

ORIGINAL ARTICLE

Maternal dental caries and pre-term birth: Results from the EPIPAP study

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Abstract

Objective. The aim of this study was to analyse the association between maternal dental caries and pre-term birth (PTB), with a particular focus on the infection-suspected causes of pre-term births. **Materials and methods.** A secondary analysis was performed on data from the EPIPAP study, a French multi-centre case-control study. Cases were 1107 women giving birth to a singleton live-born infant before 37 weeks of gestation and controls were 1094 women delivering at 37 weeks or more. A subgroup of cases was defined as women with spontaneous labour and/or pre-term premature rupture of membranes (PPROM, $n = 620$). A full-mouth dental examination was performed after delivery. The main factor of interest was the presence of decay on at least one tooth. **Results.** Crude associations between presence of tooth decay and PTB or spontaneous PTB/PPROM were significant (OR = 1.21 [1.01–1.45] and OR = 1.25 [1.01–1.55], respectively). After adjustment for two sets of potential confounders (four pre-term birth risk factors and four social characteristics), for periodontitis status and for inter-examiner variability, tooth decay was not significantly associated with either PTB or spontaneous PTB/PPROM (aOR = 1.10 [0.91–1.32] and aOR = 1.14 [0.91–1.42], respectively). **Conclusions.** This study failed to demonstrate a significant association between tooth decay and pre-term birth. However, future well-designed studies are needed to further assess the link between dental caries and adverse pregnancy outcomes.

Key Words: Dental caries, dental decay, epidemiology, pregnancy, premature birth

Introduction

Pre-term birth is a leading cause of perinatal mortality and morbidity, occurring in ~12.7% of all births in the US [1] and from 5.5–11.4% in Europe [2]. Well-established risk factors of pre-term birth include low or high maternal age, primiparity or high parity, history of prior pre-term birth, low BMI or obesity, cigarette smoking, multi-foetal pregnancy, genito-urinary infection and inflammation, incompetent cervix and abruptio placentae [3,4]. Several non-genital-tract infections such as pyelonephritis, pneumonia, appendicitis or periodontitis have also been hypothesized to increase the risk of

pre-term delivery [4]. In a previous meta-analysis of observational studies, we found a trend for maternal periodontitis to be associated with pre-term birth (OR = 2.27, 95% CI [1.06–4.85]) [5]. Results from our EPIPAP case-control study showed that this risk varied according to the complications leading to pre-term birth [6]. The main hypothesis explaining this association was the production of inflammatory mediators in the inflamed periodontal tissues, which could enter the systemic circulation and trigger an inflammatory cascade into the uterus [7].

Another highly prevalent oral disease is dental caries, a widespread, infectious disease affecting

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~40–50% of adults in industrialized countries [8–10]. Two recent studies have suggested that cariogenic oral flora could be associated with adverse pregnancy outcomes [11,12]. Moreover, secondary analyses from two observational studies assessing the link between periodontitis and pre-term birth reported a significant association between the presence of tooth decay during pregnancy and pre-term birth [13,14]. In contrast to periodontitis, tooth decay has not been reported to be directly associated with systemic disorders. On the basis of different physiopathological mechanisms (i.e. translocation of cariogenic bacteria from mouth to bloodstream or colonization of oral bacteria into the vaginal microflora), it could be hypothesized that cariogenic bacteria could be implicated in both tooth decay development and in obstetrical disorders, such as intrauterine infection, leading to pre-term birth.

The aim of this study was to analyse the association between maternal dental caries and pre-term birth, with a particular focus on pre-term births that could be related to intra-uterine infection.

Materials and methods

Study population

The current paper reports the results of the EPIPAP (EPIdeiological study on the relation between Periodontitis and Adverse Pregnancy Outcomes), a multi-centre case-control study which primarily aimed to analyse the association between periodontitis and pre-term birth according to the causes of pre-term birth [6]. The EPIPAP study was carried out between 2003 and 2006 in six maternity units in three French regions (Ile-de-France, Midi-Pyrénées and Alsace). A secondary objective of the EPIPAP study was to explore the association between maternal dental caries and pre-term birth. Cases were defined as women giving birth to a singleton live-born infant between 22–36 completed weeks of gestation (pre-term birth) [4]. Controls were women giving birth to a singleton live-born infant at term (≥ 37 weeks), randomly selected in the same maternity unit. Gestational age was estimated in a similar way in all maternity units, according to the date of last menstrual period and early ultrasound assessment (routine practice in France).

