PEDIATRIC DENTISTRY

STOMATOLOGIA DZIECIĘCA

ORIGINAL PAPERS

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New Med 2019; 23(4): 135-144

DOI: https://doi.org/10.25121/NewMed.2019.23.4.135

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The relationship between maternal nutrition in pregnancy and early childhood caries – a systematic literature review

Związek między odżywianiem w ciąży a próchnicą wczesnego okresu dzieciństwa – systematyczny przegląd literatury

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KEYWORDS

nutrition in pregnancy, early childhood caries, sugar consumption, vitamin D, calcium

SUMMARY

Introduction. Odontogenesis of deciduous teeth is dependent on the intrauterine environment and shaped, among other things, by prenatal maternal nutrition. Proper development of deciduous dentition, formation and mineralisation of the enamel and dentin determines the susceptibility to cariogenic factors. The current knowledge of the effects of prenatal nutrition and supplementation on the risk of early childhood caries (ECC) is unclear.

Aim. An evaluation of the relationship between maternal nutrition in pregnancy and the risk of early childhood caries (ECC).

Material and methods. A systematic review of literature on the association between prenatal maternal nutrition and early childhood caries was performed based on both electronic and manual search through medical databases, i.e. PubMed, EMBASE and MEDLINE, which allowed to identify 6 studies meeting the inclusion criteria. The risk of bias was evaluated using the ROBINS-I questionnaire and a quality assessment of original papers was performed using the Newcastle-Ottawa Scale (NOS).

Results. All analysed works were at a risk of bias associated with confounders affecting the intervention and interpretation of results. Four works were considered to be of good quality (NOS > 6) and two other of medium quality.

Conclusions. An increased maternal intake of vitamin D, calcium, dairy products, yoghurts and cheeses in pregnancy is an important factor reducing the risk of dental caries in their children. The risk of ECC is increased in the case of vitamin D deficiency, low intake of calcium and a diet high in fatty acids and carbohydrates.

SŁOWA KLUCZOWE

odżywianie w ciąży, próchnica wczesnego okresu dzieciństwa, spożycie cukru, witamina D, wapń

STRESZCZENIE

Wstęp. Proces rozwoju zębów mlecznych podlega wpływom środowiska wewnątrzmacicznego i jest kształtowany przez czynniki, takie jak odżywianie matki w okresie prenatalnym. Z kolei od prawidłowego rozwoju uzębienia mlecznego, tworzenia i mineralizacji

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szkliwa i zębiny zależy podatność na czynniki próchnicotwórcze. Obecny stan wiedzy dotyczącej wpływu odżywiania i suplementacji w ciąży na ryzyko wystąpienia próchnicy wczesnego okresu dzieciństwa (ang. *early childhood caries* – ECC) pozostaje niejasny.

Cel pracy. Ocena związku między odżywianiem w ciąży a ryzykiem wystąpienia próchnicy wczesnego okresu dzieciństwa.

Materiał i metody. Przeprowadzono systematyczny przegląd literatury dotyczącej związku między odżywianiem w czasie ciąży a próchnicą wczesnego okresu dzieciństwa w oparciu zarówno o elektroniczne, jak i manualne przeszukiwanie medycznych baz danych, takich jak: PubMed, EMBASE i MEDLINE, co pozwoliło zidentyfikować 6 badań spełniających kryteria włączenia. Do oceny ryzyka wystąpienia błędów systematycznych wykorzystano kwestionariusz ROBINS-I, natomiast do oceny jakości prac oryginalnych wykorzystano skalę Newcastle-Ottawa (Newcastle-Ottawa Scale – NOS).

Wyniki. Wszystkie analizowane prace były obarczone ryzykiem błędu wynikającym z obecności czynników zakłócających, wpływających na interwencję i interpretację wyników. Jakość czterech badań oceniono jako dobrą (NOS > 6), natomiast dwóch pozostałych jako średnią.

Wnioski. Zwiększone spożycie witaminy D, wapnia, produktów mlecznych, jogurtów i serów przez kobietę w trakcie ciąży stanowi istotny czynnik obniżający ryzyko wystąpienia próchnicy u dziecka. Niedobór witaminy D, niskie spożycie wapnia oraz dieta bogata w kwasy tłuszczowe i węglowodany zwiększają ryzyko wystąpienia próchnicy wczesnego okresu dzieciństwa.

