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Are intrauterine growth restriction and preterm birth associated with dental caries?

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Abstract – *Objectives:* To assess the association between two intrauterine growth restriction (IUGR) surrogates – IUGR [small for gestational age birth (SGA) and fetal growth restriction (FGR)] and preterm birth with dental caries. *Methods:* Data from the Third National Health and Nutritional Examination Survey (1988–1994) were used, including 2- to 5.9-year-old singletons ($n = 3189$). Dental caries was defined as presence of any teeth with dental caries (treated or untreated) and also as presence of at least two teeth with dental caries. Exposure variables were preterm birth (<37 gestational weeks), FGR, and SGA. Covariates included were poverty, race/ethnicity, age, sex, sucrose intake, environmental tobacco smoking, dental visits, education of head of household, breastfeeding, and use of baby bottle. Separate statistical analyses were conducted for IUGR and for preterm birth through the estimation of prevalence ratio (PR), taking complex sampling design into consideration and adjusting for confounders. Sensitivity analysis was conducted including and excluding 2-year-old children and also with the two definitions of dental caries. *Results:* In general, the inclusion of 2-year-old children and the case definition of presence of any teeth with dental caries biased the results toward the null, but with no major changes in the results. In bivariate analysis, SGA and FGR birth were both negatively but not significantly associated with dental caries while a significant positive association was found for preterm birth. Sensitivity analysis showed that the PR for preterm in bivariate analysis varied from 1.65 (95% CI 1.14–2.40) to 1.84 (95% CI 1.19–2.83). After adjusting for confounders, the PR for preterm birth varied from 1.38 (95% CI 1.00–1.89) to 1.64 (95% CI 1.22–2.20). After adjustment, the PR for SGA varied from 0.79 (95% CI 0.56–101) to 0.66 (95% CI 0.33–0.96). For children from 3 to 5.9 years old, the adjusted PR for FGR using the category 'none' as reference were mild (PR 1.10; 95% CI 0.76–1.58), moderate (PR 0.66; 95% CI 0.26–167), and severe (PR 0.59; 95% CI 0.36–0.99). These values for FGR were very similar for the other models using other classifications of case definition or inclusion of 2-year-old children. *Conclusions:* Preterm birth was found to be positively associated with dental caries while there is an indication that SGA and FGR are negatively associated with dental caries. Although the negative association is counterintuitive, it is possible that increased antibiotic use and delayed tooth eruption may explain the negative association between IUGR and dental caries.

Key words: dental caries; intrauterine growth restriction; low birth weight; preterm

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Intrauterine growth restriction (IUGR) is one of the major perinatal health problems in developing as well as in developed countries (1). The presence of IUGR has been assessed through surrogates such as low birthweight (LBW), small for gestational age (SGA) birth, fetal growth restriction (FGR), and low

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ponderal index (2, 3). In the USA, the rates of preterm birth and LBW have increased in the past decades (1).

In addition to perinatal mortality, SGA birth and LBW have been associated with chronic disorders such as respiratory diseases (4, 5), cognitive impairments (6), and risk factors for cardiovascular disease (7). However, the oral health of preterm and intrauterine growth-restricted children has received little attention, and the risk of dental caries among such children is still a matter of debate (8).

Dental caries is a disease with chronic characteristics modulated by behavior and involving colonization by *Streptococcus mutans* (9). Although its prevalence has decreased, dental caries is still the most prevalent disease among American children (10). The biological explanation for the association of IUGR and dental caries is based on the increased incidence of enamel defects (hypoplasia and/or hypomineralization) (11–14). These enamel defects have been attributed to hypocalcemia and to the physiological stress associated with perinatal outcomes, which would interfere with the secretion and maturation of enamel tissue (11, 15, 16). Enamel defects would hypothetically predispose to early colonization by *S. mutans* and to increased formation of dental biofilm (9, 17).

Despite the biological plausibility, there is a lack of empirical evidence that IUGR or preterm birth are associated with dental caries (8). This lack of evidence has primarily been attributed to the fact that most studies have been poorly designed and did not adjust for confounders (8). In fact, two recent studies involved adequate adjustment for confounders, but neither demonstrated a correlation between LBW and dental caries in primary dentition (18, 19). A significant issue that has not been addressed is the imprecision of using LBW as a surrogate for IUGR. Using LBW is imprecise because it can represent both preterm birth and rate of fetal growth (3). Although these two outcomes may occur concomitantly, they are known to have different risk factors (2, 20, 21) as well as different effects on the health of the child (4, 22). In addition, the hypothesis that enamel defects are increased is based on studies of preterm LBW and very LBW infants rather than on those involving LBW infants exclusively (12, 13, 23). Therefore, these studies did not differentiate between IUGR and preterm birth. A recent study, conducted as part of the Third National Health and Nutritional Examination Survey (NHANES III, 1988–1994), addressed the relationship between LBW and dental caries among 2- to 6-year-old children (19). The authors evaluated data on gestational age and concluded that neither LBW nor preterm birth was associated with dental caries.

Although gestational ages and birth weights are available from NHANES III data, no evaluation of the relationship between IUGR and dental caries has been performed to date. Therefore, given the significant impact of IUGR and dental caries on public health, together with the lack of information regarding such a relationship in the American population, the objective of this study was to assess the association between IUGR surrogates (birthweight adjusted for preterm birth, SGA birth, and FGR) and preterm birth with dental caries in primary teeth, limiting its scope to the population of the USA.

