Validation Of Cariogram In Caries Prediction At Woman And Their Children 4 Years After Pregnancy – Longitudinal Study

Olivera Dolic (✉ olivera.dolic@med.unibl.org)

Univerzitet u Banjoj Luci Medicinski Fakultet <https://orcid.org/0000-0002-1651-6701>

Marija Obradovic

Univerzitet u Banjoj Luci Medicinski Fakultet

Zeljka Kojic

Univerzitet u Banjoj Luci Medicinski Fakultet

Natasa Trtic

Univerzitet u Banjoj Luci Medicinski Fakultet

Slava Sukara

Univerzitet u Banjoj Luci Medicinski Fakultet

Natasa Knezevic

Univerzitet u Banjoj Luci Medicinski Fakultet

Valentina Veselinovic

Univerzitet u Banjoj Luci Medicinski Fakultet

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Abstract

Background: The Cariogram®, an algorithm based software model, for predicting caries risk has been used to assess the caries risk profile of many different groups. Early childhood caries (ECC) is the most common chronic disease in children below 71 months of age. Identifying children at greatest risk of caries to design appropriate preventive activity has been a goal of the dental profession for many years. The aim of the study was to evaluate Cariogram caries risk assessment during pregnancy with DMFT/dmft incidence at mother and their children 4-years later. Methods: The study population consisted of 96 pregnant women (average age 27.4 years at baseline) that completed clinical baseline examination and salivary tests. A caries risk assessment was made using Cariogram model and according to it, participants were divided into five risk groups. The follow-up study was initiated 4 years later and the 80 pairs of mother and children (from that pregnancy) were re-examined using the same procedure as did at baseline. An individual caries risk profile and DMFT/dmft incidence were made for each woman and child. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for two cut-offs were calculated to express the outcome. Results: There was a strong association between the risk categories of pregnant women and their offspring as well as between caries development in children and the Cariogram risk categories of their mother in pregnancy. Sensitivity and PPV for new DMFT ($\Delta\text{DMFT} > 0$) over 4 years for women was high (>80%) for those participants assessed with 0-60% “chance to avoid caries”, as well as diagnostic accuracy (74.00%). High specificity (91.00%), very high PPV (95.00%) and clinically useful values according to Youden’s index (0.53) were obtained for moderate and two lowest risk groups for dmft in children. Conclusions: With the limits of this study, Cariogram model can be useful tool for caries prediction in both groups of woman and their children based on caries risk assessment during pregnancy. The Cariogram was valid and highly predictive in caries risk assessment in children based on caries risk assessment of their mother in pregnancy.

Background

Caries is multifactorial disease and it is determined by the interaction of different microbial, genetic, immunological, behavioral, as well as environmental factors [1]. The most common chronic disease in childhood is early childhood caries (ECC) that occur in children below 71 months of age. Still remains huge problem both in developed and developing countries [2, 3]. Many studies have demonstrated the association of MS (*mutans streptococci*) with ECC [4-7]. The systematic reviews confirmed that maternal factors influence the bacterial acquisition, whereas colonization was mostly mediated by oral health and feeding habits [8, 9] during the first year of life. Cross-sectional [10] and longitudinal [11] studies have corroborated the association between parental dental status and offspring caries.

Identifying children at greatest risk of caries to design appropriate preventive activity has been a goal of the dental profession for many years. It is expected that multiple factors, combined on an appropriate scale and accounted for possible interactions may improve the prediction of caries risk. The challenge is to develop a really effective model for predicting caries risk. The Cariogram®, an algorithm based

software, assesses an individual's caries risk profile and contains many „if “conditions – it can operate with 5 million combinations of caries related factors [12]. The program offers recommendations for targeted preventive measures that should be implemented to avoid the formation of new caries lesions [13,14].

Cariogram has been used to assess the caries risk profile of schoolchildren [15,16], teenagers, young adults [17-21], orthodontic [22] and elderly patients [23]. Some studies used Cariogram to assess caries risk profile of preschool children [24-29]. In a previous study, we presented that Cariogram can be useful tool in caries risk assessment and identification of significant caries risk factors in a group of pregnant women [30], but to our knowledge, there are no studies that used Cariogram of pregnant women in offspring risk profile prediction.