Introduction

Deciduous odontogenesis begins already during foetal life. Once the deciduous crowns are fully developed in the first year of life and the mineralisation process is completed at the time of tooth eruption, the enamel shows structural stability and is not subject to metabolic processes. Therefore, the intrauterine environment, which is shaped, among other things, by prenatal maternal nutrition, is a key factor determining proper development of deciduous dentition, formation and mineralisation of the enamel and dentin, and thus susceptibility to cariogenic factors (1). The current knowledge of the effects of prenatal nutrition and supplementation on the risk of early childhood caries (ECC) is unknown. Low vitamin D levels in pregnancy were considered to be associated with reduced foetal weight (< 10 percentile), preterm birth, adverse effects on the development of the child's skeletal system and dental tissues as well as an increased risk of infectious diseases (2). Maternal hypovitaminosis (25(OH)D < 20 ng/mL or < 50 nmol/L) is an important risk factor for abnormalities in the newborn. The levels of 1,25-dihydroxyvitamin D (1,25[OH]₂D) increase in early pregnancy and are doubled in the third trimester to cover the calcium needs of the foetus during skeletal development. Karras et al. suggest that this is also associated with the physiological adaptation of the immune system to maintain the pregnancy (3). Vitamin D supplementation in pregnancy increases both umbilical cord and neonatal blood levels of this vitamin (4, 5). However, Galthen-Sørensen et al. found no evidence to support the relationship between maternal 25(OH)D levels and

skeletal development in the child based on a systematic literature review (5 observational studies) (6).

The literature describes a relationship between A- and D-hypovitaminosis and an increased risk of mineralisation disorders and enamel hypoplasia in a child, which are the risk factors for ECC (7-9). Low maternal dietary intake of calcium is considered to be associated with the so-called foetal programming in terms of, among other things, hypertension, altered lipid profile, obesity and insulin resistance (10-14). High maternal levels of carbohydrates, free fatty acids and amino acids may lead to a permanent change in appetite control, neuroendocrine function and impaired energy metabolism (developmental overnutrition hypothesis) in the foetus, leading to obesity in later life (15). The lack of appetite control in a child may promote the development of improper eating habits, such as increased frequency of meals. Furthermore, mothers who consume large amounts of carbohydrates are more likely to offer diet high in sugars to their children (16). The PICO (Patients Intervention Comparison Outcome) question was as follows: does high dietary intake of protein and calcium and low dietary intake of sugars or prenatal vitamin supplementation affect the risk of dental caries in children aged up to 71 months compared to low protein/calcium intake and high sugar intake or the lack of supplementation?

AIM

The aim of the study was to evaluate the relationship between nutrition and vitamin supplementation in pregnancy and early childhood caries basing on a systematic review of literature.

MATERIAL AND METHODS

Search strategy

Medical databases, i.e. PubMed, MEDLINE and EMBASE, were searched through for prenatal nutrition and supplementation as an exposure (I), using the following key terms: "prenatal vitamin" OR "dairy products" OR "protein deficiency" OR "calcium" OR "nutrition status" OR "intake of sugar" OR "sugar consumption" OR "vitamin" combined with: "prenatal*" OR "pregnancy" OR

"pregnant women" OR "pregnant", and the development of ECC as an effect (O) (searched terms: "early childhood caries" OR "dental caries"), in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol (17), which allowed to identify 5 studies meeting the inclusion criteria. A total of 6 studies were included in the review following an additional, manual search through the cited literature. The search strategy and the inclusion/exclusion criteria are presented in table 1 and figure 1.

Tab. 1. Search strategy

Search strategy for PICO:						
Question: Is there a relationship between prenatal nutrition and caries in the child (PICO)						
	Literature search strategy					
Population	Pregnant women and their children < 6 years old					
Intervention/exposure	Vitamin supplementation; diet high in protein, calcium and low sugar intake during pregnancy					
Comparison	No vitamin supplementation, diet low in protein and calcium, high sugar intake					
Result	ECC in the child					
Searched key terms	"Prenatal vitamin" OR "dairy products" OR "protein deficiency" OR "calcium" OR "nutrition status" OR "intake of sugar" OR "sugar consumption" OR "vitamin" combined with: "prenatal" OR "pregnancy" OR "pregnant women" OR "pregnant" AND "early childhood caries" OR "dental caries"					
	Search through medical databases					
Electronic	PubMed, MEDLINE, EMBASE					
Manual	Cited literature					
Selection criteria						
Inclusion criteria	Publications after 2000, original papers, meta-analyses, systematic reviews; language: Polish, English					
Exclusion criteria	In vitro studies, case reports, animal studies					