Materials and methods

This study used as a data source the NHANES III (1988–1994) – a cross-sectional survey of a complex, multistage, stratified, clustered sample intended to be representative of the civilian non-institutionalized American population more than 6 months of age (24). This analysis included singleton White, African–American, and Mexican–American children 2–5.9 years of age having undergone complete examinations for dental caries and for whom birth certificates were available. Information on gestational age and birthweight was taken from birth certificates available in the 'Natality Data' section of the NHANES III database (25), which contains information from the birth certificates of 94% of all children under the age of 6 years.

For the study population defined, birth certificates were available for 92.7% (n = 3888). Only singletons were included in our study (n = 3788), and information on both gestational age and birthweight was available for 97.8% of those (n = 3621). To avoid misclassification of IUGR, we excluded children presenting implausible values for gestational age (>44 weeks; n = 84) (26) and birth weights that were improbable for the gestational ages (n = 61) (26, 27). We also excluded children whose gestational age and birthweight were recorded as 26 weeks (n = 17) and 1200 g (n = 17), respectively. These exclusions were performed because these values grouped children with less than 26 weeks and less than 1200 g which would result in misclassification of

IUGR. Complete dental examination was available for 3189 children.

Dental examinations were performed by six trained and calibrated examiners at the Medical Examination Center of NHANES III. Dental caries was defined according to decayed and filled (primary) teeth (dft) index. Detailed information on the examination procedures used in the NHANES III can be found elsewhere (28). We classified children with dental caries using two case definitions: (i) children with more than one tooth with dental caries and (ii) children with any teeth with dental caries. The reasons for using two case definitions are the following. The first case definition was used because having a single tooth with dental caries does not necessarily indicate that a child is at increased risk of dental caries. A single tooth with dental caries may represent an incorrect placement of a restoration or a unique lesion caused by a specific enamel defect or dental fissure. Therefore, using a case definition of at least two teeth with dental caries will avoid misclassification. The second definition was used for comparison with other studies.

We identified IUGR by assessing LBW adjusted for preterm birth, SGA birth, and FGR. We defined LBW as <2500 g, and preterm birth was defined as being born at <37 weeks of gestational age. SGA birth was calculated by using the reference values for the 10th percentile of birthweight reference data described by Alexander et al. (29). As those authors did not provide information on the 50th percentile of growth distribution, the FGR – measured through the fetal growth ratio, which describes the relationship between birthweight and the 50th percentile of birthweight for each gestational age from reference data (32) – was calculated using the reference data presented by Zhang and Bowes (27). Based on the calculation of the fetal growth ratio, FGR is classified as none (0.85+), mild (0.85–0.80), moderate (0.79–0.75), or severe (<0.75) (30).

Covariates

Covariate information was taken from questionnaires completed during interviews of parents or guardians and from dental examination records. Covariates included known determinants of dental caries and possible confounders, as well as possible effect modifiers. Known determinants of dental caries were race/ethnicity and age, as well as socioeconomic variables such as poverty level and education of head of household. Possible confounders included sucrose intake, carbohydrate intake, and environmental exposure to tobacco smoke, as well as breastfeeding. The possible effect modifiers evaluated were fluoride supplement intake, frequency of dental visits, and urbanization classification (rural or urban residence). Residing in an urban area can be considered a weak but acceptable surrogate for water fluoridation.

Race/ethnicity was categorized as Whites, African–Americans, and Mexican–Americans. Head of household education level at the time of interview was categorized as <12, 12 or >12 years of schooling. Poverty level was defined as the ratio of observed annual family income by the poverty threshold (>3.5, 1.301–3.5 or <1.301) (31).

Daily intakes of sucrose and carbohydrates were obtained from a 24-h food-frequency questionnaire. Carbohydrate intake (g/day) and sucrose intake (g/day) were categorized by their median values. Categorization into quartiles did not change our results. Environmental exposure to tobacco smoke, which has been associated with dental caries (32), was measured by means of a proxy by determining the number of smokers who smoke inside the home where the child lives (0, 1–2 or >2). A proxy was used because data on serum cotinine levels, a more objective measure of environmental tobacco smoke exposure (32), were not available for the age range we evaluated in this study. Breastfeeding was also considered as a possible confounder because it has been associated with dental caries (19) and because preterm infants are less likely to be breastfed because of difficulty in suction (35). The breastfeeding variable was categorized according to Schulman (19) as bottle-feeding until 19 months and bottle-feeding after 19 months. Fluoride supplementation was defined as the intake of any vitamin supplement containing fluoride or prescription fluoride within the preceding month, either or both having been ingested regularly for more than 3 months. The frequency of dental visits was categorized as never having been to a dentist, going to a dentist only when necessary, or visiting a dentist on a regular basis (every year or every 2 years). We also included in the analysis the census region of the country (northeast, central-west, south or west) and urbanization classification (urban or rural).

Statistical analysis

One of our concerns about Schulman's study (19) was that inclusion of 2-year-old children would have biased his results toward the null. The bias would happen because recently erupted teeth and teeth still erupting would have a very short period of time at risk to develop the disease. Therefore, we performed a sensitivity analysis including and excluding 2-year-old children, and with the two dental caries definitions.