Therefore, the aim of this study was to evaluate baseline caries risk assessment according to Cariogram during pregnancy with the DMFT/dmft development at mother and their children after 4-years.

The null hypothesis was that there is no association between children's caries risk profiles by Cariogram and caries risk profiles (by Cariogram) of their mothers during pregnancy.

Methods

Study group

This longitudinal study was performed as a follow up of the study previously presented by Dolic et al [30]. The baseline survey was carried out in 2007 (January to April) and follow-up in 2011 (January to April). The study population consisted of 96 pregnant women who were between 20 and 42 years old (average age 27, 4 years) at the start of the study. They lived in different socio-economic areas of the city of Banja Luka, Bosnia and Herzegovina. Banja Luka is the second-largest city in Bosnia and Herzegovina. In 2006, Banja

Luka had a total population of 170,000. There is no official data about pregnant women as well as the prevalence of caries in pregnant women in this area. Pregnant women were recruited at the Pregnancy counseling center at Public Hospital Banja Luka, the only counseling center in this city. The sample size was calculated by simple random sample selection, with confidence level 95% and confidence interval 10. There is no official data about pregnant women, but 1452 children were born in 2006 in Banja Luka. Among the 213 pregnant women who were initially eligible, 96 fulfilled the inclusion criteria and were included in the study. The study included only pregnant women a) who were in last trimester of a normal, single fetus pregnancy, b) who didn't have high-risk pregnancies, C) who didn't have previous medical conditions, pregnancy complications, or pregnancy-related issues that required hospitalization, d) who did not have any chronic disease, e) who had not taken antibiotics or other drugs during pregnancy, f) who gave their written consent to participate in research.

The follow-up study was initiated 4 years later and the mother and their children (from that pregnancy) were re-examined by the same examiner, using the same procedure as that followed at baseline. The examiner was previously trained in using the dmft/DMFT on a group of ten 4-year-old and ten adult subjects with a wide range of levels of caries not included in the final sample. The examiner then examined a group of twenty-five 4-year-old and twenty-five adult subjects not included in the final sample twice, on successive days. Duplicate examinations performed on twenty-five 4-year-old and twenty-five adult subjects at the start of the study, about half-way through and at the end of the study. Kappa statistics were used to test the intra-investigator reliability. The kappa values estimated from repeat examination for the intra-consistency of the fieldwork investigator was kappa >0.87. The follow-up sample included 80 pairs of mother-child (83, 33 % recall rate), with 16 participants dropout- 10 did not want to participate in the follow-up study and 6 had moved from the area.

In Banja Luka, pregnant women and children up to the age of 15 have access to free dental care at public dental clinics. At baseline and follow-up the women were given detailed written and verbal information about the outline of the study, and they signed informed consent for themselves and their children. During the study period, the participants were not informed about any result and they received regular dental care. Pregnant women were referred to their dentists to obtain necessary dental care concerning individual needs. All the participants were residents in areas with low natural fluoride content in the drinking water supply (<0.30 mg/l).

The research has been conducted in full accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards and ethical approval for the study was obtained from the Research Committee of Faculty of Medicine, University of Banja Luka.

Clinical examination

The study consisted of five steps: a questionnaire, interview, clinical examination, saliva sampling, and assess caries risk using the Cariogram. Interview/questionnaire was taken only to assess the personal data needed for calculating one's caries risk by Cariogram [30]. The questionnaire contained questions about: general health and medication, diet and oral hygiene habits including tooth brushing frequency and the use of fluoride. The guardians were responsible for completing the child's questionnaire.