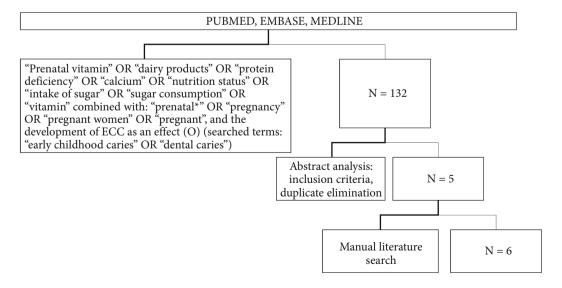


Fig. 1. Search strategy according to PRISMA (17)

The quality and risk of bias assessment

The qualified studies were assessed independently by two investigators using the The Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) assessment tool ver. 1.08.2016 (18). Also, the quality was evaluated based on the Newcastle Ottawa Scale (19). Contentious issues were discussed. Final assessment was performed jointly by all investigators involved. Key factors potentially disturbing study results, i.e. the socioeconomic status, age, maternal education, the course of pregnancy (maternal comorbidities, preterm birth, low birth weight), the number of teeth in a child, dietary exposure to sugars, the lack of calibration of the investigators, dental assessment in daylight with no previous dental surface cleaning, the lack of radiological assessment, were identified based on the literature. Each study was briefly characterised (country, type of study, age and number of participants, definition of intervention/exposure and final result, findings, conclusions and confounders).

RESULTS

Database search findings

The electronic search through databases and the manual search through literature allowed to identify 6 studies meeting the inclusion criteria.

Characteristics of the works

Four prospective cohort studies, a longitudinal observational study and a retrospective cohort study were included in the analysis. The discussed works are summarised in table 2.

The included studies evaluated the relationship between ECC and vitamin D levels/diary intake (n = 3) (20-22), calcium supplementation/dairy intake (n = 2) (23, 24) and high sugar intake (n = 1) (25).

Three studies evaluated prenatal vitamin D levels and the risk of ECC. Schroth et al. demonstrated a statistically significant negative correlation between serum maternal

Tab. 2. Characteristics of the analysed studies

Study/authors, year, country	Type of study, participants	Results	Conclusions	Factors affecting quality
Schroth et al. 2014 (20) Canada	A prospective cohort study; determination of 25(OH)D, total calcium, phosphorus and alkaline phosphatase serum levels in the second/early third trimester (n = 200); dental evaluation in 135 children aged up to 1 year (64%); dmft assessment, d = non-cavity and cavity decay; ECC confounders controlled in multiple logistic regression analysis: socioeconomic factors, infant feeding practices, season and enamel hypoplasia	32.5% of women with 25(OH)D deficiency, 36% of children with ECC; higher d component in children whose mothers had lower 25(OH)D levels; ECC more common in children whose mothers had lower 25(OH)D levels	Prenatal vitamin D deficiency increases the risk of ECC	 No randomisation Confounders Unrepresentative study group, large proportion of lost patients No justification for the sample size No calibration of investigators or the assessment of Kappa compatibility index
Tanaka et al. 2015 (21) Japan	A prospective cohort study; dmft assessment at 36-46 months of age in 1210 children of mothers participating in a questionnaire assessing dietary vitamin D intake based on a 1-month dietary diary; dental status copied from child's dental health records by parents	A 6% reduction in the risk of ECC with increased in- take of vitamin D per each microgram per day	Increased maternal prenatal vitamin D intake reduced the risk of ECC in children	 No randomisation Confounders Study group unrepresentative for the Japanese population Large proportion of lost patients No calibration of investigators or the assessment of Kappa compatibility index for dentists Data from the study were copied by mothers – possible mistakes/distorted data

Tab. 2. c.d.

