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Original Article

Combined deficiencies of 25-hydroxyvitamin D and anemia in preschool children with severe early childhood caries: A case–control study

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Abstract

Background: Severe early childhood caries (S-ECC) is common and has adverse affects on children's health. Children with S-ECC have been shown to have anemia or vitamin D deficiency. No studies have assessed the presence of combined deficiencies with S-ECC. The purpose of our study was to examine whether those with S-ECC had a higher prevalence of combined anemia and low 25-hydroxyvitamin D (25(OH)D) compared to controls. Covariates associated with elevated parathyroid hormone (PTH), previously noted in S-ECC, were examined.

Methods: This is a re-analyses of a previously described cross-sectional case–control study; data were collected between 2009 and 2011. Children with S-ECC were recruited on the day of dental surgery and controls from the community. Blood was drawn for complete blood count, ferritin, 25(OH)D and PTH. Families completed a questionnaire.

Results: A total of 266 children participated (S-ECC n=144); the mean age was 40.8 ± 14.1 months. Children with S-ECC were more likely to have low 25(OH)D, hemoglobin, elevated PTH or iron-deficiency anemia compared to controls. Significant differences between groups were seen for a combined deficiency of low hemoglobin (<110 g/L) *and* 25(OH)D < 50 nmol/L; controls 0/114 versus S-ECC 15/140 (P<0.001). In an adjusted regression model, PTH was negatively associated with 25(OH)D (P<0.001) and higher income (P<0.02); it was positively associated with less regular milk consumption (P=0.001).

Conclusions: Combined deficiencies of vitamin D and anemia are more prevalent in children with S-ECC; the etiology remains unclear. A detailed diet history is key in those with S-ECC to assess risks for deficiencies.

Keywords: *Anemia; Caries; Child; Hypovitaminosis D; Preschool; Vitamin D.*

Early childhood caries (ECC) is common and is defined as any decay involving the primary dentition in children under 6 years (1). The prevalence of ECC in Canadian children may be as high as 40 to 50%, depending on the population (2). Severe early childhood caries (S-ECC) is a more aggressive manifestation that frequently necessitates dental treatment under general anaesthesia (3). Those with S-ECC often suffer from pain, sleep disturbance, behaviour changes and altered eating habits (2).

Children with S-ECC have been found to have lower vitamin D status or iron status or anemia in recent cross-sectional studies (4–6). At this time, it is not clear if altered nutritional status is secondary to the caries limiting the

consumption of nutrient-rich foods or other factors. The predisposition to S-ECC may stem from dietary inadequacies especially because children of lower socioeconomic status (SES) are often at higher risk for S-ECC (5). Other etiologies for these nutritional disturbances include chronic inflammation or chronic infectious disease (2). Caries can be considered a chronic infectious disease, as tooth-adherent bacteria such as *Streptococci mutans* metabolize sugars, produce acids and demineralize tooth structure (3).

The World Health Organization defines anemia in children less than 60 months of age as a hemoglobin (Hgb) less than 110 g/L (7). Anemia attributable to iron deficiency is usually microcytic, with a mean corpuscular volume (MCV) less than 80 fL and a marker of low iron stores (8). Recently, Schroth et al. have shown that children with S-ECC have lower hemoglobin, lower ferritin and are more likely to have iron deficiency anemia (IDA) than controls (5). Schroth found that 75% of the children in the S-ECC group had isolated low hemoglobin, which has been confirmed by others (4,5).

Vitamin D deficiency, typically defined as 25-hydroxyvitamin D (25(OH)D) < 30 nmol/L, may be associated with poorer oral health (9). This deficiency has been shown to contribute to enamel hypoplasia, dental caries and periodontal disease (10,11). 25-hydroxyvitamin D or its metabolites may also play an immunological role with antimicrobial peptides such as cathelicidin and defensins, which act against oral pathogens (12). In the same cohort described above, children with S-ECC had significantly lower 25(OH)D than healthy age-matched controls (6). Additionally, elevated parathyroid hormone (PTH) concentrations were seen more frequently in those with S-ECC compared to controls. Elevated PTH concentrations may be seen with low 25(OH)D, insufficient dietary calcium intake or inflammation (13,14).