All examinations were performed by one trained and calibrated examiner in the morning, between the meals and at least one hour after a meal and after teeth brushing to avoid possible contaminations during saliva sampling especially for microbial tests. A plane mirror, World Health Organization Community Periodontal Index (WHO-CPI) probe, and air syringe were used in the clinical visual-tactile examination following WHO criteria [26]. Clearly visible lesions with cavities on tooth surfaces were classified as dental caries (i.e.d3-level cavities), whereas changes in transparency, initial enamel demineralization with intact surfaces and no cavitation were noted as intact teeth. The teeth were not professionally cleaned and no radiographs were taken. Caries prevalence was registered at the Decayed-Missed-Filled-Teeth (DMFT) level. The oral hygiene and oral biofilm amount were estimated using a mirror and periodontal probe following the Sillness and Löe plaque index [31].

Saliva sampling consisted of: measurement of the saliva secretion rate, measurements of saliva buffer capacity using a Dentobuff® Strip test, measurements of *mutans streptococci* in the saliva using a Dentocult® SM Strip mutans test and measurements of lactobacilli in the saliva using a Dentocult® LB test according to the manual of the manufacturer. Paraffin-stimulated whole saliva was collected for 5 minutes and the secretion rate was expressed as ml/min. Buffer capacity was categorized as high, medium or low. The density of colonies (*Streptococcus mutans* and *Lactobacillus*) was compared with a chart provided by the manufacturer (Orion Diagnostica, Finland).

Data for the computerized caries risk assessment were entered into the Cariogram to obtain an individual caries risk profile. The following five Cariogram categories were used: “very high risk” = 0-20% chance to avoid caries; “high risk” = 21-40% chance to avoid caries; “moderate risk” = 41-60% chance to avoid caries; “low risk” = 61-80% chance to avoid caries; and “very low risk” = 81-100% chance to avoid caries.

The patient and the patient’s ordinary dental team were not informed about the calculated Cariogram risk category. The patient's regular dental team was responsible for restorative dental care during the entire study period.

Statistical methods

All data were processed with the SPSS software (version 16.0, Chicago Ill., USA). χ^2 test of contingency was used to compare the difference between groups. Differences between baseline and follow up DMFT/dmft between different cariogram groups were assessed using Kruskal Wallis ANOVA. Student's test for independent samples (if the difference variance observed characteristics were not statistically significant) and nonparametric Mann-Whitney test (if the difference in the variance of the observed characteristics statistically significant) were used to compare the mean values of the characteristics. Likelihood ratio and Youden's index were used for the measure of diagnostic accuracy. Youden's index was used for the evaluation of the overall discriminative power of a diagnostic procedure.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated from two-by-two tables. P values less than 0.05 were considered statistically significant.

Results

Risk categories for children in regard to risk categories of their mother during pregnancy are shown in Figure 1. The results displayed that 85.00% (n = 68) of the children were in the same risk category as their mother during pregnancy (at baseline). A higher-risk category than their mother during pregnancy had 10% (n=8) of children. Decreased risk than their mother during pregnancy had only 5% (n=4) of children (P < 0.001).

The distribution of women with new DMFT in relation to the baseline Cariogram risk category, mean DMFT at baseline and 4 years follow up, as well as mean DMFT increment is shown in Table 1. The positive relationship was statistically significant and the women in very high and high risk categories had

more DMFT than those in very low risk group ($p < 0.05$). The difference in mean DMFT at the baseline and follow up for a very low group was not statistically significant.

Sensitivity, specificity and predictive values for Cariogram over 4 years for women are displayed in Table 2. Sensitivity (Se) and specificity (Sp) of the Cariogram were compared at two cut-off points. The moderate risk group was combined with the low risk and very low group and it was taken as cut off 1. As cut off 2, it was combined the moderate, the high and very high risk groups. Sensitivity and PPV was high ($> 80\%$) for cut-off 2, for those assessed with 0-60% "chance to avoid caries", as well as diagnostic accuracy (74.00%). When the moderate risk combined with the two lowest risk groups sensitivity, diagnostic accuracy and NPV were lower than 60%.

The distribution of children with dmft in relation to the Cariogram risk category of their mother in pregnancy and mean dmft of children are shown in Table 3. The percentage of " $\Delta \text{dmft} = 0$ and $\Delta \text{dmft} > 0$ " was calculated from the total No. of pregnant women in each risk category. The children of high and very high risk mothers in pregnancy had more dmft than those in very low risk group ($p < 0.05$).