Study/authors, year, country	Type of study, participants	Results	Conclusions	Factors affecting quality
Singleton et al. 2019 (22) USA, Alaska	A retrospective cohort study; 76 prenatal mother/infant pairs with prenatal blood ≥ 16 week of gestation and 57 infants with cord blood assessed for vitamin D level; dmft scores of children aged 12-35 months and 36-59 months calculated using electronic dental records. Controlled confounders: breastfeeding, gestational age and birth weight, maternal age, smoking	Children 12 to 35 months of age with deficient cord blood (25(OH)D < 30 nmol/L) had a mean dmft score twice as high as children who were nondeficient at birth (9.3 vs. 4.7; P = 0.002). No significant difference in mean dmft scores for children aged 36 to 59 months with deficient versus nondeficient cord blood 25(OH)D (10.9 vs. 8.7; P = 0.14). No significant difference in mean dmft scores for children aged 12 to 35 months whose mothers had sufficient (≥ 50 nmol/L) v. insufficient (< 50 to ≥ 30 nmol/L) 25(OH)D during prenatal visits (9.0 vs. 7.4; P = 0.48). Children with deficient vitamin D levels in cord blood had a dmft score at 12 to 35 months 2-fold higher than children with nondeficient cord blood	Prenatal vitamin D levels may influence the primary dentition and the development of ECC. Improving vitamin D status in pregnant women might affect ECC rates in their infants	 Low sample size No adjustment for confounding factors: dental hygiene, sugar-sweetened beverage use, access to running water
Thitasomakul et al. 2009 (23) Thailand	495 children aged 9, 12 and 18 months were examined; data regarding mothers and hygiene/dietary behaviours were acquired during qualification in the 2 nd trimester of pregnancy and during follow-up visits of children	Increase in caries between 9 and 12 months of age = 1.1 (± 2.6), higher in children whose mothers did not supplement Ca and did not consume milk on a daily basis during pregnancy; breastfed. Increased caries between 12 and 18 months of age = 4.2 (± 5.1), higher in breastfed children and children consuming sugar-containing snacks	A relationship was demonstrated between the lack of prenatal calcium supplementation and breastfeeding and increased caries in children up to 18 months old	 No randomisation Confounders present No justification for the sample size
Tanaka et al. 2012 (24) Japan	315 mother-child pairs; a retrospective dietary diary kept by a pregnant woman and regarding the preceding month (dairy products: milk, yoghurt, cheeses) and data on maternal age, course of pregnancy, education, socio-economic status, habits, breastfeeding, hygiene, fluoride prophylaxis and child's nutrition; dental evaluation – df (41-50 months of age) performed by a hygienist	23.5% of children with ECC; mean df = 0.87; tooth brushing 2 x in 46% of children, fluoride prophylaxis in 83%; a negative correlation between the amount of consumed cheese and the risk of ECC	The more cheese consumed during pregnancy, the lower the risk of ECC. A tendency for reduced risk of ECC with increased intake of dairy products, yoghurts; insignificant milk consumption	 No randomisation No evaluation of nutrition assessment questionnaire Confounders Unrepresentative study group – a large proportion of group lost for the final examination No justification for the sample size No calibration of investigators or the assessment of Kappa compatibility index

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Tab. 2. c.d.

Study/authors, year, country	Type of study, participants	Results	Conclusions	Factors affecting quality
Wigen et al. 2011 (25) Norway	A prospective cohort study; 1348 mother-child pairs; dmft assessed by hygienists without calibration in a dental office setting; X-ray if indicated; d = cavitated carious lesions; a questionnaire in pregnancy and at 18 months of age as well as dental visit at the age of 5 years (maternal health, lifestyle and habits). Prenatal nutrition – a questionnaire of daily nutrient intake: sugars, fats and total energy	11% of 5-year-olds had d > 0; the risk of ECC was higher in non-Western children (OR 5.0), children of mothers with overweight (OR 2.4), obesity (OR 1.5), low level of education (OR 2.0), smoking habits (OR 1.9), higher sugar (OR 1.6) and fat intake (OR 1.6) as well as asthma and allergy (OR 1.4)	Multivariate regression analysis: maternal obesity and high dietary sugar and fat intake increase the risk of caries in 5-year-olds	 No calibration of hygienists Assessment of investigator compliance only for X-ray Confounders Preterm children and children with low births weight were not excluded Possible underestimation of dietary questionnaire data

25(OH)D – 25-hydroxycholecalciferol; df – the number of decayed or filled deciduous teeth; dmft – the number of decayed, missing or filled deciduous teeth; d – the number of decayed deciduous teeth; OR – odds ratio

vitamin D (25(OH)D) precursor levels and the rates of ECC among children from an Aboriginal community in Canada (20). Among 200 pregnant women, 25(OH)D deficiency (< 35 nmol/L) was found in 32.5%; caries was detected in their children more frequently compared to those whose mothers had 25(OH)D levels > 75 nmol/L. Tanaka et al. conducted a prospective cohort study in 1,210 children (36-46 months old) of Japanese mothers participating in a questionnaire, which assessed their dietary intake of vitamin D based on a 1-month food frequency questionnaire (FFQ) (21). The authors observed a 6% reduction in the risk of ECC with increased maternal vitamin D intake per every microgram per day. Singleton et al. used prenatal blood samples drawn at 16 week of gestation or later and cord blood drawn at birth for the analysis of vitamin D levels and electronic dental records to calculate dmft scores in children aged 12-35 months and 36-59 months in Alaska (22). They observed a 2-fold higher dmft scores at 12 to 35 months in children with deficient vitamin D levels in cord blood (22).

