excluded. In total 283 women were recruited; 141 women were assigned to the supplementation group and 142 served as controls.

All participants completed a short questionnaire administered by a staff member via interview. The questionnaire collected basic information on demographics, nutrition, intake of foods containing vitamin D, and amount of sunlight exposure. Additional information regarding education level, and SES was also obtained.

Those in the intervention group received two orally administrated doses of 50,000 IU vitamin D at scheduled prenatal visits, which was administered by a nurse in the outpatient clinic. The first dose was given during the second trimester, while the second dose was given during the third trimester. This supplementation was in addition to their regular prenatal vitamins.

At delivery, a sample of cord blood was taken and assayed for 25(OH)D. Samples were analyzed by Hospitals in Common Laboratory, based out of Mount Sinai Hospital in Toronto, Canada using Chemiluminescence Immunoassay. 25(OH)D is recognized as the main circulating form of vitamin D. The key thresholds used to quantify 25(OH)D levels within this study were ≥ 75 nmol/L (optimal based on HICL and HSC), ≥ 50 nmol/L (adequate based on Institute of Medicine (IOM)), and < 35 nmol/L (common threshold used to denote deficiency).[5,22-25]

Participants and their infants were then invited to return for a follow-up examination around the child's first birthday. Multiple contacts via phone and mail were made. An interview style questionnaire was administered collecting information on demographics, birth weight, current infant height and weight, prematurity, and current or past health problems. Information regarding diet, oral hygiene, timing of the eruption of the first tooth, and dental home status were also obtained. The primary dentition was assessed by the principal investigator (RJS) for signs of caries and developmental defects of enamel, but was blinded to groupings and cord 25(OH)D levels. ECC and S-ECC were defined according to current standards.[3] Caries scores using the dmft index (i.e. combined total for decayed, missing, and filled primary teeth) were also recorded. Developmental defects, such as enamel hypoplasia were assessed and the results were recorded.[26]

Data from questionnaires and dental screenings were entered into a Microsoft Office Excel database. The data were imported and analyzed by a statistical computer program, NCSS Version 9 (Kaysville, Utah). Analysis involved descriptive statistics (frequencies, means ± Standard Deviations (SD)), and bivariate tests Chi-square tests, t-tests, and analysis of variance (ANOVA). A p value ≤ 0.05 was considered significant.

RESULTS:

A total of 283 women were enrolled (mean age: 23.4 ± 5.6 years); 141 women were in the supplementation group, while 142 served as controls. There were no significant differences in mean age between those in the intervention or control groups (22.9 ± 5.3 years vs. 24.0 ± 5.9, p=0.11). Overall, there was no significant difference in the number of children participants had in the intervention and control groups (2.0 ± 1.6 vs. 2.2 ± 1.8, p=0.38). A total of 128 participants (45.4%) indicated that this was their first pregnancy; 46.8% of women in the intervention group and 44.0% in the control group were primiparous (p=0.63). Likewise, there were no significant differences between the groups with respect to socioeconomic characteristics like household income (p = 0.99), receiving social assistance (p=0.26), education level (p = 0.85), and employment level of the mother (p=0.72) or mother's partner (p = 0.46) (Table 1).

The groups were relatively well matched for prenatal vitamin use (p=0.21), skin color (p = 0.34), and milk consumption (p = 0.141) (Table 1). However, it appeared that fewer participants in the intervention group had heard of vitamin D (70.2% vs. 81.0%, p=0.035).

Cord 25(OH)D concentrations were available for 216 participants (76.3%) and the mean 25(OH)D level was 49.6 ± 24.3 nmol/L (Table 2). There was no statistical difference in the mean 25(OH)D cord levels between participants in the supplementation or control groups (p = 0.087, one-tailed test). When using 75 nmol/L cut-off, there was no difference between the two groups; 20.6% of participants in the supplementation group had levels ≥ 75 nmol/L compared to 15.6% in the control group (p=0.34). However, when the Institute of Medicine cut-off for

vitamin D adequacy (50 nmol/L) was applied, 50.5% of participants in the supplementation group met or exceeded this threshold compared to only 37.6% among controls. Unfortunately, this failed to reach statistical significance ($p = 0.057$).

A total of 175 participants (61.8%) returned with their infant for the follow-up visit. Some reasons for loss-to-follow-up included moving outside of Winnipeg (n=4; 1 intervention and 3 controls), fetal demise (n=9; 6 intervention and 3 controls), and child placed in foster care (n=11, 7 intervention and 4 controls). Figure 1 highlights the number of participants completing the various phases of the investigation.

The proportion of participants returning to complete the follow-up portion of the study was consistent between the supplementation and controls groups (63.8% vs. 59.9%, p=0.49). However, returning participants had significantly higher cord 25(OH)D levels than those lost-to-follow-up (52.6 ± 23.1 nmol/L vs. 44.0 ± 25.7, p=0.013). Those returning for the follow-up assessment were also significantly older than those lost-to-follow-up (24.1 ± 5.6 years vs. 22.3 ± 5.5, p=0.01). Likewise, those completing the study were significantly more likely to have completed high school or beyond than those lost to follow-up (50.9% vs. 37.0%, p=0.024). They were also significantly more likely to have taken prenatal vitamins than those lost-to-follow-up (86.3% vs. 75.9%, p=0.028). Interestingly, there was no difference in the proportion of participants receiving government assistance between those returning and those lost (42.8% vs. 50.0%, p=0.24) or in the proportion who were regular milk drinkers (88.0% vs. 86.1%, p=0.45). However, women returning for follow-up were less likely to be of lower income than those lost (64.0% vs. 80.0%, p=0.042). There was also no difference in the prevalence of participants who identified as Aboriginal between those returning and those lost to follow-up (p=0.086).