All analysis was performed for each IUGR surrogate separately. Bivariate and stratified analyses were followed by Poisson regression modeling of PRs in order to assess the association between each IUGR surrogate and dental caries. The PR is the correct measurement of association for a cross-sectional survey. In particular, for common events, such as the prevalence of dental caries in this study (from 15.4% to 21.17%, depending on the case definition and the study population included), logistic regression leads to an overestimation of the measure of association provided (odds ratio) compared with the desired PR. Such overestimation can also interfere with the correct modeling process because the selection of confounders is based on the effect size (34). We also conducted an analysis of the dft index as a continuous variable using negative binomial regression. However, as the findings were very similar, we decided to present only the estimation of PR, which is more easily understood. Poisson regression models were built using a stepwise procedure with backward elimination of variables. All analyses were performed using the 'survey procedure' command in the STATA 8.0 program (35), thereby taking the sampling design into account.

All covariates associated with dental caries at values of $P \leq 0.2$ were included in the models. We also included known confounders and possible effect modifiers, even those not reaching the 0.2 cut-off point. Known risk factors for dental caries and confounders for IUGR surrogates or preterm that changed coefficients more than 10% were kept in the models. Plausible interactions were also tested: race/ethnicity, education of head of household, dental visits, use of bottle-feeding after 19 months, poverty, and fluoride supplement intake. Additional models including FGR as a continuous explanatory variable were also carried out in order to test for linear trend.

Results

The final analytical sample consisted of 3189 children 2–5.9 years old (which we will refer to 5 years old), 21.2% (SE 1.5) of them with dental caries. For this age group, children had on average 1.0 (SE 0.1) tooth and 1.7 surfaces (SE 0.2) with dental caries. There were 2341 3- to 6-year-old children with a prevalence of dental caries of 25.9% (SE 1.9). The average number of teeth affected by dental caries was 1.5 with surface average of 2.2 (SE 0.3).

Background characteristics of the study population are described in Table 1. Bivariate analysis for dental caries, including both classifications of dental caries, is shown in Tables 2 and 3 for 2–5- and 3–5-year-old children, respectively. Independent of the age group or dental caries definition, these tables show that preterm birth was positively and statistically associated with dental caries. Moreover, low birthweight (LBW) although positively associated with dental caries did not reach statistical significance. SGA and FGR, although not statistically significant, tended to be negatively associated with dental caries. Moreover, including 2-year-old children and use of a more loose definition of dental caries can lead the point estimators toward the null.

Table 4 shows the final model for the analysis of preterm birth and LBW. After adjusting for major confounders, independent of inclusion of 2-year-old children, and independent of the dental caries definition, preterm birth was statistically significantly associated with dental caries. An important observation is that LBW reversed its association when adjusted by preterm, becoming negatively associated with dental caries. However, this association was not statistically significant.

To ensure that multicollinearity between preterm birth and IUGR surrogates did not interfere with our results, we conducted several analyses. Adding preterm birth to the models did not lead to inflation of P-values or to a considerable change in the confidence intervals, which would provide evidence of multicollinearity.

Table 5 shows the models for SGA. In these models preterm birth was only significant when excluding 2-year-old children. However, we can observe that the point estimators for preterm birth increase as the case definition gets more stringent and with the exclusion of 2-year-old children. SGA maintains its trend of negative association with dental caries. A similar analysis for FGR is shown in Table 6 with similar pattern of results. There is a tendency that moderate and severe FGR are negatively associated with dental caries compared with no and mild FGR. As mild FGR is considered a borderline category near normality, and because

Table 1. Background characteristics of children aged 3–5 years ($n = 3189$), NHANES III (1988–1994)

Characteristics	2- to 5-year olds ($n = 3189$)			3- to 5-year olds ($n = 2341$)		
	n[a]	%[b]	SE[c]	n[a]	%[b]	SE[c]
Race/ethnicity						
White	1031	72.6	1.4	720	73.1	1.5
African–American	1083	17.7	1.3	815	17.6	1.4
Mexican–American	1075	9.6	0.9	806	9.3	0.9
Poverty ratio						
>3.500	326	19.3	1.6	224	18.3	1.7
1.301–3.500	764	34.6	1.6	896	36.1	1.8
<1.301	1867	46.2	1.6	1058	45.6	1.8
Head of household education (years)						
>12	945	43.4	1.8	670	42.0	2.0
= 12	1053	35.0	1.3	783	36.0	1.4
<12	1086	21.7	1.1	812	22.0	1.3
Number of smokers in the home						
None	1976	61.2	2.1	1438	61.8	2.1
1–2	790	22.2	1.6	600	22.8	1.6
>2	421	16.6	1.5	305	15.4	1.5
Dental visits						
Never	1867	52.0	1.5	1142	41.4	1.9
As needed	349	8.4	0.8	309	9.7	0.9
Regularly	953	39.6	1.5	881	48.9	1.9
Fluoride supplementation						
No	3123	96.4	1.3	2289	96.9	1.5
Yes	66	3.6	1.3	52	3.9	1.5
Sucrose intake (g/day)						
<35.0	1451	47.7	1.6	963	44.4	1.8
≥35.0	1416	52.3	1.6	1119	55.6	1.8
Breast-feeding						
No	1777	46.1	1.7	1325	46.0	2.0
Yes	1411	53.9	1.7	1018	54.0	2.0
Bottle-feeding after 19 months						
No	2157	72.2	1.5	1614	73.3	1.5
Yes	1032	27.8	1.5	727	26.7	1.5
Carbohydrate intake (g/day)						
<161.0	838	25.1	1.6	535	22.5	1.8
161.0–202.2	672	25.1	1.2	458	22.9	1.4
202.3–249.1	640	24.7	1.2	493	26.6	1.4
≥249.2	717	25.1	1.4	596	27.9	1.5
Dental caries (dft > 0)						
No	2284	78.8	1.5	1529	74.1	1.9
Yes	907	21.2	1.5	815	25.9	1.9
Dental caries (dft > 1)						
No	2502	84.5	1.4	1725	81.2	1.8
Yes	689	15.5	1.4	619	18.9	1.8
Preterm birth (weeks)						
≥37	2914	93.4	0.7	2137	93.5	0.8
<37	275	6.6	0.7	204	6.5	0.8
Low birthweight (g)						
≥2500	2997	94.8	0.6	2198	94.5	0.7
<2500	192	5.3	0.6	143	5.5	0.7
Small for gestational age birth						
No	2747	88.2	1.0	2010	87.7	1.2
Yes	442	11.8	1.0	331	12.3	1.2
Fetal growth restriction						
None	2751	87.7	0.9	2003	86.7	1.1
Mild	179	5.0	0.6	136	5.3	0.7
Moderate	122	3.6	0.5	97	4.1	0.7
Severe	137	3.7	0.5	105	3.9	0.6