Two studies evaluated calcium supplementation and dietary intake and ECC (23, 24). Thitasomakul et al. examined 495 children aged 9, 12 and 18 months and observed increased caries between 9 and 12 months of age in children whose mothers reported lack of calcium supplementation and non-daily milk consumption during pregnancy (23). Tanaka et al. assessed prenatal dietary intake of dairy and calcium products in 315 Japanese mother-child pairs based on a dietary questionnaire including the total intake of dairy products (milk, yoghurts and cheese) (24). A statistically significant negative correlation with the risk of ECC at an average age of 41-50 months was reported in children of

mothers with high prenatal consumption of cheese. It was observed that the risk of ECC in children decreased with higher consumption of cheese, whereas the negative correlation between consumption of dairy products, calcium and yoghurts was at the limit of statistical significance. No correlation was found between maternal intake of milk and ECC in the child.

One study determined the relationship between ECC and maternal obesity, combined with high dietary intake of sugar and fat. Wigen et al. demonstrated a higher risk of ECC in children from families of non-Western origin (OR 5.0), children of mothers with overweight (OR 2.4) or obesity (OR 1.5), low education (OR 2.0), smoking habits (OR 1.9), higher sugar (OR 1.6) and fat (OR 1.6) intake, as well as asthma or allergy (OR 1.4), based on a prospective cohort study in 1348 mother-child pairs in Norway, which involved a questionnaire (eating habits, lifestyle, habits) for pregnancy and 18-month-year-old child and dental evaluation in 5-year-old children (25).

Bias and quality assessment

Bias evaluation is presented in table 3. Four works were considered to be of good quality (NOS > 6) and two other of medium quality (tab. 4). The analysed studies had a risk of data distortion due to methodological limitations and confounders.

Discussion

D-hypovitaminosis is associated with an increased risk of mineralisation disorders and enamel hypoplasia, which are well documented risk factors for ECC (26-28).

Tab. 3. Assessment of the risk of bias according to The Risk Of Bias In Non-randomised Studies – of Interventions (ROBINS-I) assessment tool (18)

Study	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Risk of bias judgement
Schroth et al. 2014 (20)	Y	Y	N	N	N	N	Y
Tanaka et al. 2015 (21)	Y	Y	Y	Y	Y	Y	Y
Singleton et al. 2019 (22)	Y	Y	Y	N	N	N	Y
Thitasomakul et al. 2009 (23)	Y	Y	Y	Y	Y	Y	Y
Tanaka et al. 2012 (24)	Y	Y	Y	N	Y	Y	Y
Wigen et al. 2011 (25)	Y	N	Y	N	Y	Y	Y

Y (yes) / N (no)

Tab. 4. Quality assessment according to Newcastle-Ottawa Scale (19)

Study	Selection	Comparability	Outcome	Score
Schroth et al. 2014 (20)	***	*	**	6
Tanaka et al. 2015 (21)	***	**	***	8
Singleton et al. 2019 (22)	***	**	***	8
Thitasomakul et al. 2009 (23)	***	*	**	6
Tanaka et al. 2012 (24)	***	*	**	6
Wigen et al. 2011 (25)	***	*	***	8

Studies exploring the correlation between maternal vitamin D level and ECC demonstrated that ECC incidence is greater in children of mothers with low level of vitamin D and low dairy intake, but due to methodological aspects (evaluation of serum maternal vitamin D level or vitamin D level in cord blood v. dietary questionnaire), they cannot be compared (20-22). Moreover, Schroth et al. (20) conducted their among Aboriginal women with low socioeconomic status, therefore the results cannot be extrapolated to the entire population. The questionnaire did not include all risk factors for ECC, thus an assessment of confounders was not possible. Singleton et al. we were

not able to adjust for key confounding factors such as dental hygiene, sugar-sweetened beverage use, or access to running water, which affect dental caries (22).