The mean age of returning children was 19.7 ± 8.1 months and did not significantly differ between those from mothers in the intervention and control groups (19.4 ± 7.8 months vs. 20.0 ± 8.5, p=0.60). Overall, 52% were male. Mean weights, heights, and head circumference measures of returning infants were 12.7 ± 6.3 kg, 83.9 ± 9.4 cm, and 48.6 ± 1.7 cm, respectively.

Table 3 reports results derived from the follow-up study visit questionnaire. There were no differences in how much milk mothers consumed during pregnancy (p = 0.26), prenatal vitamins taken during pregnancy (p = 0.907), or the child's current health (p = 0.67) between the supplementation and control groups. Socio-economical factors such as dental insurance for the child (p = 0.641) and government assistance (p = 0.49) also demonstrated insignificance. (Table 3).

Overall, 26.3% of children (46/175) had ECC, or technically speaking, S-ECC. The mean decayed tooth (dt) score among all children was 0.94 ± 2.16 teeth (range 0-16). The total mean dt, mt, ft and dmft scores for all children appear in Table 4. While 22.2% of children from mothers in the intervention group had S-ECC compared to 30.6% in the control group, there was no apparent difference in the proportion of children with S-ECC between the two groups (p=0.21). Caries tooth and tooth surface scores did not appear to statistically differ between children born to mothers in the supplementation and control groups (Table 4).

Poisson regression was performed to investigate the relationship between cord 25(OH)D concentrations and dt scores. Overall, a significant inverse relationship was revealed as children with higher cord 25(OH)D levels had significantly lower dt scores (p=0.0011).

Table 5 compares prenatal and post-natal data for children with S-ECC to those caries-free. Prenatal variables such as mothers age (p=0.12), taking vitamin D during pregnancy

(p=0.95), and mother's education level (p=0.063) showed no significance in prevalence. However, mothers of infants with ECC were significantly more likely to receive government assistance (p=0.011), have a household income below $28 000 (p=0.0024), be unemployed (p=0.00019), and rate their own dental health as poor (p=0.024). Interestingly, infants of mothers receiving the Healthy Baby Prenatal Benefit were more likely to have ECC (P = 0.00024) as well.

Although cord levels of 25(OH)D in children with ECC were lower than caries-free children (50.6 ± 21.6 nmol/ vs. 53.3 ± 23.7 nmol/L), the difference was not significant (Table 5). Post-natal characteristics such as sex (p=0.71), birth weight (p=0.55), and prematurity (p=0.88), were not associated with ECC. ECC was not associated with breast feeding (p=0.66) or bottle-feeding (p=0.088). However infants with ECC were bottle-fed for a longer duration than caries-free children (18.4 ± 9.0 vs 14.3 ± 4.9 months; p=0.0079). Frequent milk drinking (p=0.36) and snacking (p=0.33) revealed no significant association with ECC. Children with ECC were significantly older than children without ECC (23.8 ± 8.8 vs 18.2 ± 7.3 months; p<0.0001). Those with ECC were also more likely to have enamel hypoplasia (p=0.0063) and developmental defects of enamel (p=0.0086) than caries-free children. Mothers of children with ECC were significantly more likely to rate their child's dental health as poor than those of caries-free children (p=0.0001).

DISCUSSION:

This prospective study attempted to explore whether high dose vitamin D supplementation (100,000 IU) during pregnancy was associated with improved cord 25(OH)D levels and

improved infant oral health status. It also allowed us to observe which children went on to develop ECC during early life. Overall, 81.9% of our cohort demonstrated suboptimal cord levels of 25(OH)D, defined as concentrations of < 75 nmol/L. This is a concern as the developing fetus is dependent on the mother for vitamin D, which has a key role in the development and calcification of bones and teeth. It was recently reported that pregnant women with inadequate vitamin D status are at a higher risk for having offspring who develop ECC.[14] Unfortunately, much of this damage cannot be reversed with post-natal supplementation.[12,15]

Early research has demonstrated an association between vitamin D status (via diet and sun exposure) and caries[9,27]. Higher vitamin D is linked to lower caries incidence, decreased caries severity, decreased enamel hypoplasia, and higher caries resistance.[9] However, few studies have been conducted which examine the link between cord 25(OH)D levels at birth and caries development in offspring. While our current study did not find a direct link between supplementation and a lower incidence of ECC, we did identify that children of mothers with higher cord 25(OH)D levels had significantly lower dt caries scores (p=0.0011). This relationship is consistent with a study published in 2014 in Winnipeg that reported for the first time that maternal prenatal levels impact ECC incidence.[14]

The mean cord 25(OH)D of all sampled participants in this study (49.6 nmol/L) just failed to reach the Institute of Medicine's threshold for vitamin D adequacy. This was similar to the mean 25(OH)D reported in our prospective study looking at maternal 25(OH)D prenatal levels and caries in offspring (48 nmol/L).[14] Surprisingly, we did not identify a statistically significant difference in mean 25(OH)D levels between those in the supplementation and control groups (51.6 ± 22.1 nmol/L vs. 47.4 ± 26.2). It could be argued the dosage of vitamin D administered

(two doses of 50,000 IU) was very modest and insufficient to bring pregnant women up to what would be considered optimal or adequate levels. A higher dose or more frequent administration may have been needed to increase the plasma levels. For instance, daily doses of 400 IU/day of vitamin $D_3$ for a period of eight weeks generally only leads to an increase of 11 nmol/L in healthy adults.[28] Therefore, intakes of cholecalciferol in the range of 400 IU and fortified foods are unable to produce marked increases in 25(OH)D levels to optimal ranges if baseline levels are low.[29] A limitation of this study was that those in the supplementation group received two doses 50,000 IU of vitamin $D_2$. There is evidence that reveals that vitamin $D_3$ is being better at sustaining higher 25(OH)D levels for a longer period of time than vitamin $D_2$.[30,31] Considering this, it is interesting that hospital pharmacies in Canada carry plant based high dose vitamin D supplements.