[a]Total number might vary due to missing values for independent variables.
[b]Weighted percentage.
[c]SE, standard error.

Table 2. Bivariate analysis of background variables, oral health-related characteristics, IUGR surrogates and preterm birth in relation to dental caries among children aged 2–5 years NHANES III (1988–1994)

	dft > 0[a]					dft > 1				
	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value
Age (years)										
2	7.2	0.8	1.00		<0.01	4.8	0.7	1.00		<0.01
3	12.6	1.8	1.99	1.32–3.00		9.4	1.5	1.93	1.21–3.09	
4	27.9	2.6	4.42	3.19–6.13		18.4	1.9	3.80	2.59–5.57	
5	37.2	3.2	5.90	4.25–8.18		28.6	3.7	5.91	3.90–8.96	
Race/ethnicity										
White	17.2	1.8	1.00		<0.01	12.2	1.7	1.00		<0.01
African–American	28.1	2.1	1.63	1.27–2.09		21.5	1.9	1.76	1.30–2.37	
Mexican–American	38.3	2.4	2.22	1.74–2.84		29.2	1.8	2.39	1.78–3.20	
Poverty ratio										
>3.500	8.1	2.0	1.00		<0.01	5.7	1.8	1.00		<0.01
1.301–3.500	17.9	1.6	2.22	1.42–3.47		11.0	1.5	1.92	1.12–3.30	
<1.301	28.9	25	3.59	2.14–6.01		22.7	2.4	3.96	2.11–7.45	
Maternal age at birth (years)										
<20	29.9	3.5	1.00		<0.01	21.4	2.9	1.00		<0.01
20–29	22.2	1.7	0.74	0.57–0.97		16.6	1.6	0.78	0.57–1.05	
>29	15.5	2.0	0.52	0.40–0.67		10.7	1.7	0.50	0.36–0.69	
Head of household education (years)										
>12	15.2	1.7	1.00		<0.01	9.5	1.4	1.00		<0.01
= 12	21.7	2.1	1.43	1.11–1.85		16.3	1.9	1.72	1.25–2.37	
<12	31.7	2.7	2.09	1.68–2.59		25.5	2.9	2.68	1.97–3.65	
Number of smokers in the home										
None	17.6	1.3	1.00		<0.01	12.2	1.0	1.00		<0.01
1–2	28.6	3.2	1.62	1.32–2.00		22.7	3.3	1.86	1.43–2.40	
>2	24.6	4.1	1.40	1.10–1.78		18.0	2.6	1.47	1.06–2.04	
Dental visits										
Never	14.2	1.1	1.00		<0.01	9.7	0.9	1.00		<0.01
As needed	36.0	4.3	2.53	1.93–3.31		27.7	3.6	2.87	2.12–3.88	
Regularly	26.8	2.8	1.88	1.51–2.34		20.4	2.6	2.11	1.67–2.66	
Fluoride supplementation										
No	21.0	1.3	1.00		0.52	15.4	1.3	1.00		<0.57
Yes	26.9	10.6	1.28	0.59–2.77		19.1	7.5	1.24	0.58–2.67	
Carbohydrate intake (g/day)										
<161.0	17.7	2.2	1.00		0.03	14.0	2.0	1.00		0.2319
161.0–202.2	15.5	1.8	0.88	0.66–1.18		11.7	2.1	0.79	0.55–1.14	
202.3–249.1	23.5	2.8	1.33	1.01–1.75		17.5	2.5	1.08	0.78–1.51	
≥249.2	25.3	2.4	1.44	1.05–1.96		17.0	2.0	1.02	0.69–1.51	
Sucrose intake										
<35 g/day	15.6	1.3	1.00		<0.01	12.7	1.3	1.00		0.06
≥35 g/day	24.9	2.7	1.60	1.23–2.08		17.2	2.3	1.35	0.98–1.87	
Bottle-feeding										
≤19 months	19.5	1.2	1.00		0.02	14.0	1.0	1.00		0.02
>19 months	25.4	2.9	1.30	1.05–1.61		19.4	2.9	1.39	1.06–1.82	
Breast-feeding										
No	25.6	1.8	1.00		<0.01	12.3	1.6	1.00		<0.01
Yes	17.4	1.9	0.68	0.54–0.86		19.3	1.5	0.64	0.51–0.80	
Preterm birth										
≥37 weeks	20.3	1.3	1.00		<0.01	14.7	1.3	1.00		0.01
<37 weeks	33.5	6.8	1.65	1.14–2.40		26.3	5.9	1.78	1.14–2.78	
Low birthweight										
≥2500 g	20.8	1.5	1.00		0.09	15.3	1.4	1.00		0.12
<2500 g	28.4	5.2	1.37	0.95–1.97		22.0	4.8	1.46	0.90–2.35	
Small for gestational age birth										
No	21.6	1.5	1.00		0.96	15.6	1.4	1.00		0.82
Yes	21.0	2.7	0.99	0.76–1.29		15.1	2.3	0.97	0.74–1.28	