The mechanism of action of low vitamin D precursor level in the period of deciduous mineralisation has not been explained. The authors suggest that enamel developing in such an environment is less resistant to acids. In analysed studies the influence of vitamin D was considered only in relation to mineralised tooth tissue (prenatal mineralisation). However, low level of (25(OH)D) is associated with immunodeficiency (29, 30), which may affect the environment of maternal oral cavity in favour of cariogenic micro-

flora. High maternal levels of oral bacteria is a risk factor of early transmission of cariopathogens to oral cavity of a child and ECC (31, 32). The impact of vitamin D level and oral bacterial load of pregnant women and ECC has not yet been investigated.

The normal level of calcium in blood plasma and Ca/P ratio is particularly important during odontogenesis and skeletal development. Calcium deficiency impedes mineralisation of forming hard tissues of the teeth. Mineralisation of primary dentition begins ca. 13 weeks of gestation, permanent teeth - perinatally. The mature enamel in erupted teeth is not remodelled during an individual's life. Hypocalcaemia during pregnancy and in the first years of a child's life may be the cause of developmental defect hypomineralisation of enamel and dentin (27, 30, 33-38). Studies of enamel of hypomineralised teeth showed a higher content of carbon and a lower content of calcium and phosphorus in comparison with normal enamel (38). Calcium deficiency is also conducive to reducing the size of the teeth, shortening their roots as well as delaying tooth eruption and premature exfoliation of milk teeth (33-36). In addition, hypocalcaemia at the time of odontogenesis promotes the accumulation of lead in the tissues of the teeth, which is the cause of their greater susceptibility to decay (39). The degree of mineralisation of dental tissues determines their sensitivity to bacterial and non-bacterial acids as well as mechanical factors. Teeth containing insufficient amount of minerals are more susceptible to decay, erosion and mechanical wear (27, 30).

The studies assessing calcium supplementation and dairy intake in pregnancy and ECC demonstrated a decreased risk of ECC with higher dairy consumption (23, 24). The mechanism underlying the effects of dairy intake on child's dentition remains unexplained; it has been suggested that an increased intake of dairy products increases total level of body calcium. However, the lack of calcium supplementation during pregnancy does not necessarily mean that serum calcium levels are low. The presented studies are also affected by multiple confounders and thus should be interpreted with caution. In the study of Thitasomakul et al. a high proportion of mothers (35%) admitted that they did not brush their children's teeth until participation in the

study at the age of 9 months; no information was provided on the use of toothpaste or other fluorine-containing products (23). Tanaka et al. collected questionnaires via e-mail and the results might prove to be false due to the tendency to respond in line with the expectations of researchers as they determined the frequency of consumption of dairy products only in the preceding month, which does not reflect the nutritional pattern throughout pregnancy (24). Dental evaluation was performed by hygienists trained in the detection of caries, however, with no calibration or an assessment of the Kappa (compatibility) factor or an X-ray evaluation of caries on interproximal surfaces – therefore the rates of caries could be underestimated. The study group was characterised by a higher education level compared to the general Japanese population, which could have influenced the level of health awareness and may account for the 50% lower percentage of children with ECC compared to population data.

Apart from changes in appetite control, neuroendocrine function and metabolism, consuming a large amount of sugars during pregnancy promotes the child's preference for sweet taste by stimulating taste buds in the developing fetus (40, 41). Frequent and high carbohydrate intake may increase cariogenic bacteria counts in maternal oral cavity and increase the risk of early transmission of *Streptococcus mutans*. Wigen et al. demonstrated a higher risk of ECC in children of obese mothers, and those who reported higher sugar and fat intake (25). Limitations of the study are as follows: dental status assessment by hygienists with no calibration. Tooth decay was diagnosed when a cavity was identified, therefore the percentage (11%) of children with caries (d > 0) may be underestimated. The dietary questionnaire data may also be underestimated.

Conclusions

It was found, based on the review, that increased maternal intake of vitamin D, dairy products, yoghurts and cheese during pregnancy as well as calcium supplementation are important factors reducing the risk of caries in children. The risk of ECC is increased in the case of maternal vitamin D deficiency and the lack of calcium supplementation as well as diet rich in fatty acids and carbohydrates.

CONFLICT OF INTEREST KONFLIKT INTERESÓW

None Brak konfliktu interesów

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submitted/nadesłano: 10.10.2019 accepted/zaakceptowano do druku: 31.10.2019