Despite our ability to demonstrate an association between vitamin D supplementation and the incidence of ECC, the idea that vitamin D supplementation could reduce the risk for caries is still plausible as evidenced by the meta-analysis of past studies on the topic of vitamin D and caries.[27] There is evidence that supplementation with both $D_2$, $D_3$, and solar irradiation are all associated with a reduced risk for caries in children. Our finding of an inverse relationship between 25(OH)D and the dt score on Poisson regression would also suggest that better prenatal 25(OH)D levels may be protective against caries.

This study draws attention to the increased prevalence of caries in Canadian children with low socioeconomic status. Overall, 23.6% of the children presented with S-ECC. Our findings suggest this specific population is subject to increased risk factors for ECC. Children with ECC were significantly more likely to have mothers who receive government assistance

(p=0.011), have a household income less than $28 000 (p=0.0024), and are unemployed (p=0.00019). Interestingly, this study did not find an association between education level and infant caries rate (p=0.063). It is also interesting to note that mothers receiving the Healthy Baby Prenatal Benefit were more likely to have children with ECC (p=0.00024). However, this finding may be confounded by the involvement of other risk factors such as income, or employment. ECC is highly associated with the social determinants of health.[7] Low parental education and family income are known to heighten the risk for dental problems in during early childhood.[32-35]

Several studies highlight the relationship between bottle use and caries incidence. Common bottle-feeding habits, such as prolonged bottle use, bedtime bottle use, and sugar addition promote caries development in young children.[2,8] Similarly, this study found that infants with ECC were bottle-fed for a longer duration than caries-free infants (p=0.0079). However, the use of a bottle at bedtime did not demonstrate a significant association with ECC. Other notable predictors for ECC include child's age (p<0.0001), and presence of enamel hypoplasia (p=0.0063). This mirrors what was found in an earlier prospective study on the association between maternal 25(OH)D levels and caries in infants.[14]

There was no significant difference in the percentage of children with ECC between the intervention and control groups. Similarly no difference was seen in caries tooth and tooth surface scores between children born to mothers of either group. However, this observation may be explained by the non significant difference in vitamin D status between the two experimental groups.

There were several limitations to this study. 38.2% of participants did not complete the study, however the proportion of returning mothers did not differ between the supplement and control groups (p=0.49). Unfortunately, the returning participants had significantly higher vitamin D levels than those lost-to-follow-up (p=0.013). Had more mothers returned, we might have been able to determine whether there was an association between supplementation and reduced risk for caries. This study was also limited as the vitamin D dosage may have been too low or given too infrequently to cause a significant difference in cord 25(OH)D levels between the two experimental groups. The mean 25(OH)D level among those in the supplementation group was only 51.6 nmol/L. The form of vitamin D administered, vitamin $D_2$, is also sustained at lower 25(OH)D values than that of vitamin $D_3$. Future studies may benefit by investigating different dosage regimens, and vitamin D subtype. This study may also be limited as the population was chosen by convenience rather than randomized. However, a population at high-risk for low vitamin D status and ECC was intended for this study, in order to make it generalizable to the urban inner city population. Another limitation was that we only measured 25(OH)D levels via cord blood. Had we included a prenatal baseline level (prior to any high dose supplementation) we would have been able to see the true effect that the vitamin $D_2$ actually had.

Strengths of the study include the prospective design and the moderately sized and deliberately chosen sample. Cohort studies also have the advantage of decreased bias. In addition, the dental assessments were completed by a single practitioner who was blinded to which experimental group the participant belonged to. The design of the experiment allowed

for the observation of natural caries development and for the assessment of multiple outcomes after altering a single factor, 25(OH)D level.

CONCLUSION:

The vitamin D supplementation used in this study was insufficient to produce superior cord 25(OH)D levels compared to controls. The prevalence of ECC between the two groups also did not differ. However, there was a significant inverse relationship between 25(OH)D levels and the number of decayed primary teeth. The amount and form of supplementation used in this investigation was unable to yield improvements in early childhood oral health.

1. Evans EW, Hayes C, Palmer CA, Bermudez OI, Cohen SA, Must A. Dietary intake and severe early childhood caries in low-income, young children. *J Acad Nutr Diet*. 2013;113(8):1057-1061.

2. Colak H, Dulgergil CT, Dalli M, Hamidi MM. Early childhood caries update: A review of causes, diagnoses, and treatments. *J Nat Sci Biol Med*. 2013;4(1):29-38.

3. American Academy on Pediatric Dentistry, American Academy of Pediatrics. Policy on early childhood caries (ECC): Classifications, consequences, and preventive strategies. *Pediatr Dent*. 2008;30(7 Suppl):40-43.

4. Schroth RJ, Harrison RL, Moffatt ME. Oral health of indigenous children and the influence of early childhood caries on childhood health and well-being. *Pediatr Clin North Am*. 2009;56(6):1481-1499.

5. Schroth RJ, Jeal NS, Kliewer E, Sellers EA. The relationship between vitamin D and severe early childhood caries: A pilot study. *Int J Vitam Nutr Res*. 2012;82(1):53-62.

6. Douglass JM, Douglass AB, Silk HJ. A practical guide to infant oral health. *Am Fam Physician*. 2004;70(11):2113-2120.