Table 2. Continued

	dft > 0[a]					dft > 1				
	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value
Fetal growth restriction										
None	20.8	1.5	1.00		0.66	15.4	1.3	1.00		0.66
Mild	27.5	5.9	1.32	0.84–2.07		18.4	5.2	1.19	0.70–2.03	
Moderate	22.4	6.5	1.06	0.58–1.94		17.3	3.3	1.12	0.76–1.65	
Severe	19.7	3.5	0.95	0.67–1.34		11.8	4.3	0.77	0.37–1.59	

[a]Dft, decayed and filled (primary) teeth index.
[b]Weighted percentage.
[c]SE, standard error.
[d]PR, prevalence ratio.
[e]95% CI, 95% confidence interval.

Table 3. Bivariate analysis of background variables, oral health-related characteristics, IUGR surrogates and preterm birth in relation to dental caries among children aged 3–5 years NHANES III (1988–1994)

	dft > 0[a]					dft > 1				
	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value
Age (years)										
3	12.6	1.8	1.00		<0.01	9.4	1.5	1.00		<0.01
4	27.9	2.6	2.22	1.58–3.12		18.4	1.9	1.97	1.37–2.83	
5	37.2	3.2	2.96	2.22–3.95		28.6	3.7	3.06	2.18–4.30	
Race/ethnicity										
White	21.4	2.4	1.00		<0.01	15.1	2.3	1.00		<0.01
African–American	34.1	2.4	1.60	1.23–2.08		25.6	2.3	1.71	1.24–2.36	
Mexican–American	45.8	2.9	2.14	1.64–2.80		35.6	2.2	2.36	1.72–3.25	
Poverty ratio										
>3.500	10.3	2.7	1.00		<0.01	7.7	2.5	1.00		0.01
1.301–3.500	22.2	2.0	2.03	1.29–3.19		16.0	1.6	2.07	1.16–3.70	
<1.301	34.6	3.2	3.17	1.87–5.36		29.2	3.9	3.79	1.94–7.40	
Maternal age at birth (years)										
<20	35.1	4.4	1.00		<0.01	25.1	3.5	1.00		0.01
20–29	27.3	2.3	0.78	0.59–1.03		20.3	2.2	0.81	0.59–1.10	
>29	19.2	2.5	0.55	0.41–0.74		13.5	2.2	0.54	0.39–0.75	
Head of household education (years)										
>12	19.9	2.3	1.00		0.01	12.4	2.0	1.00		0.01
= 12	25.9	2.6	1.30	1.01–1.68		19.2	2.4	1.54	1.12–2.13	
<12	36.5	3.6	1.83	1.46–2.31		29.7	3.8	2.38	1.70–3.35	
Number of smokers in the home										
None	21.7	1.7	1.00		<0.01	15.0	1.4	1.00		<0.01
1–2	34.9	4.0	1.61	1.31–1.98		27.6	4.3	1.84	1.41–2.41	
>2	29.3	3.8	1.35	1.02–1.80		21.3	3.6	1.42	0.99–2.04	
Dental visits										
Never	19.7	1.6	1.00		<0.01	13.2	1.3	1.00		<0.01
As needed	38.8	4.7	1.96	1.51–2.55		29.6	3.9	2.25	1.66–3.06	
Regularly	28.2	3.1	1.43	1.13–1.81		21.5	2.8	1.64	1.28–2.09	
Fluoride supplementation										
No	25.6	1.7	1.00		0.60	18.7	1.7	1.00		0.71
Yes	31.9	12.8	1.25	0.57–2.70		22.9	8.9	0.82	0.28–2.37	
Carbohydrate intake (g/day)										
<161.0	23.4	3.3	1.00		0.19	18.8	3.1	1.00		0.36
161.0–202.2	19.7	2.5	0.84	0.64–1.12		14.8	2.6	0.79	0.55–1.14	
202.3–249.1	27.3	3.3	1.17	0.87–1.58		20.3	3.0	1.08	0.78–1.51	
≥249.2	28.5	2.5	1.22	0.89–1.67		19.6	2.3	1.02	0.69–1.51	
Sucrose intake										
<35 g/day	19.6	1.9	1.00		<0.01	11.0	1.6	1.00		0.19
≥35 g/day	29.4	3.2	1.50	1.14–1.98		13.1	1.7	1.27	0.89–1.80	