For both cases and controls, exclusion criteria were: women aged under 18, women not understanding French, HIV infection, unbalanced diabetes or any medical condition that required antibiotic prophylaxis for dental examination and periodontal probing, women with fewer than six teeth and infants born with a severe congenital malformation. The study was approved by the French data protection authority. All the women included gave their written informed consent.

Data

A full-mouth dental examination was performed within 2–4 days post-partum in the post-delivery wards of the maternity units. Women were examined in a sitting position. Eleven dentists were in charge of carrying out the dental examinations in this multi-centre study. Examiners were given clear instructions prior to the observation period, to assess dental caries according to the World Health Organization (WHO) diagnosis criteria [15]. Given the pathogenesis of dental caries, it was considered that tooth decay observed within 4 days post-partum was already present during pregnancy. Third molars were not considered for examination. The numbers of decayed, filled and missing dental surfaces were recorded using sterile dental mirrors and explorers. Radiographs were not taken. Caries were recorded at the surface level of the teeth. Four surfaces were coded for incisors and canines and five surfaces for premolars and molars.

- A decayed surface (DS) was recorded when a carious lesion could be observed, including any carious lesion which was contiguous with the margin of a filling. A carious lesion was defined as ‘an unmistakable cavity, undermined enamel or a detectably softened floor or wall’ [15]. A decayed tooth (DT) was a tooth with at least one carious lesion on at least one of its surfaces. A woman was considered as having tooth decay (yes/no) if at least one of her teeth presented a decayed surface.
- A surface was recorded as filled if there was a restoration without decayed surface elsewhere on the surface. A filled tooth (FT) was a tooth with at least one filled surface (FS) and without decayed surface elsewhere on the tooth.
- Missing surfaces (MS) and missing teeth (MT) were also reported, although the presumed reasons for surface and tooth loss were not recorded.
- A surface that showed no evidence of carious lesion or filling material was considered as a sound surface. A tooth with all of its surfaces coded as sound was recorded as sound.

The sum of decayed, missing and filled surfaces (DMFS index) and the sum of decayed, missing and filled teeth (DMFT index) were calculated for each subject according to the WHO standards [15].

Both plaque and calculus scores were measured during the oral examination, using the Silness-Löe plaque index [16] and the Greene and Vermillion calculus index [17], at four sites per tooth. A woman was classified as having a high quantity of plaque if the examiner reported at least one site with visible plaque on at least one tooth. Similarly, a woman was classified as having a high quantity of calculus if the examiner reported at least one site with calculus

covering more than one third of the exposed tooth surface of at least one tooth. Finally, women were classified as having no periodontitis, localized periodontitis (2–3 teeth) or generalized periodontitis (≥ 4 teeth). Details on the periodontal examination and periodontitis definitions, based on measures of clinical attachment level (3 mm threshold) and pocket depth (4 mm threshold), have been published in a previous report [6]. Briefly, examinations were performed with a PCPUNC-15 (Hu-Friedy®) periodontal probe, at six sites per tooth. Localized periodontitis was defined as PD ≥ 4 mm and CAL ≥ 3 mm on the same site on two or three teeth, generalized periodontitis as PD ≥ 4 mm and CAL ≥ 3 mm on the same site on four or more teeth.

All dental examiners were blinded to the cause of pre-term birth and to medical and socio-demographic data. Maternal characteristics were obtained through a standardized interview of the women after the dental examination and medical characteristics were obtained from the women's medical records. Characteristics of interest included maternal age (18–24, 25–29, 30–34 and ≥ 35 years), parity of the mother (primiparous vs multiparous), smoking status during pregnancy (non-smoker before pregnancy, stopped smoking during pregnancy, smoker during pregnancy) and the Body Mass Index (BMI). BMI was calculated by dividing the weight (in kilograms) by the square of the height (in metres) and assessed using self-reported values of height and weight before pregnancy (< 18.5 , 18.5–25, 25–30 and ≥ 30 kg/m²). Social characteristics were nationality (French or not), marital status (married, unmarried couple, living alone), educational level (primary and secondary compulsory education, sixth form, university) and employment during pregnancy (yes/no).