7. Canadian Dental Association. CDA position on early childhood caries. http://www.cda-adc.ca/_files/position_statements/earlyChildhoodCaries.pdf. Updated April 2010. Accessed 07/21, 2015.

8. Schroth RJ, Smith PJ, Whalen JC, Lekic C, Moffatt ME. Prevalence of caries among preschool-aged children in a northern manitoba community. *J Can Dent Assoc*. 2005;71(1):27.

9. Mellanby M, Pattison CL. The action of vitamin D in preventing the spread and promoting the arrest of caries in children. *Br Med J*. 1928;2(3545):1079-1082.

10. Mellanby M, Pattison CL. Remarks on THE INFLUENCE OF A CEREAL-FREE DIET RICH IN VITAMIN D AND CALCIUM ON DENTAL CARIES IN CHILDREN. *Br Med J*. 1932;1(3715):507-510.

11. Taylor GF, Day CD. Dental caries, vitamin D, and mineral deficiencies. *Br Med J*. 1939;1(4087):919-921.

12. Kaushal M, Magon N. Vitamin D in pregnancy: A metabolic outlook. *Indian J Endocrinol Metab*. 2013;17(1):76-82.

13. Calvo MS, Whiting SJ. Prevalence of vitamin D insufficiency in canada and the united states: Importance to health status and efficacy of current food fortification and dietary supplement use. *Nutr Rev*. 2003;61(3):107-113.

14. Schroth RJ, Lavelle C, Tate R, Bruce S, Billings RJ, Moffatt ME. Prenatal vitamin D and dental caries in infants. *Pediatrics*. 2014.

15. Li W, Green TJ, Innis SM, et al. Suboptimal vitamin D levels in pregnant women despite supplement use. *Can J Public Health*. 2011;102(4):308-312.

16. Vatanparast H, Calvo MS, Green TJ, Whiting SJ. Despite mandatory fortification of staple foods, vitamin D intakes of canadian children and adults are inadequate. *J Steroid Biochem Mol Biol*. 2010;121(1-2):301-303.

17. Calvo MS, Whiting SJ. Survey of current vitamin D food fortification practices in the united states and canada. *J Steroid Biochem Mol Biol*. 2013;136:211-213.

18. Vitamin D and calcium: Updated dietary reference intakes. http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php#a1. Updated 2012. Accessed 07/10, 2014.

19. Vitamin D supplementation: Recommendations for canadian mothers and infants. http://www.cps.ca/en/documents/position/vitamin-d. Updated 2013. Accessed 07/14, 2014.

20. Schroth RJ, Levi JA, Sellers EA, Friel J, Kliewer E, Moffatt ME. Vitamin D status of children with severe early childhood caries: A case-control study. *BMC Pediatr*. 2013;13:174-2431-13-174.

21. Cockburn F, Belton NR, Purvis RJ, et al. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J*. 1980;281(6232):11-14.

22. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357(3):266-281.

23. Whiting SJ, Calvo MS. Overview of the proceedings from experimental biology 2005 symposium: Optimizing vitamin D intake for populations with special needs: Barriers to effective food fortification and supplementation. *J Nutr*. 2006;136(4):1114-1116.

24. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int*. 2005;16(7):713-716.

25. Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. . 2011.

26. An epidemiological index of developmental defects of dental enamel (DDE index). commission on oral health, research and epidemiology. *Int Dent J*. 1982;32(2):159-167.

27. Hujoel PP. Vitamin D and dental caries in controlled clinical trials: Systematic review and meta-analysis. *Nutr Rev*. 2013;71(2):88-97.

28. Schwalfenberg G. Not enough vitamin D: Health consequences for canadians. *Can Fam Physician*. 2007;53(5):841-854.

29. Heaney RP. The vitamin D requirement in health and disease. *J Steroid Biochem Mol Biol*. 2005;97(1-2):13-19.

30. Trang HM, Cole DE, Rubin LA, Pierratos A, Siu S, Vieth R. Evidence that vitamin D3 increases serum 25-hydroxyvitamin D more efficiently than does vitamin D2. *Am J Clin Nutr*. 1998;68(4):854-858.

31. Glendenning P, Chew GT, Seymour HM, et al. Serum 25-hydroxyvitamin D levels in vitamin D-insufficient hip fracture patients after supplementation with ergocalciferol and cholecalciferol. *Bone*. 2009;45(5):870-875.

32. Schroth RJ, Moffatt ME. Determinants of early childhood caries (ECC) in a rural manitoba community: A pilot study. *Pediatr Dent*. 2005;27(2):114-120.

33. Schroth RJ, Halchuk S, Star L. Prevalence and risk factors of caregiver reported severe early childhood caries in manitoba first nations children: Results from the RHS phase 2 (2008-2010). *Int J Circumpolar Health*. 2013;72:10.3402/ijch.v72i0.21167. eCollection 2013.

34. Hallett KB, O'Rourke PK. Social and behavioural determinants of early childhood caries. *Aust Dent J*. 2003;48(1):27-33.

35. Schroth RJ, Cheba V. Determining the prevalence and risk factors for early childhood caries in a community dental health clinic. *Pediatr Dent*. 2007;29(5):387-396.