Table 3. Continued

	dft > 0[a]					dft > 1				
	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value	%[b]	SE[c]	PR[d]	95% CI[e]	*P*-value
Bottle-feeding										
≤19 months	24.0	1.6	1.00		0.02	17.0	1.5	1.00		0.02
>19 months	31.1	3.8	1.29	1.04–1.62		24.0	3.9	1.42	1.07–1.88	
Breast-feeding										
No	30.6	2.3	1.00		<0.01	23.0	2.0	1.00		<0.01
Yes	21.9	2.5	0.71	0.57–0.90		15.3	2.1	0.67	0.54–0.83	
Preterm birth										
≥37 weeks	24.7	1.7	1.00		<0.01	17.9	1.7	1.00		0.06
<37 weeks	42.4	8.3	1.72	1.22–2.42		32.9	7.4	1.84	1.19–2.83	
Low birthweight										
≥2500 g	25.5	1.9	1.00		0.23	18.6	1.9	1.00		0.26
<2500 g	32.1	6.5	1.26	0.86–1.84		24.2	5.4	1.30	0.82–2.07	
Small for gestational age birth										
No	26.2	2.0	1.00		0.55	19.2	1.8	1.00		0.35
Yes	23.9	3.6	0.92	0.68–1.23		16.5	3.1	0.86	0.63–1.18	
Fetal growth restriction										
None	25.7	2.0	1.00		0.43	19.2	1.8	1.00		0.55
Mild	33.7	6.5	1.31	0.88–1.95		22.4	6.3	1.18	0.70–1.98	
Moderate	24.3	7.5	0.95	0.50–1.80		16.9	4.2	0.89	0.58–1.37	
Severe	19.9	4.7	0.77	0.51–1.18		12.4	4.9	0.65	0.29–1.44	

[a]dft, decayed and filled (primary) teeth index.
[b]Weighted percentage.
[c]SE, standard error.
[d]PR, prevalence ratio.
[e]95% CI, 95% confidence interval.

the sample size for moderate and severe FGR are small we also performed the analysis collapsing no and mild category and the moderate and severe categories that we call low FGR and high FGR. For models including 2- to 5-year-old children, the PRs comparing low FGR with high FGR were 0.65 (95% CI 0.34–1.27) for the presence of any tooth with dental caries and 0.78 (95% CI 0.57–1.09) for case definition of at least two teeth with dental caries; the PR values were 0.59 (95% CI 0.60–0.28) and 0.40 (95% CI 0.23–0.81; $P = 0.0102$), for 3- to 5-year-old children, respectively.

Discussion

In the present study, dental caries was associated positively with preterm birth but tends to be negatively associated with IUGR. The positive association between dental caries and preterm birth was significant independent of the inclusion of 2-year-old children or the case definition. A similar independence of results could be observed for the negative association, although not always statistically significant, between dental caries and SGA or FGR. As we predicted, inclusion of 2-year-old children and a more loose definition of dental caries seem to bias the results toward the null. An explanation for these biases would be a systematic selection bias when excluding 2-year-old children or a directional misclassification bias by using a more stringent case definition. However, we have no reason to believe that excluding 2-year-old children would result in selection bias, nor that using a more stringent case definition would create a directional misclassification. The inclusion of 2-year-old children represents an entrance 1/4 of the study sample with a very short period of time at risk because of their recent erupted teeth and very low prevalence of dental caries. A more loose definition for dental caries and inclusion of very young children may be the reason why no statistical association was found in other studies.

As the negative association between dental caries and IUGR suggested in this study is counterintuitive, we should interpret this finding with caution. It is possible that this negative association is the result of chance, being a particular characteristic of this data set. This negative association does not seem to be a result of any interaction, at least with the information available from NHANES III. In addition, the imprecision of the specific reference

Table 4. Models for dental caries according to low birthweight and preterm birth among children aged 2–5 years, NHANES III (1988–1994)

	2- to 5-year olds				3- to 5-year olds			
	dft > 0[a]		dft > 1		dft > 0		dft > 1	
	PR[b]	95% CI[c]	PR[b]	95% CI[c]	PR[b]	95% CI[c]	PR[b]	95% CI[c]
Race/ethnicity								
White	1.00		1.00		1.00		1.00	
African–American	1.58	1.23–2.03	1.52	1.14–2.04	1.60	1.21–2.13	1.54	1.11–2.13
Mexican–American	1.86	1.29–2.67	1.75	1.18–2.60	1.86	1.25–2.77	1.75	1.15–2.65
Poverty ratio								
>3.500	1.00		1.00		1.00		1.00	
1.301–3.500	1.83	1.10–3.03	1.58	0.88–2.84	1.82	1.09–3.03	1.62	0.89–2.96
<1.301	2.61	1.38–4.94	2.81	1.35–5.83	2.44	1.28–4.64	2.71	1.28–5.71
Number of smokers in the home								
None	1.00		1.00		1.00		1.00	
1–2	1.42	1.13–1.78	1.69	1.29–2.20	1.42	1.12–1.81	1.68	1.25–2.26
>2	1.39	1.02–1.89	1.65	1.13–2.40	1.34	0.96–1.89	1.60	1.08–2.39
Dental visits								
Never	1.00		1.00		1.00		1.00	
As needed	1.50	1.15–1.94	1.79	1.32–2.43	1.44	1.10–1.87	1.70	1.24–2.33
Regularly	1.63	1.31–2.03	2.16	1.74–2.69	1.60	1.26–2.03	2.14	1.71–2.68
Bottle-feeding								
≤19 months	1.00		1.00		1.00		1.00	
>19 months	1.44	1.21–1.71	1.52	1.22–1.90	1.41	1.19–1.68	1.47	1.19–1.82
Low birthweight								
No	1.00		1.00		1.00		1.00	
Yes	0.79	0.53–1.19	0.78	0.45–1.04	0.71	0.51–0.98	0.67	0.44–1.02
Preterm birth								
No	1.00		1.00		1.00		1.00	
Yes	1.38	1.00–1.89	1.49	1.01–2.19	1.52	1.18–1.94	1.64	1.22–2.20

Note: Models were also adjusted for child's sex and age, maternal age at birth, fluoride supplementation, carbohydrate intake, and head of household education.
[a]dft, decayed and filled (primary) teeth index.
[b]PR, prevalence ratio.
[c]95% CI, 95 percent confidence interval.

data for estimating SGA birth does not seem to be responsible for our results because independent of the three reference data used (27, 29, 36), the results were very similar (data not shown). The results were also similar when low FGR, which has been proposed to be a better proxy for IUGR than is SGA birth (30), was used. Furthermore, when we tested the interaction between LBW and preterm birth, we observed that children who were not born preterm but presented LBW (possibly because of IUGR) were less likely to have dental caries than the others. Additional support for our conclusion is found in the trend analysis performed for FGR. The higher the severity of the FGR, the lower was the risk of dental caries, suggesting a dose–response gradient.