The original EPIPAP study design included an analysis according to the causes of pre-term birth. For the present analysis, we chose to analyse the association between the presence of tooth decay and overall pre-term birth, but also according to a pathophysiological hypothesis. Pre-term birth can result from any of three sets of clinical conditions: medically indicated pre-term birth, pre-term premature rupture of membranes (PPROM) and spontaneous pre-term birth [18]. All case women were grouped in the overall pre-term birth group (PTB group). Among the PTB group, we defined a sub-group of women for whom premature delivery could have been related to intra-uterine infection [19]: women with spontaneous pre-term labour, pre-term birth after PPRM (rupture of membranes occurring 12 h or more before the onset of labour) and induced pre-term birth for chorioamnionitis or fever. This pre-term birth sub-group was named the 'spontaneous PTB/PPROM group'.

Statistical analysis

Dental quantitative variables were presented using means and standard deviations. PTB cases and spontaneous PTB/PPROM cases were compared to controls. Comparisons between cases and controls were performed using general linear models (*F*-test) adjusted for dental examiner.

Dental categorical variables were presented using observed numbers and percentages. Comparisons between cases and controls were made using logistic regression models (Wald Chi² test), adjusted for dental examiner. Characteristics of the case and control women were compared using Chi² tests.

The relation between pre-term birth (either PTB or spontaneous PTB/PPROM) and the presence of tooth decay was analysed using logistic regression models. Analyses were adjusted for variables selected on the basis of the literature. We controlled for the effects of four well established risk factors for pre-term birth (age, parity, smoking status and BMI before pregnancy) [3,4], for four social characteristics (nationality, marital status, educational level and employment during pregnancy) and for periodontitis [4]. Inter-examiner variability was taken into account by adjustment in all the analyses. Results were adjusted odds ratios (aOR) and their 95% confidence intervals.

The significance level was set at $p \leq 0.05$. Post-hoc calculation revealed that the present analysis had a power of 65% to detect a 5% difference in tooth decay frequency between cases and controls, at a 5% significance level. Statistical analyses were performed using SAS software version 9 (SAS Institute Inc., Cary, NC).

Results

The total inclusion rate among women having given birth to a pre-term singleton liveborn child in the six maternity units was 53% for all 3 years of the study. A total of 1108 cases and 1094 controls were included in the EPIPAP primary study [6]. Of these, only one case woman did not consent to the dental caries examination. This woman had a medically indicated pre-term birth infant. Thus, the sample size studied in the present analysis was 1107 PTB cases and 1094 controls. Among PTB cases, 620 were in the spontaneous PTB/PPROM group. During the last year of recruitment, detailed reasons for the non-inclusion of cases were collected according to inclusion criteria: 720 women gave birth to a pre-term singleton liveborn child and 340 were not included; 25 (7.4% of the non-included subjects) did not speak French, 40 (11.8%) had medical exclusion criteria, 45 (13.2%) women declined the examination,

114 (33.5%) were discharged before examination and 116 (34.1%) were not examined because no examiner was available.

The mean number of DMFS was significantly higher for PTB cases than for control women ($p = 0.02$) (Table I). Mean DMFT was 8.23 (SD = 4.80) among controls, 8.55 (SD = 4.97) among PTB cases ($p = 0.08$) and 8.44 (SD = 4.77) among spontaneous PTB/PPROM cases ($p = 0.27$). Among women who had at least one decayed tooth, the mean number of decayed teeth was 3.16 (SD = 2.82) for controls, 3.01 (SD = 2.50, $p = 0.99$) for PTB cases and 3.01 (SD = 2.48, $p = 0.82$) for spontaneous PTB/PPROM cases.

The frequency of women with tooth decay was significantly higher in the PTB group and in the spontaneous PTB/PPROM group (Table II). High quantity of calculus was borderline significantly associated with PTB. Other dental characteristics were not linked to PTB.