To our knowledge, no one has previously examined if children with S-ECC are more likely to have combined low concentrations of 25(OH)D and anemia. We hypothesize these combined deficiencies will be more likely in those with S-ECC compared to caries-free controls. Our primary objective was to examine whether preschoolers with S-ECC had higher prevalence of combined anemia (Hgb<110 g/L) and low serum 25(OH)D (<50 nmol/L) compared to controls. Our secondary objectives were to explore the potential mechanisms for the raised PTH in those with S-ECC compared to controls and to assess if there was a difference in the prevalence of combined low ferritin and 25(OH)D in those with and without S-ECC.

METHODS

This is a re-analyses of a previously described cross-sectional case–control study using the original data set (5,6). Children with dental caries were recruited from the Misericordia Hospital in Winnipeg, Manitoba at the time of dental surgery and age-matched controls were recruited from the community by advertisement. Data were collected between October 2009 and August 2011. A total of 266 children under 72 months of age were recruited, 144 with severe early childhood caries and 122 caries-free controls. Parental consent was obtained in the collection of the original data set.

Blood was collected at the time of the dental surgery or by a research nurse for cases and controls, respectively. Laboratory investigations included PTH, calcium, and albumin (Cobas, 8000, Laval, Canada) as well as ferritin and hemoglobin as part of a complete CBC (Sysmex XE5000, Japan); 25(OH)D levels were also measured (Roche Electro-chemiluminescent Immunoassay, Laval, Canada). A 25(OH)D < 50 nmol/L was considered inadequate and ≥ 75 nmol/L was considered optimal; both were used in these analyses. For PTH, the reference range is 1.1 to 5.5 pmol/L. Ferritin < 45 pmol/L was considered low (4) as was hemoglobin < 110 g/L (7,8). Iron deficiency (ID) was defined if both hemoglobin and ferritin concentrations were low; IDA was defined as having two out of three abnormal blood tests for hemoglobin, ferritin and/or MCV (4).

A questionnaire about pregnancy, birth history, child's oral and overall health, nutritional intake, supplements, employment status and family income was completed by caregivers as administered by staff. Regular milk intake was defined as five or more glasses (~250 mL) consumed per week (5,6).

In the previously reported control group, the prevalence of combined low hemoglobin and low 25(OH)D was 0/114 (Table 3). With n=130, power=80% and α=0.05, a two-sided binomial test of proportions indicate sufficient power to detect an increase of ≥ 6% in the affected cases.

Descriptive analyses were completed, including means, medians and correlations between variables. Paired t tests (continuous numeric variables) and chi-square or Fisher exact tests (categorical variables) were performed to assess combined deficiencies for cases and controls. Linear regression models were developed to assess PTH concentrations and control for potentially confounding variables (e.g., sex, season, household income, etc.). Routine regression diagnostics were performed. A P value of < 0.05 was considered significant. STATA (College Station, TX) and R were used for statistical analyses (Vienna, Austria) (15).

Ethics approval was received by the University of Manitoba Health Research Ethics Board for both the original and amended protocol.

RESULTS

A total of 266 children (48.9% female, 51.1% male) participated in the study. The mean age was 40.8 ± 14.1 months; there was no significant difference in age or sex between the two groups (Table 1).

Children with S-ECC were heavier and had higher BMI z-scores than the children in the control group (P<0.03, P=0.001, respectively) and came from families with lower household incomes (P<0.001). There were also differences in season when the blood was drawn (P=0.04), with more children in the control group assessed during the winter months (October to April).

As previously reported, those with S-ECC were more likely to have inadequate 25(OH)D levels, elevated PTH, low hemoglobin, low ferritin or iron deficiency anemia compared to controls (Table 2) (5,6). When combined deficiencies were analyzed, significant differences between groups were seen for low hemoglobin *and* low 25(OH)D level (< 50 or < 75 nmol/L) and iron deficiency or iron deficiency anemia only with a 25(OH)D < 75 nmol/L (OR=11.5, P=0.004) (Table 3). No children in the caries-free control group had a combined deficiency of low hemoglobin and low 25(OH)D level. There was no significant difference between groups for combined deficiencies of low 25(OH)D and low ferritin or low 25(OH)D and low MCV.