Sensitivity, specificity and predictive values for dmft ($\Delta \text{DMFT} > 0$) in children are displayed in Table 4. Sensitivity (Se) and specificity (Sp) of the baseline Cariogram (pregnant women) were compared at two cut-off points on the same way as for women. The moderate risk group was combined with the low risk and very low group and it was taken as cut off 1. As cut off 2, it was combined the moderate, the high and very high risk groups. High specificity (91.00%), very high PPV (95.00%) and clinically useful values according to Youden's index (0.53) were obtained for cut-off 1 (moderate and two lowest risk groups). When the moderate risk combined with the two lowest risk groups sensitivity and PPV were higher than 82%.

Discussion

Oral health has been an important aspect of an adult, as well as, children well-being and quality of life. Untreated dental caries associated with discomfort/pain can affect weight gain, normal growth and child's development, therefore preventive and therapeutic measures must be based on the most current scientific and clinical knowledge available [3]. Although the Health Insurance Fund of Bosnia and Herzegovina covers full costs of dental care for children younger than 15-years, the ECC prevalence is extremely high and most of the lesions are untreated [3]. In countries like Bosnia and Herzegovina, with high caries prevalence, caries risk assessment is very important, but there is only data about caries risk assessment in the 12-years-old children [19] and pregnant women [30].

In the present study, the majority of participants (women and children) were at high risk of caries according to Cariogram. It was found that 22.50% of 4-years-old children are in a very high and 26.25% of 4-years-old children are in high risk group. Garg et al. also showed the highest percentage of 5-years-old children (66.2 %) developed new caries lesions in the category of high risk group by Cariogram [29]. Steckslen-Blickset al. investigated the existing caries risk factors in 2- years- old children and displayed that 51% of the sample had a low chance (or very high risk) of avoiding caries in the future [24]. Study

concerning Greek (2-6 years old) preschool children reported the highest number of patients in a moderate caries risk group (65%) and only 29% in a high risk group by Cariogram [26]. The study conducted in Macedonia among 4-5-years-old children showed that 55.10% children had a moderate dental caries risk and 40.82% children had a high dental caries risk according to Cariogram [28].

It is very difficult to compare the results of Cariogram for pregnant women in the present study, as no studies were conducted on pregnant women and their offspring for caries risk assessment by Cariogram. Study performed in children and adult populations in Turkey showed that the majority of their participants had a high risk for caries, while Celik et al. reported the majority Turkish adults (20–21 years old) with medium and low caries risk by Cariogram (33% and 24%, respectively) [32,33]. In the study of Sonbul et al. the prevalence rates of caries risk in adults by Cariogram with several dental restorations in Saudi Arabia were high [34]. On the other hand, there are many studies with different models for caries risk assessment focusing mother's caries risk at pregnancy and subsequent risk of their children in the future. The studies suggest that infants acquire mutans streptococci from their mothers and only after the eruption of primary teeth [35, 36]. There have been numerous studies that have linked the presence of caries in mothers with the incidence of caries in children. The influence of maternal caries status on the same in preschool children was also confirmed in studies in Turkey [37], Thailand [38] and New York [39], while it was not significant in the Japanese study [40].

In a cross-sectional study conducted on the eight-year-old child- mother couples in Mendota, California, in a low-income rural community of Hispanics, it was found that the presence of untreated caries in mothers almost doubled untreated caries in children [41]. A study by Roberts et al in Iowa, states that tooth loss due to caries in caregivers was significantly associated with the prevalence of caries in their children [42]. A study in the African-American population in Detroit found that the incidence of caries in parents or caregivers increased the likelihood of caries lesions in children [43]. Studies in Finland from 2000 and 2005 also confirm the importance of family-related factors [44,45].

Factors such as low socioeconomic status, low maternal education, and unemployed mother are significant in many studies [46-51].

In the review of Kirthiga M. et al. from 2019 the important risk factors (OR greater than one) amid high-income countries were: low maternal education; smoking during pregnancy; maternal age younger than 25 years and negative parental attitudes [52].