One limitation of our study is the lack of information on oral hygiene and water fluoridation. However, we could not find evidence in the literature that water fluoridation was associated with the occurrence of IUGR, indicating that it could not be a confounder. As IUGR is primarily associated with low socioeconomic level, it seems unreasonable that the poorest communities in the US would be more likely to have water fluoridation than the others. If so, underprivileged groups also would tend to have less dental caries than the richest ones, which is contrary to what has been observed (37). However, if there is any socioeconomic pattern associated with water fluoridation in the US, we suppose this could at least be in part controlled by the fact that we took ethnicity and certain socioeconomic variables into consideration.

Another potential limitation of our study is the lack of information on serum levels of cotinine (32) and blood lead levels (38), both of which have been associated with dental caries. Blood lead levels were only available for a small part of our sample. The biological explanation for these associations relies on impairment of enamel deposition and

Table 5. Models for dental caries according small for gestational age (SGA) birth among children aged 2–5 years, NHANES III (1988–1994)

	2- to 5-year olds				3- to 5-year olds			
	dft > 0[a]		dft > 1		dft > 0		dft > 1	
	PR[b]	95% CI[c]	PR	95% CI	PR	95% CI	PR	95% CI
Race/ethnicity								
White	1.00		1.00		1.00		1.00	
African–American	1.57	1.31–2.02	1.51	1.13–2.01	1.59	1.20–2.10	1.55	1.12–2.15
Mexican-American	1.88	1.31–2.68	1.77	1.20–2.62	1.88	1.28–2.78	1.77	1.17–2.66
Poverty Ratio								
>3.500	1.00		1.00		1.00		1.00	
1.301–3.500	1.83	1.10–3.05	1.58	0.88–2.85	1.82	1.08–3.06	1.62	0.88–2.95
<1.301	2.63	1.38–5.00	2.83	1.35–5.92	2.47	1.29–4.74	2.75	1.29–5.87
Number of smokers in the home								
None	1.00		1.00		1.00		1.00	
1–2	1.43	1.14–1.79	1.70	1.31–2.22	1.44	1.13–1.83	1.69	1.26–2.28
>2	1.42	1.05–1.94	1.69	1.16–2.46	1.38	0.98–1.95	1.67	1.12–2.49
Dental visits								
Never	1.00		1.00		1.00		1.00	
As needed	1.48	1.14–1.91	1.76	1.30–2.38	1.41	1.08–1.84	1.68	1.24–2.28
Regularly	1.61	1.30–2.00	2.13	1.72–2.64	1.57	1.24–1.98	2.10	1.70–2.59
Bottle-feeding								
≤19 months	1.00		1.00				1.00	
>19 months	1.42	1.20–1.69	1.50	1.22–1.86	1.39	1.17–1.65	1.47	1.19–1.81
SGA birth								
No	1.00		1.00		1.00		1.00	
Yes	0.79	0.56–1.01	0.72	0.52–0.99	0.73	0.50–1.01	0.66	0.33–0.96
Preterm birth								
No	1.00		1.00		1.00		1.00	
Yes	1.25	0.97–1.62	1.34	0.98–1.84	1.32	1.03–1.69	1.38	1.03–1.85

Note: models were also adjusted for child's sex and age, maternal age at birth, fluoride supplementation, carbohydrate intake, and head of household education.
[a]dft, decayed and filled (primary) teeth index.
[b]PR, prevalence ratio.
[c]95% CI, 95 percent confidence interval.

maturation (32, 38). However, only smoking has been associated with perinatal outcomes, and there is little evidence of a causal association between lead exposure and perinatal outcomes (39–41) to be considered a confounder for dental caries. In order to control for environmental exposure to tobacco smoke, we used the number of smokers in the home.

An important concern in any NHANES III data analysis is the possibility of missing values for covariates, which results in exclusion of the individual from the multivariate analysis. In an attempt to understand the possible impact of the missing values in our final models, the covariates with missing information were recoded to include a category discriminating the missing values. We then reconstructed the models, each time replacing one variable with missing values with the corresponding recoded variable as well as using simultaneous substitution. After exhaustive analysis, we could not find any major differences between the original models and the reconstructed models. Therefore, we decided to present the original models that included the variables with missing values.

An explanation for the negative association between IUGR and dental caries is the possible delay in tooth eruption, which has been reported among preterm LBW children (15, 42). Unfortunately, we were not able to find studies dissociating the effect of IUGR from preterm birth on tooth eruption. Delay in tooth eruption of primary teeth would delay colonization with *S. mutans*, resulting in lower prevalence of dental caries. It can also be hypothesized that increased utilization of antibiotics contributes to the lower prevalence of dental caries among growth-retarded children as pulmonary infections in the first years of life are more severe in such children (22, 43). Antibiotic use is thought to reduce dental caries by inhibiting colonization by cariogenic bacteria (44).