Table 4 illustrates the univariate regression model demonstrating an elevated PTH concentration in children with S-ECC. The adjusted model showed that PTH was negatively associated with 25(OH)D concentrations (P<0.001), serum calcium (P=0.051) or improved household income (P=0.017). It was positively associated with less regular milk consumption (P=0.001). Age, sex and season had no significant effect.

DISCUSSION

We are likely the first to note that children with S-ECC had combined low 25(OH)D *and* anemia, while the controls did not. One could speculate the anemia is possibly an anemia of chronic disease (ACD) because the MCVs were generally normal and not different than those in the control group. The ferritins were more likely to be low in the S-ECC group but still nearly 70% of those with S-ECC had normal values. Because ferritin is an acute phase reactant, mild IDA may be underestimated (this required two or three tests to be low—Hgb, ferritin and MCV). If underestimating IDA, we could speculate that combined deficiencies were secondary to nutrient poor diets. The lower SES of the S-ECC group could fit with this hypothesis. The clustering of ID and IDA with 25(OH)D <75 nmol/L is consistent with this speculation. Since the ID or IDA combination may be inflated with the generous 25(OH)D cut-off of 75 nmol/L, we prefer to only discuss the findings with the more conservative 50 nmol/L threshold.

In reality, the anemia may well be of mixed etiology (such as IDA, ACD or hemoglobinopathies including thalassemia trait). Part of the reason for trying to dissect this is the question of when or if to screen clinically or via laboratory testing children at risk and supplement iron or vitamin D, if needed. To distinguish between iron-deficiency anemia and anemia of chronic disease, more definitive testing with sedimentation rates, C-reactive protein (CRP), and serum levels of erythropoietin or soluble transferrin receptors, could be considered for future studies, although bone marrow iron stores are still regarded as the gold-standard (16).

Because we were limited in the number of children with combined deficiencies, we could not explore all possible confounders such as season of procurement of the sample or diet that might explain lower vitamin D status. We did see that 10 out of 15 children with S-ECC with combined deficiencies had their sample procured in Oct-April, which might partially explain our observation of combined deficiencies. Nonetheless, five children with caries still had low 25(OH)D tested in summer and anemia. Lower status could also be explained by poorer intake of vitamin D rich foods, such as fortified milk, margarine or fatty fishes or lower use of supplements.

Table 1. Characteristics of children

Variable		Mean	Study group				P value
			Caries-free controls		S-ECC		
			N=122		N=144		
			N (%)	95% CI	N (%)	95% CI	
Age		40.8 ± 14.1	39.3 ± 16.3	36.4, 42.3	42 ± 11.8	40.1, 43.9	0.1
Sex	Male	136	66 (54.1)	0.44, 0.63	70 (48.6)	0.40, 0.57	0.4
	Female	130	56 (45.9)	0.37, 0.55	74 (51.4)	0.43, 0.60	
Weight (z-score)		0.67 ± 1.14	0.51 ± 1.11	0.31, 0.71	0.82 ± 1.15	0.63, 1.01	0.03
Height (z-score)		0.16 ± 1.19	0.20 ± 1.18	–0.01, 0.42	0.11 ± 1.21	–0.01, 0.30	0.5
BMI (z-score)		0.84 ± 1.39	0.54 ± 1.32	0.30, 0.78	1.10 ± 1.40	0.87, 1.34	0.001
Season	Winter		77 (63.6)	0.54, 0.72	72 (50.7)	0.42, 0.59	0.04
	Summer		44 (36.4)	0.28, 0.46	70 (49.3)	0.41, 0.58	
Household income	≤$28,000/year		34 (28.1)	0.20, 0.37	85 (64.4)	0.56, 0.73	<0.001
	>$28,000/year		87 (71.9)	0.63, 0.80	47 (35.6)	0.27, 0.44	