**Figure 1: Cohort sizes during different phases**

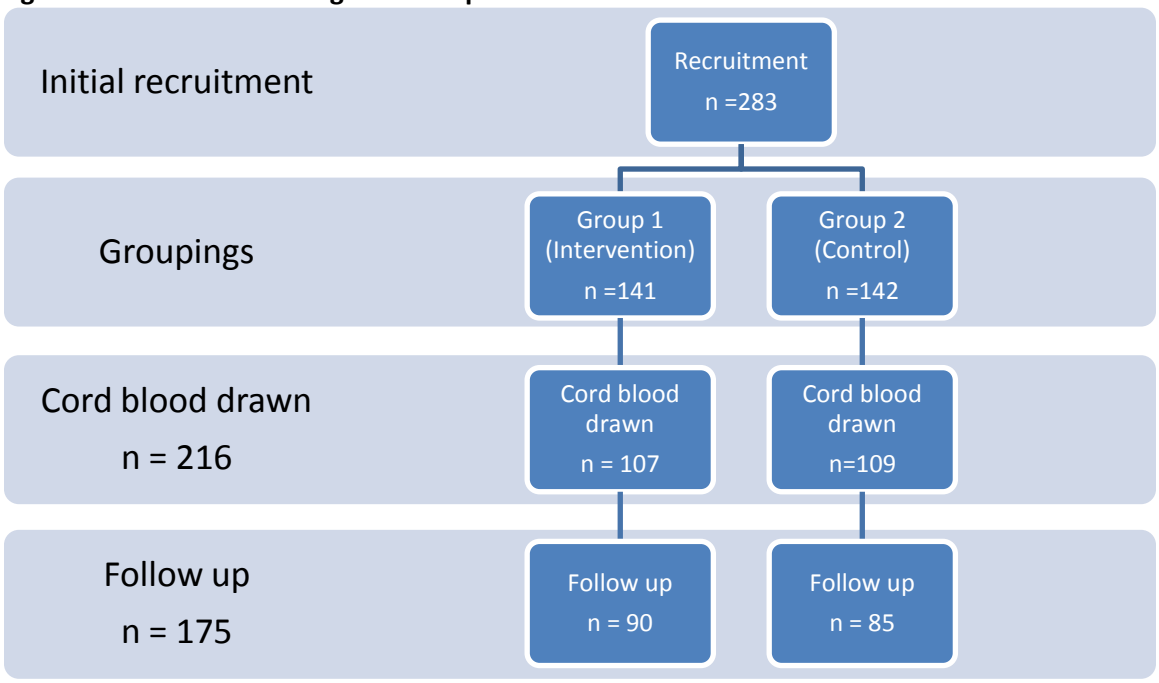


**Table 1: Maternal prenatal characteristics**

| Variable | Total Population N (%) | Intervention Group N (%) | Control Group N (%) | P Value |
|---|---|---|---|---|
| First pregnancy | | | | |
| Yes | 128 (45.4%) | 66 (46.8%) | 62 (44.0%) | 0.63 |
| No | 154 (54.6%) | 75 (53.2%) | 79 (56.0%) | |
| Doctor recommended taking vitamins during pregnancy | | | | |
| Yes | 234 (82.7%) | 120 (85.1%) | 114 (80.3%) | 0.28 |
| No | 49 (17.3%) | 21 (14.9%) | 28 (19.7%) | |
| Frequency of vitamins during pregnancy | | | | |
| Often | 174 (61.9%) | 90 (64.7%) | 84 (59.2%) | 0.17 |
| Sometimes | 46 (16.4%) | 26 (18.7%) | 20 (14.1%) | |
| Rarely | 19 (6.8%) | 6 (4.3%) | 13 (9.2%) | |
| Never | 42 (14.9%) | 17 (12.2%) | 25 (17.6%) | |
| Prenatal vitamins | | | | |
| Yes | 232 (82.3%) | 120 (85.1%) | 112 (79.4%) | 0.21 |
| No | 50 (17.7%) | 21 (14.9%) | 29 (20.6%) | |
| Heard of Vitamin D | | | | |
| Yes | 214 (75.6%) | 99 (70.2%) | 115 (81.0%) | **0.035** |
| No | 69 (24.4%) | 42 (29.8%) | 27 (19.0%) | |
| Eat fish | | | | |
| Often/Sometimes | 77 (27.2%) | 33 (23.4%) | 44 (31.0%) | 0.15 |
| Rarely/Never | 206 (72.8%) | 108 (76.6%) | 98 (69.0%) | |

| | | | | |
|---|---|---|---|---|
| Eat eggs | | | | |
| Often/Sometimes | 236 (83.7%) | 118 (84.3%) | 118 (83.1%) | 0.79 |
| Rarely/Never | 46 (16.3%) | 22 (15.7%) | 24 (16.9%) | |
| Eat margarine | | | | |
| Often/Sometimes | 235 (83.3%) | 118 (84.3%) | 117 (82.4%) | 0.67 |
| Rarely/Never | 47 (16.7%) | 22 (15.7%) | 25 (17.6%) | |
| Drink milk | | | | |
| Often/Sometimes | 249 (88.0%) | 119 (84.4%) | 130 (91.5%) | |
| Rarely/Never | 34 (12.0%) | 22 (15.6%) | 12 (8.5%) | 0.064 |
| Skin color | | | | |
| Dark | 103 (8.3%) | 8 (5.8%) | 15 (10.7%) | 0.34 |
| Mid | 151 (54.5%) | 77 (56.2%) | 74 (52.9%) | |
| Light | 103 (37.2%) | 52 (38.0%) | 51 (36.4%) | |
| Healthy Baby Prenatal Benefit | | | | |
| Yes | 142 (50.4%) | 68 (48.6%) | 74 (52.1%) | 0.55 |
| No/Just applied | 140 (49.6%) | 72 (51.4%) | 68 (47.9%) | |
| Dental health important | | | | |
| Yes | 264 (95.0%) | 135 (96.4%) | 129 (93.5%) | 0.26 |
| No | 14 (5.0%) | 5 (3.6%) | 9 (6.5%) | |
| How do you rate your own dental health | | | | |
| Good | 104 (37.0%) | 52 (37.1%) | 52 (36.9%) | 0.66 |
| Fair | 153 (54.4%) | 74 (52.9%) | 79 (56.0%) | |
| Poor | 24 (8.5%) | 14 (10.0%) | 10 (7.1%) | |
| Education level | | | | |
| < Grade 12 | 153 (54.5%) | 77 (55.0%) | 76 (53.9%) | 0.85 |
| ≥ Grade 12 | 128 (45.5%) | 63 (45.0%) | 65 (46.1%) | |
| Government assistance | | | | |
| Yes | 127 (45.5%) | 68 (48.9%) | 59 (42.1%) | 0.26 |
| No | 152 (54.5%) | 71 (51.1%) | 81 (57.9%) | |
| Mother's employment | | | | |
| Full or part time | 74 (26.1%) | 36 (25.5%) | 38 (26.8%) | 0.81 |
| Unemployed/other | 209 (73.9%) | 105 (74.5%) | 104 (73.2%) | |
| Partner's employment | | | | |
| Full or part time | 142 (63.9%) | 79 (68.1%) | 63 (59.4%) | 0.18 |
| Unemployed/other | 80 (36.1%) | 37 (31.9%) | 43 (40.6%) | |
| Household income | | | | |
| < $28000 | 113 (40.1%) | 53 (37.6%) | 60 (42.6%) | 0.48 |
| >$28000 | 51 (18.1%) | 24 (17.0%) | 27 (19.1%) | (0.99 when not |
| Not sure | 118 (41.8%) | 64 (45.4%) | 54 (38.3%) | sure excluded) |
| Ethnic background | | | | |
| Caucasian | 60 (21.4%) | 29 (20.7%) | 31 (22.0%) | 0.34 |