In the early caries risk assessment by Cariogram studies, researchers identified and measured various caries related factors and correlated them to the current caries status of the individual, i.e. after 1-3 years, in longitudinal studies. Data obtained from these studies often used a simple correlation for analyses. Stamm et al. state that useful risk assessment program should be one with high simplicity, sensitivity, and specificity [53]. Often, it may be very impractical to be achieved simultaneously simplicity and accuracy. But in more recent years, sensitivity/specificity, predictive powers, and Youden's index have been applied for validation in Cariogram studies [54-56].

The principle of sensitivity/specificity is to use a specific cut-off value for the factor under investigation and to define a specific outcome of the test. In present study, the relatively high negative predictive values are found for both cut-off and both aims: (1) to validate baseline caries risk classifications according to Cariogram with the actual caries development over a 4-year period in a group of women; (2) validate (baseline?) caries risk classification of pregnant women according to Cariogram with the offspring actual caries development after 4 years. The similar results are found in Holgerson longitudinal study in Sweden, which showed that validation of a modified Cariogram in 2-years-old preschool children resulted in high sensitivity for future caries 5 years later, but the method lacked precision and accuracy [25].

The predictive ability of Cariogram for pregnant women at both cut-off points had specificity lower than 70%, which may be categorized in high-risk group some individuals with actual low caries risk and unnecessary preventive measures may be taken. But, on the other hand, according to PPV (>78%) in both cut-offs, it can be seen that a higher percentage of patients will develop caries. PPV is even higher (95%-cut off 1, 85%-cut off 2) for a possibility of caries developing in offspring if pregnant women are in a higher risk of caries according to Cariogram.

In recent studies from Hong Kong, the results showed that the Cariogram for preschool children generally exhibited a higher accuracy [27,57]. In the present study, for validation of caries experience in children using Cariogram model of their mothers during pregnancy, accuracy was higher than 70% for both cut-offs. Also, validation used in this study obtained clinically useful values according to Youden's index, when moderate and two lowest risk groups have combined.

The limitations of the study are the relatively small sample size, which is a consequence of the factors for inclusion in the study and the small number of pregnant women in the region of Banja Luka. Early childhood caries is associated with many other factors not included in the Cariogram program, so this would also be the limitation of the current study. Although Cariogram requires laboratory tests it is easily applicable and according to research, it was valid for certain population groups [15, 23, 25, 27, 29, 54, 55, 56]. Guided by this, the main reason for use of Cariogram in this study and the strength of the study was that an important aspect is a benefit to the children, i.e. early preventive measures which would be taken for children based on high risk of caries of their mothers in pregnancy.

Conclusions

With the limits of this study, Cariogram model can be a useful tool for caries prediction in both groups of woman and their children based on caries risk assessment during pregnancy. The Cariogram was valid and highly predictive in caries risk assessment in children based on caries risk assessment of their mother in pregnancy.

Abbreviations

Early childhood caries (EEC); World Health Organization Community Periodontal Index (WHO-CPI) probe; Decayed-Missed-Filled-Teeth (DMFT); Sensitivity (Se); specificity (Sp); positive predictive value (PPV); negative predictive value (NPV).

Declarations

Availability of data and materials

This study is a part of the Ph.D. thesis and all data and materials (ethical approval, consent to participate and publish) can be found in official documents at the University of Banja Luka archive on the native language.

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Competing interests

The authors declare that they have no competing interests. The authors alone are responsible for the content and writing of the paper. The authors do not hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript. The authors as well do not hold or currently applying for any patents relating to the content of the manuscript, and never had received fundings from an organization that holds or has applied for patents relating to the content of the manuscript. There are no nonfinancial competing interests (political, personal, religious, academic, ideological, intellectual, commercial or any other).

Authors' contributions

OD: conceptualized and designed study, supervised and evaluated the data collection, critically reviewed the manuscript. OD and MO have made substantial contributions to statistical analyses and interpretation of the results. MO, ZK, NT, SS, NK, VV critically reviewed the manuscript. All authors have contributed to and read the final draft. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The research has been conducted in full accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards and ethical approval for the study was obtained from the Research Committee of Faculty of Medicine, University of Banja Luka. All participants gave their written consent to participate in research. The guardians were responsible for the child's written consent to participate in research.