BMI Body Mass Index; CI confidence interval; S-ECC Severe early childhood caries

Table 2. Laboratory values by group

Variable	Study group				P value
	Caries-free controls		S-ECC		
	N (%)	95% CI	N (%)	95% CI	
25(OH)D < 50 nmol/L	14/121 (11.6%)	0.06, 0.19	29/141 (20.6%)	0.14, 0.28	0.05
25(OH)D < 75 nmol/L	52/121 (43%)	0.34, 0.52	84/141 (59.6%)	0.51, 0.68	0.007
High PTH > 5.5 pmol/L	7/114 (6.1%)	0.03, 0.12	85/140 (60.7%)	0.52, 0.69	<0.001
Low Hemoglobin < 110 g/L	5/114 (4.4%)	0.01, 0.10	64/140 (45.7%)	0.37, 0.54	<0.001
Low Ferritin < 45 pmol/L	24/118 (20.3%)	0.13, 0.29	45/140 (32.1%)	0.25, 0.41	0.03
Low MCV < 75 fL	18/114 (15.8%)	0.10, 0.24	23/140 (16.4%)	0.11, 0.24	0.9
Iron deficiency	3/114 (2.6%)	0.01, 0.07	26/140 (18.6%)	0.13, 0.26	<0.001
Iron deficiency anemia	7/114 (6.1%)	0.03, 0.12	34/140 (24.3%)	0.17, 0.32	<0.001

CI confidence interval; MCV mean corpuscular volume; PTH parathyroid hormone; S-ECC Severe early childhood caries

Table 3. Combined deficiencies by group

Variable	Study group				P value
	Caries-free controls		S-ECC		
	N (%)	95% CI	N (%)	95% CI	
25(OH)D < 50 nmol/L + Hgb < 110 g/L	0/114 (0%)	0, 0.03	15/140 (10.7%)	0.06, 0.17	<0.001
25(OH)D < 75 nmol/L + Hgb < 110 g/L	0/114 (0%)	0, 0.03	38/140 (27.1%)	0.20, 0.35	<0.001
25(OH)D < 50 nmol/L + Fer < 45 pmol/L	4/118 (3.4%)	0, 0.08	6/140 (4.3%)	0.02, 0.09	0.8
25(OH)D < 75 nmol/L + Fer < 45 pmol/L	11/118 (9.3%)	0.05, 0.16	19/140 (13.6%)	0.08, 0.20	0.3
25(OH)D < 50 nmol/L + MCV < 75 fL	1/114 (0.9%)	0, 0.05	1/140 (0.7%)	0, 0.04	1.0
25(OH)D < 75 nmol/L + MCV < 75 fL	7/114 (6.1%)	0.03, 0.12	8/140 (5.7%)	0.02, 0.11	1.0
25(OH)D < 50 nmol/L + ID	0/114 (0%)	0, 0.03	3/140 (2.1%)	0, 0.06	0.3
25(OH)D < 75 nmol/L + ID	0/114 (0%)	0, 0.03	12/140 (8.6%)	0.05, 0.15	<0.001
25(OH)D < 50 nmol/L + IDA	0/114 (0%)	0, 0.03	3/140 (2.1%)	0, 0.06	0.3
25(OH)D < 75 nmol/L + IDA	1/114 (0.9%)	0, 0.05	13/140 (9.3%)	0.05, 0.15	0.004

CI confidence interval; Fer ferritin; Hgb hemoglobin; ID iron deficiency; IDA iron deficiency anemia; S-ECC Severe early childhood caries

Table 4. Univariate and multivariable regression for PTH concentration

Variable	Regression coefficient	95% confidence interval	P value
Intercept	32.90	/	/
S-ECC*	26.18	21.78, 30.59	<0.001
Multivariable regressions			
Intercept	94.48	/	/
S-ECC*	16.84	11.04, 22.65	<0.001
Age (months)	–0.002	–0.158, 0.154	1.0
Sex†	3.22	–0.89, 7.32	0.1
Season‡	3.57	–0.98, 8.11	0.1
Household income**	–5.48	–9.97, –0.99	0.02
Calcium (mmol/L)	–21.03	–42.19, 0.12	0.05
Regular milk drinker††	13.2	5.61, 20.79	0.001
25(OH) D level (nmol/L)	–0.12	–0.18, –0.06	<0.001

*Referent = caries free-controls. †Referent = male. ‡Referent = winter. **Referent = income <$28,000/year. ††Referent = 5 or more glasses/week

Vitamin D supplementation of children (in the form of vitamin D2, D3 and irradiation) has been shown to lower the risk for dental caries in a meta-analysis (17). Vitamin D metabolites play a role in tooth formation and levels in early childhood may ultimately impact secondary teeth as they form. It is possible that maternal vitamin D status plays a more important role in primary teeth than vitamin D status of children at the time of dental caries in early childhood (18,19). We do not have information on maternal vitamin D status during pregnancy for this cohort.