| | | | | |
|---|---|---|---|---|
| Aboriginal | 183 (65.1%) | 95 (67.9%) | 88 (62.4%) | |
| Black | 10 (3.6%) | 6 (4.3%) | 4 (2.8%) | |
| Asian | 18 (6.4%) | 7 (5.0%) | 11 (7.8%) | |
| Other | 4 (1.4%) | 0 | 4 (2.8%) | |
| Preferred not to answer | 6 (2.1%) | 3 (2.1%) | 3 (2.1%) | |
| Aboriginal heritage | | | | |
| Yes | 183 (65.1%) | 95 (67.9%) | 88 (62.4%) | 0.34 |
| No | 98 (34.9%) | 45 (32.1%) | 53 (37.6%) | |

**Table 2: Serum concentrations of 25(OH)D via cord blood analysis**

| | **Total population** | **Intervention Group** | **Control Group** | **p value** |
|---|---|---|---|---|
| Number of available 25(OH)D results | 216 (76.3%) | 107 (75.9%) | 109 (76.8%) | |
| Mean 25(OH)D nmol/L | 49.6 ± 24.3 | 51.6 ± 22.1 | 47.4 ± 26.2 | 0.087* |
| 25(OH)D | | | | |
| <75 nmol/L | 177 (81.9%) | 85 (79.4%) | 92 (84.4%) | 0.34 |
| ≥75 nmol/L | 39 (18.1%) | 22 (20.6%) | 17 (15.6%) | |
| 25(OH)D | | | | |
| <50 nmol/L | 121 (56.0%) | 53 (49.5%) | 68 (62.4%) | 0.057 |
| ≥50 nmol/L | 95 (44.0%) | 54 (50.5%) | 41 (37.6%) | |

*one tailed

**Table 3: Infant follow up questionnaire**

| **Variable** | **Total n(%)** | **Intervention Group n(%)** | **Control Group n(%)** | **P value** |
|---|---|---|---|---|
| Premature | | | | |
| Yes | 18 (10.3%) | 8 (8.9%) | 10 (11.8%) | 0.53 |
| No | 157 (89.7%) | 82 (91.1%) | 75 (88.2%) | |
| Child has serious health problems at birth | | | | 0.57 |
| Yes | 49(30.3%) | 29 (32.1%) | 24 (28.2%) | |
| No | 112(69.7%) | 61 (67.8%) | 61 (71.8%) | |
| Prenatal vitamins | | | | |
| Yes | 146 (83.4%) | 76 (84.4%) | 70 (82.3%) | 0.71 |
| No | 29 (16.6%) | 14 (15.6%) | 15 (17.7%) | |
| Vitamin D supplements | | | | |
| Yes | 8 (4.6%) | 4 (4.4%) | 4 (4.7%) | 0.93 |