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Table 1. Crosstabulation of DMFT incidence at 4-year-follow up with overall caries risk level predicted by Cariogram at baseline

Baseline risk category by Cariogram of pregnant women	No of pregnant women		No of pregnant women with Δ DMFT > 0		Baseline DMFT (Mean, SD)	Follow-up DMFT (Mean, SD)	Mean DMFT increment	95% CI *for mean DMFT increment	p value*
	n	%	n	%					
Very high	13	16.25	9	69.23	20.15 $\pm$ 3.67	22.17 $\pm$ 4.00	2.92 $\pm$ 2.02	1.70-4.14	0.000
High	24	30.00	20	83.33	16.83 $\pm$ 2.63	18.67 $\pm$ 2.59	1.83 $\pm$ 1.24	1.31-2.36	0.000
Moderate	18	22.50	15	83.33	15.28 $\pm$ 3.91	16.11 $\pm$ 3.53	1.44 $\pm$ 1.34	0.78-2.11	0.000
Low	13	16.25	5	38.46	13.77 $\pm$ 2.78	14.67 $\pm$ 3.68	1.08 $\pm$ 1.71	0.05-2.11	0.042
Very low	12	15.00	5	41.67	11.92 $\pm$ 3.50	12.10 $\pm$ 4.09	0.75 $\pm$ 1.22	0.02-1.52	0.056
Total	80	100.00	54	68.00	15.79 $\pm$ 4.16	17.43 $\pm$ 4.74	1.64 $\pm$ 1.60	1.28-1.99	0.000

p < 0.05 statistically significant; p < 0.001 extremely statistically significant

Table 2. Sensitivity, specificity and predictive values for Cariogram over 4-years for women

Cariogram (for women) cut-off	Se ^a	Sp ^b	PPV ^c	NPV ^c	Youden index ^d	Diagnostic accuracy	LR +	LR -
Cut-off 1	54.0	69.0	78.0	42.0	0.23	59.0	1.7453	0.6687
Cut-off 2	81.0	58.0	80.0	60.0	0.39	74.0	1.9259	0.3209

aSensitivity

bSpecificity

cPPV = positive predictive value; NPV = negative predictive value.

dJ = sensitivity + specificity -1.

LR-Likelihood ratio

Table 3. Distribution of children with dmft in relation to the Cariogram risk category of their mother in pregnancy

Baseline risk category of pregnant women	No of pregnant women		No of children with Δ dmft = 0		No of children with Δ dmft> 0		dmft of children (Mean, SD)	Chi-square
	n	%	n	%	n	%		p value
Very high	13	16.25	0	0.00	13	100.00	10.94±3.96	0.000
High	24	30.00	2	8.33	22	91.67	5.90±2.84	
Moderate	18	22.50	6	33.33	12	66.67	3.73±2.71	
Low	13	16.25	3	23.08	10	76.92	1.00±0.91	
Very low	12	15.00	12	100.00	0	0.00	0.08±0.28	
Total	80	100.00	23	28.75	57	71.25	4.89±4.70	

p< 0.05 statistically significant; p< 0.001 extremely statistically significant

Table 4. Sensitivity, specificity and predictive values for Cariogram in children compared to baseline mothers risk level

Cariogram (for women) cut-off	Se ^a	Sp ^b	PPV ^c	NPV ^c	Youden-index ^d	Diagnostic accuracy	LR +	LR -
Cut-off 1	61.0	91.0	95.0	49.0	0.53	70.0	7.0614	0.4227
Cut-off 2	82.0	65.0	85.0	60.0	0.48	78.0	2.3706	0.239

aSensitivity

bSpecificity

cPPV = positive predictive value; NPV = negative predictive value.

dJ = sensitivity + specificity -1.

LR-Likelihood ratio

Figures

Figure 1

Risk categories for children in regard to risk categories of their mother during pregnancy