Others have shown that combined deficiencies of 25(OH)D and iron are also prevalent in populations of healthy children (20–23). In one study, Jin et al. demonstrated that 67% of children less than 24 months with iron deficiency anemia also had vitamin D deficiency (25(OH)D < 50 nmol/L) and 53% of those children with iron deficiency (defined as ferritin < 27 pmol/L) had vitamin D deficiency compared to 29% of normal controls (20). Yoon et al. also demonstrated increased iron deficiency anemia in children under 2 years of age with vitamin D deficiency (25.5% compared to 12% of controls) (21). Mechanistically, vitamin D metabolism may play a role in erythropoiesis while iron-dependent enzymes are required for activation of vitamin D metabolites (24,25).

Alternatively, the combination of low vitamin D status and anemia could be coincidental. For example, this could just be ACD and moderately low vitamin D status, particularly for those sampled in winter. Prospective cohort studies of children at risk might help to delineate the different mechanisms for the anemia. How both may play a role in the etiology of S-ECC is unclear. Poorer dietary vitamin D or calcium may impair enamel formation. However, these deficiencies may just be proxies for lower SES where having tools and knowledge to start early tooth cleaning, eliminating baby bottles and the use of fluoride containing toothpaste might be limited. The higher BMI and weight z-scores may reflect choices of food calorically dense but nutritionally poor often consumed by those of lower SES (26,27).

We had wondered whether the higher PTH in the S-ECC group might reflect poor calcium intake (poorer nutritional intake in general), especially given the increased numbers of families earning very low incomes and lower 25(OH)D concentrations in the S-ECC group. We were motivated to perform these analyses because of established associations between poor vitamin D or calcium intakes and developmental defects of enamel (18,28). Nevertheless, adding the variable 'regular' milk consumption into the regression model did not negate the group effect even after adjustment for 25(OH)D concentration and season. To date, others have noted that PTH concentrations may be high in adults with periodontal disease (29). Another possible mechanism is that inflammation has been associated with elevated PTH, although other studies have seen suppressed concentrations (13,14). Perhaps the elevated PTH concentration and anemia reflect inflammatory processes.

This study is one of the first to look at combined deficiencies of vitamin D and anemia in children with dental caries. It was well powered to analyze the primary outcome. There was a reasonable breadth of information available on study participants for analysis. Certain laboratory variables were not available that may have been useful for analysis including serum iron, iron saturation and CRP to better assess inflammation. Another limitation was the small number of children identified with a combined deficiency including none of the controls; this limited the intention to do more sophisticated statistical analyses.

CONCLUSION

Some children with S-ECC have combined deficiencies; given the relatively low frequency we do not encourage laboratory investigation. However, a good dietary history and discussion with the family about iron, vitamin D and possibly calcium rich diets may be warranted when seeing children with S-ECC, especially those of lower income. Future studies with more detailed assessment of nutritional status before and after dental surgery may be helpful to clarify some of these remaining questions.

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References

1. American Academy of Pediatric Dentistry. Policy on early childhood caries (ECC): Classifications, consequences and preventive strategies. Pediatr Dent 2016;38(6):52–54.
2. 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):1481–99.
3. American Academy of Pediatric Dentistry. Policy on early childhood caries (ECC): Classifications, consequences, and preventive strategies. Pediatr Dent 2015;37:50–2.
4. Clarke M, Locker D, Berall G, Pencharz P, Kenny DJ, Judd P. Malnourishment in a population of young children with severe early childhood caries. Pediatr Dent 2006;28(3):254–9.
5. Schroth RJ, Levi J, Kliewer E, Friel J, Moffatt ME. Association between iron status, iron deficiency anaemia, and severe early childhood caries: A case-control study. BMC Pediatr 2013;13:22.
6. 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.
7. World Health Organization. Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity. Geneva,

Switzerland: World Health Organization, 2011:6. Report No: WHO/NMH/NHD/MNM/11.1. Vitamin and Mineral Nutrition Information System.