| | | | | |
|---|---|---|---|---|
| No | 167 (95.4%) | 86 (95.6%) | 81 (95.3%) | |
| Drink milk during pregnancy | | | | 0.26 |
| Often/Sometimes | 149 (85.1%) | 74 (82.2%) | 75 (88.2%) | |
| Rarely/Never | 26 (14.9%) | 16 (17.8%) | 10 (11.8%) | |
| Child's current health | | | | 0.67 |
| Very good | 125 (71.4%) | 63 (70.0%) | 62 (72.9%) | |
| Good | 50 (28.6%) | 27 (30.0%) | 23 (27.1%) | |
| Child have medical problems | | | | < 0.001 |
| Yes | 37 (21.3%) | 28 (31.5%) | 9 (10.6%) | |
| No | 137 (78.7%) | 61 (68.5%) | 76 (89.4%) | |
| Rickets | | | | |
| Yes | 0 | 0 | 0 | N/A |
| No | 175 (100%) | 90 (100%) | 85 (100%) | |
| Hypocalcemic seizures | | | | |
| Yes | 0 | 0 | 0 | N/A |
| No | 175 (100%) | 90 (100%) | 85 (100%) | |
| Current condition of child's mouth | | | | |
| Very good | 84 (48.6%) | 46 (48.6%) | 38 (45.2%) | 0.69 |
| Good | 71 (41.0%) | 34 (41.0%) | 37 (44.1%) | |
| Poor | 18 (10.4%) | 9 (10.4%) | 9 (10.7%) | |
| Believe child has dental problems | | | | |
| Yes | 37 (21.2%) | 19 (21.1%) | 18 (21.2%) | 0.99 |
| No | 138 (78.9%) | 71 (78.9%) | 67 (78.8%) | |
| Child have gov. insurance for dental care | | | | 0.64 |
| Yes | 127(79.4%) | 67(78.8%) | 60(80.0%) | |
| No | 32(20.0%) | 17(20.0%) | 15(20.0%) | |
| Don't know | 1(0.6%) | 1(1.2%) | 0(0.0%) | |
| Government assistance | | | | |
| Yes | 101 (58.1%) | 50 (55.6%) | 51 (60.7%) | 0.49 |
| No | 73 (41.9%) | 40 (44.4%) | 33 (39.3%) | |
| Received Healthy Baby Prenatal Benefit | | | | |
| Yes | 123 (70.3%) | 60 (66.7%) | 63 (74.1%) | 0.28 |
| No | 52 (29.7%) | 30 (33.3%) | 22 (25.9%) | |
| Season of birth | | | | |
| May-Oct | 62(46.6%) | 31(44.9%) | 31(48.4%) | 0.48 |
| Nov-Apr | 71(53.4%) | 38(55.1%) | 33(51.6%) | |

**Table 4: Dental outcomes of children**

| Dental Outcomes | All children | Intervention Group | Control Group | P value |
|---|---|---|---|---|
| S-ECC | | | | |
| Yes | 46 (26.3%) | 20 (22.2%) | 26 (30.6%) | 0.21 |
| No | 129 (73.7%) | 70 (77.8%) | 59 (69.4%) | |
| dt score | 0.94 ± 2.16 (range 0-16) | O.87 ± 2.39 | 1.01 ± 1.89 | 0.66 |
| mt score | 0.05 ± 0.37 (range 0-4) | 0.04 ± 0.42 | 0.05 ± 0.31 | 0.95 |
| ft score | 0.04 ± 0.46 (range 0-6) | 0.01 ± 0.11 | 0.07 ± 0.65 | 0.41 |
| dmft score | 1.03 ± 2.28 (range 0-16) | 0.92 ± 2.42 | 1.14 ± 2.11 | 0.52 |
| ds score | 1.29 ± 3.57 (range 0-31) | 1.39 ± 4.42 | 1.19 ± 2.39 | 0.71 |
| ms score | 0.18 ± 1.48 (range 0-16) | 0.18 ± 1.69 | 0.19 ± 1.23 | 0.95 |
| fs score | 0.17 ± 2.12 (range 0-28) | 0.01 ± 0.11 | 0.33 ± 3.06 | 0.34 |
| dmfs score | 1.65 ± 4.69 (range 0-37) | 1.57 ± 4.69 | 1.73 ± 4.71 | 0.81 |
| Enamel hypoplasia | | | | |
| Yes | 12 (7.1%) | 4 (33.3%) | 8 (66.6%) | 0.16 |
| No | 158 (92.9%) | 86 (54.4%) | 72 (45.6%) | |
| Enamel opacity | | | | |
| Yes | 39 (24.4%) | 23 (59.0%) | 16 (41.0%) | 0.35 |
| No | 121 (75.6%) | 61 (50.4%) | 60 (49.6%) | |
| Development defects of enamel | | | | |
| Yes | 47 (29.4%) | 26 (55.3%) | 21 (44.7%) | 0.65 |
| No | 113 (70.6%) | 58 (51.3%) | 55 (48.7%) | |

**Table 5: Association between prenatal and post-natal factors and S-ECC**

| Variable | S-ECC | Caries-Free | P value |
|---|---|---|---|
| Prenatal Characteristics | | | |
| Mean age of mother (years) | 23.0 ± 5.5 | 24.5 ± 5.6 | 0.12 |
| Vitamin D during pregnancy | | | |
| Yes | 38 (82.6%) | 106 (82.2%) | 0.95 |
| No | 8 (7.4%) | 23 (7.8%) | |
| Prenatal vitamins | | | |
| Yes | 36 (80.0%) | 114 (88.4%) | 0.16 |
| No | 9 (20.0%) | 15 (11.6%) | |