Table 6. Models for dental caries according the fetal growth restriction (FGR) among children aged 2–5 years, NHANES III (1988–1994)

	2- to 5-year olds				3- to 5-year olds			
	dft > 0[a]		dft > 1		dft > 0		dft > 1	
	PR[b]	95% CI[c]	PR	95% CI	PR	95% CI	PR	95% CI
Race/ethnicity								
White	1.00		1.00		1.00		1.00	
African-American	1.59	1.24–2.04	1.53	1.15–2.04	1.61	1.22–2.14	1.57	1.13–2.19
Mexican-American	1.86	1.30–2.68	1.77	1.20–2.62	1.87	1.26–2.78	1.80	1.18–2.75
Poverty Ratio								
>3.500	1.00		1.00		1.00		1.00	
1.301–3.500	1.83	1.10–3.05	1.56	0.86–2.81	1.81	1.07–3.06	1.59	0.86–2.92
<1.301	2.63	1.38–5.00	2.79	1.34–5.80	2.45	1.27–4.73	2.69	1.27–5.67
Number of smokers in the home								
None	1.00		1.00		1.00		1.00	
1–2	1.43	1.14–1.79	1.69	1.30–2.20	1.44	1.13–1.82	1.69	1.27–2.25
>2	1.42	1.04–1.93	1.68	1.15–2.44	1.37	0.97–1.94	1.66	1.11–2.49
Dental visits								
Never	1.00		1.00		1.00		1.00	
As needed	1.49	1.15–1.92	1.77	1.31–2.39	1.43	1.10–1.85	1.68	1.24–2.29
Regularly	1.62	1.31–2.01	2.14	1.73–2.66	1.59	1.26–2.00	2.13	1.68–2.69
Bottle-feeding								
≤19 months	1.00		1.00		1.00		1.00	
>19 months	1.43	1.20–1.69	1.51	1.22–1.86	1.39	1.17–1.65	1.51	1.24–1.84
FGR								
None	1.00		1.00		1.00		1.00	
Mild	0.98	0.71–1.36	1.06	0.74–1.52	1.04	0.75–1.44	1.10	0.76–1.58
Moderate	0.94	0.50–1.75	0.71	0.31–1.62	0.92	0.47–1.78	0.66	0.26–1.67
Severe	0.70	0.48–1.01	0.74	0.49–1.12	0.58	0.38–0.90	0.59	0.36–0.99
Preterm birth								
No	1.00		1.00		1.00		1.00	
Yes	1.27	0.97–1.66	1.37	1.00–1.89	1.34	1.03–1.74	1.43	1.05–1.94

Note: models were also adjusted for child's sex and age, maternal age at birth, fluoride supplementation, carbohydrate intake, and head of household education.
[a]dft, decayed and filled (primary) teeth index.
[b]PR, prevalence ratio.
[c]95% CI, 95 percent confidence interval.

We can further hypothesize that the well-known increased lung maturation among IUGR fetuses compared with preterm children is analogous to dental development (45, 46). If a similar increased maturation also affects tooth germs, IUGR children might present enamel structure that is more nearly normal in comparison with that seen in preterm children.

Unfortunately, we could not find any human or animal studies of tooth development in which the effect of IUGR was dissociated from preterm birth. Therefore, it is possible that our results are attributable to a sum of events, such as delay in tooth eruption together with increased antibiotic intake and accelerated enamel maturation among IUGR children.

Another possible explanation for our results is the improvement in positive health behaviors among IUGR children. However, we could not find IUGR to correlate with low sucrose, carbohydrate intake or frequency of dental visits. Having been breastfed is in fact associated with neonatal conditions as most preterm children have difficulties in suction and are thus introduced to exclusive bottle-feeding very early in life (47). Nevertheless, the duration of bottle-feeding was no greater among such children.

The study of the association of dental caries and perinatal outcomes is challenging because of the presence of several confounders, especially those associated with socioeconomic status and health behaviors. These confounders are very difficult to measure, in particular because they rely on personal information and change over time. In addition, there are common risk factors for both conditions, related to maternal behaviors (e.g. smoking), prenatal care and socioeconomic status, which may reveal, in a broad sense, negative maternal health behaviors (18, 48–50). Therefore, it is possible that IUGR and preterm birth are only markers for negative health behaviors commonly associated with dental caries.

We found no data in the literature regarding the independent effect of IUGR on dental caries with which we could compare our results. Schulman (19) recently conducted an analysis of preterm birth using NHANES III data but found no association between preterm birth and dental caries. Despite the fact that the same data set was used, there are some differences in our analysis that might explain the contradictory findings. For example, the classification of gestational age in four categories (>44, 44–37, 33–36, and <33 weeks), with those with <33 weeks with a very small sample size. In spite of the small sample size, the bivariate analysis clearly showed an increased prevalence of dental caries among preterm children. Moreover, whereas Schulman (19) modeled decayed and filled surfaces as a continuous variable using Poisson regression, we estimated PR.

In spite of some limitations such as the cross-sectional design, this study has several strengths. One advantage was the large sample size and the availability of data on the most significant risk factors for dental caries, on gestational age and on the most significant confounders. In addition, data on LBW taken from birth certificates avoid information bias related to the faulty recollections of parents or guardians. Furthermore, this is the first study to address the various effects of IUGR and preterm birth on dental caries.

In conclusion, we found a positive association between preterm birth and dental caries, and a negative association between IUGR and dental caries. As preterm delivery has been increasing in the US, further studies are needed in order to confirm and better understand the associations identified in this study.

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