8. Baker RD, Greer FR; Committee on Nutrition American Academy of Pediatrics. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). Pediatrics 2010;126(5):1040–50.
9. Berdal A, Bailleul-Forestier I, Davideau JL, Lezot F. Dento-alveolar bone complex and vitamin D. In: Feldman D, Pike J, Glorieux F, eds. Vitamin D. Burlington: Elsevier Academic Press, 2005:599–607.
10. Grant WB. A review of the role of solar ultraviolet-B irradiance and vitamin D in reducing risk of dental caries. Dermatoendocrinology 2008;3:193–8.
11. 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):1079–82.
12. Hewison M. Vitamin D and the immune system: New perspectives on an old theme. Rheum Dis Clin North Am 2012;38(1):125–39.
13. Cheng SP, Liu CL, Liu TP, Hsu YC, Lee JJ. Association between parathyroid hormone levels and inflammatory markers among US adults. Mediators Inflamm 2014;2014:709024.
14. Ogard CG, Engelmann MD, Kistorp C, Nielsen SL, Vestergaard H. Increased plasma N-terminal pro-B-type natriuretic peptide and markers of inflammation related to atherosclerosis in patients with primary hyperparathyroidism. Clin Endocrinol (Oxf) 2005;63(5):493–8.
15. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing. [Internet]. 2016 (cited November 9, 2016). https://www.R-project.org/.
16. World Health Organization, UNICEF, United Nations University. Iron Deficiency Anaemia: Assessment, Prevention, and Control. Geneva, Switzerland: World Health Organization, 2001:114. Report No: WHO/NHD/01.3.
17. Hujoel PP. Vitamin D and dental caries in controlled clinical trials: Systematic review and meta-analysis. Nutr Rev 2013;71(2):88–97.
18. Schroth RJ, Lavelle C, Tate R, Bruce S, Billings RJ, Moffatt ME. Prenatal vitamin D and dental caries in infants. Pediatrics 2014;133(5):e1277–84.
19. Tanaka K, Hitsumoto S, Miyake Y et al. Higher vitamin D intake during pregnancy is associated with reduced risk of dental caries in young japanese children. Ann Epidemiol 2015;25(8):620–5.
20. Jin HJ, Lee JH, Kim MK. The prevalence of vitamin D deficiency in iron-deficient and normal children under the age of 24 months. Blood Res 2013;48(1):40–5.
21. Yoon JH, Park CS, Seo JY, Choi YS, Ahn YM. Clinical characteristics and prevalence of vitamin D insufficiency in children less than two years of age. Korean J Pediatr 2011;54(7):298–303.
22. Yoon JW, Kim SW, Yoo EG, Kim MK. Prevalence and risk factors for vitamin D deficiency in children with iron deficiency anemia. Korean J Pediatr 2012;55(6):206–11.
23. Atkinson MA, Melamed ML, Kumar J et al. Vitamin D, race, and risk for anemia in children. J Pediatr 2014;164(1):153–158.e1.
24. Alon DB, Chaimovitz C, Dvilansky A et al. Novel role of 1,25(OH)(2)D(3) in induction of erythroid progenitor cell proliferation. Exp Hematol 2002;30(5):403–9.
25. Lac PT, Choi K, Liu IA, Meguerditchian S, Rasgon SA, Sim JJ. The effects of changing vitamin D levels on anemia in chronic kidney disease patients: A retrospective cohort review. Clin Nephrol 2010;74(1):25–32.
26. Davidson K, Schroth RJ, Levi JA, Yaffe AB, Mittermuller BA, Sellers EA. Higher body mass index associated with severe early childhood caries. BMC Pediatr 2016;16:137.
27. Pinket AS, De Craemer M, Huybrechts I et al. Diet quality in european pre-schoolers: Evaluation based on diet quality indices and association with gender, socio-economic status and overweight, the toybox-study. Public Health Nutr 2016;19(13):2441–50.
28. 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):11–4.
29. Schulze-Späte U, Turner R, Wang Y et al. Relationship of bone metabolism biomarkers and periodontal disease: The osteoporotic fractures in men (mros) study. J Clin Endocrinol Metab 2015;100(6):2425–33.