| | | | |
|---|---|---|---|
| Mother's education level | | | |
| < Grade 12 | 28 (60.9%) | 57 (44.9%) | 0.063 |
| ≥ Grade 12 | 18 (39.1%) | 70 (55.1%) | |
| Government assistance | | | |
| Yes | 26 (59.1%) | 48 (37.2%) | **0.011** |
| No | 18 (40.9%) | 81 (62.8%) | |
| Rating of own dental health | | | |
| Good | 13 (28.3%) | 54 (41.8%) | **0.024** |
| Fair | 23 (50.0%) | 65 (50.4%) | |
| Poor | 10 (21.7%) | 10 (7.8%) | |
| Household income | | | |
| < $28,000 | 24 (88.9%) | 49 (56.3%) | **0.0024*** |
| ≥ $28,000 | 3 (11.1%) | 38 (43.7%) | |
| Mother's employment | | | |
| Full or part time | 5 (10.9%) | 53 (41.1%) | **0.00019** |
| Unemployed/other | 41 (89.1%) | 76 (58.9%) | |
| First pregnancy | | | |
| Yes | 15 (32.6%) | 70 (54.7%) | **0.010** |
| No | 31 (67.4%) | 58 (45.3%) | |
| Number of kids | 2.07 ± 1.53 | 2.02 ± 1.46 | 0.88 |
| Heard of vitamin D | | | |
| Yes | 33 (71.7%) | 105 (81.4%) | 0.17 |
| No | 13 (28.3%) | 24 (18.6%) | |
| Able to buy healthy foods | | | |
| Yes | 38 (82.6%) | 119 (92.2%) | 0.065 |
| No | 8 (17.4%) | 10 (7.8%) | |
| Healthy Baby Prenatal Benefit | | | |
| Yes | 36 (78.3%) | 60 (46.9%) | **0.00024** |
| No | 10 (21.7%) | 68 (53.1%) | |
| Milk intake | | | |
| Often/Sometimes | 40 (87.0%) | 116 (89.9%) | 0.58 |
| Rarely/Never | 6 (13.0%) | 13 (10.1%) | |
| Partner's employment | | | |
| Full or part time | 19 (52.8%) | 78 (72.9%) | **0.025** |
| Unemployed/other | 17 (47.2%) | 29 (27.1%) | |
| Aboriginal heritage | | | |
| Yes | 32 (69.6%) | 74 (58.3%) | 0.18 |
| No | 14 (30.4%) | 53 (41.7%) | |
| Post-natal Characteristics | | | |
| Mean 25(OH)D nmol/L | 50.6 ± 21.6 | 53.3 ± 23.7 | 0.54 |
| 75 nmol/L cutoff | | | |
| ≥ 75 nmol/L | 7 (17.9%) | 21 (20.6%) | 0.73 |
| < 75 nmol/L | 32 (82.1%) | 81 (79.4%) | |
| 50 nmol/L cutoff | | | |
| ≥ 50 nmol/L | 19 (48.7%) | 51 (50.0%) | 0.89 |

| | | | |
|---|---|---|---|
| < 50 nmol/L | 20 (51.3%) | 51 (50.0%) | |
| Sex | | | |
| Male | 25 (54.3%) | 66 (51.2%) | 0.71 |
| Female | 21 (45.7%) | 63 (48.8%) | |
| Mean age of child (months) | 23.8 ± 8.8 | 18.2 ± 7.3 | **<0.0001** |
| Premature | | | |
| Yes | 5 (10.9%) | 13 (10.1%) | 0.88 |
| No | 41 (89.1%) | 116 (89.9%) | |
| Birth weight (grams) | 3435.6 ± 812.1 | 3511.1 ± 703.8 | 0.55 |
| Current weight (kg) | 13.4 ± 2.6 | 12.5 ± 7.1 | 0.22 |
| Current height (cm) | 88.4 ± 9.3 | 82.3 ± 9.0 | <0.001 |
| Current head circumference (cm) | 49.4 ± 1.7 | 48.3 ± 1.6 | 0.0001 |
| Number of children in household | 2.2 ± 1.8 | 2.1 ± 1.3 | 0.77 |
| Mother's rating of child's dental health | | | |
| Very good | 10 (22.7%) | 74 (57.2%) | **0.0001** |
| Good | 22 (50.0%) | 49 (38.0%) | |
| Poor | 12 (27.3%) | 6 (4.7%) | |
| Enamel hypoplasia | | | |
| Yes | 7 (16.3%) | 5 (3.9%) | **0.0063** |
| No | 36 (83.7%) | 122 (96.1%) | |
| Developmental defects of enamel | | | |
| Yes | 19 (45.2%) | 28 (23.7%) | **0.0086** |
| No | 23 (54.8%) | 90 (76.3%) | |
| Child's current health | | | |
| Good | 16 (34.8%) | 34 (26.4%) | 0.28 |
| Very good | 30 (65.2%) | 95 (73.6%) | |
| Child has health problems | | | |
| Yes | 13 (28.3%) | 24 (18.8%) | 0.18 |
| No | 33 (71.7%) | 104 (81.2%) | |
| Age first tooth erupted | 5.6 ± 2.5 | 6.4 ± 2.7 | 0.10 |
| Child has dental problems | | | |
| Yes | 22 (47.8%) | 15 (11.6%) | **0.0001** |
| No | 24 (52.2%) | 114 (88.4%) | |
| Started brushing/cleaning teeth | | | |
| Yes | 43 (93.5%) | 113 (87.6%) | 0.41* |
| No | 3 (6.5%) | 16 (12.4%) | |
| Breast fed | | | |
| Yes | 29 (63.0%) | 86 (66.7%) | 0.66 |
| No | 17 (37.0%) | 43 (33.3%) | |

| | | | |
|---|---|---|---|
| Breast fed duration (months) | 7.6 ± 6.9 | 7.2 ± 5.5 | 0.73 |
| Bottle-fed | | | |
| Yes | 39 (86.7%) | 120 (94.5%) | 0.088 |
| No | 6 (13.3%) | 7 (5.5%) | |
| Bottle-fed duration (months) | 18.4 ± 9.0 | 14.3 ± 4.9 | **0.0079** |
| Bottle at bedtime | | | |
| Yes | 31 (68.9%) | 70 (54.3%) | 0.087 |
| No | 14 (31.1%) | 59 (45.7%) | |
| Age solids introduced (months) | 6.8 ±2.5 | 6.2 ± 2.3 | 0.12 |
| Snack between meals frequency | | | |
| Often/sometimes | 45 (97.8%) | 122 (94.6%) | 0.33* |
| Rarely/never | 1 (2.2%) | 7 (5.4%) | |
| Milk drinker | | | |
| Regular | 44 (95.6%) | 116 (89.9%) | 0.36* |
| Other | 2 (4.4%) | 13 (10.1%) | |

*Fishers Exact Test