Table III shows the maternal characteristics according to the case-control status. PTB cases and spontaneous PTB/PPROM cases were less frequently of French nationality and more often had a low educational level, lived alone, were not employed during pregnancy and smoked before or during pregnancy.

The associations between presence of tooth decay and PTB or spontaneous PTB/PPROM were significant when adjusted for dental examiner only (aOR = 1.21 [1.01–1.45] and aOR = 1.25 [1.01–1.55], respectively). When adjusted for the four well-known pre-term birth risk factors, the four social characteristics, periodontitis and dental examiner, tooth decay was no longer significantly associated with either PTB or spontaneous PTB/PPROM (Table IV). Table IV shows the adjusted odds ratios for all factors included in the logistic regression model, which allows comparison of the size order of the OR associated with tooth decay with that of the other variables.

Discussion

Crude associations between tooth decay and pre-term birth were significant. Adjustment for pre-term birth risk factors, social characteristics and periodontitis led to loss of significance of the associations.

A limitation of this study was that dental examiners were blinded for the causes of pre-term birth, but not totally blinded for the case-control status. The study design planned to blind dental examiners to the pre-term/at term status of the birth and they were not informed of this status. Nonetheless, if when the dental examiner entered the room, the baby was not there or was very small, the dental examiner could have guessed that he/she was pre-term. Dental examiners did check and record information about gestational age and the cause of the pre-term birth from the medical record, but only after both the examination and the interview. Although this was a retrospective study, we found that the control group had socio-demographic characteristics similar to those of the French national sample of births [20]. Another limitation of this study was that it was a secondary analysis of a study initially designed to investigate the association between pre-term birth and periodontitis. This could have led to some drawbacks, even if the case-control approach remained relevant to explore the association between dental caries and pre-term birth. First, the 11 dentists were standardized for intra- and inter-examiner reproducibility regarding the assessment of dental caries: dental examiners were given clear instructions prior to the observation period to assess dental caries according to the WHO diagnosis criteria. However, a kappa coefficient calculation was not performed. We chose to account for possible residual inter-examiner variability by adjusting for examiner in the statistical models. In any case, given that each dentist examined cases and controls in the same maternity unit, possible intra- and inter-examiner variability would result in a non-differential measurement error that would

Table I. Distribution of decayed, missing and filled surfaces/teeth among controls, PTB cases and spontaneous PTB/PPROM cases.

Indices	Controls ($n = 1094$)	PTB cases ($n = 1107$)		Spontaneous PTB/PPROM cases ($n = 620$)	
	Mean \pm SD	Mean \pm SD	p^*	Mean \pm SD	p^{**}
Decayed surfaces (DS)	2.80 \pm 5.77	2.96 \pm 5.04	0.36	2.92 \pm 4.84	0.50
Decayed and filled surfaces (DFS)	15.84 \pm 14.11	16.65 \pm 14.31	0.21	16.28 \pm 13.73	0.56
Decayed, missing and filled surfaces (DMFS)	21.18 \pm 17.20	23.06 \pm 18.45	0.02	22.40 \pm 17.50	0.16
Decayed teeth (DT)	1.63 \pm 2.57	1.71 \pm 2.41	0.23	1.68 \pm 2.38	0.35
Decayed and filled teeth (DFT)	7.14 \pm 4.38	7.25 \pm 4.46	0.46	7.20 \pm 4.32	0.66
Decayed, missing and filled teeth (DMFT)	8.23 \pm 4.80	8.55 \pm 4.97	0.08	8.44 \pm 4.77	0.27

*Calculated using general linear models (F -test), pre-term birth (PTB) compared to controls (adjusted for dental examiner).

**Calculated using general linear models (F -test), spontaneous PTB or PPROM compared to controls (adjusted for dental examiner).

Table II. Dental characteristics of controls, PTB cases and spontaneous PTB/PPROM cases.

	Controls (<i>n</i> = 1094)		PTB cases (<i>n</i> = 1107)			Spontaneous PTB/PPROM cases (<i>n</i> = 620)		
	<i>n</i>	%	<i>n</i>	%	<i>p</i> [*]	<i>n</i>	%	<i>p</i> ^{**}
Tooth decay					0.03			0.03
No	529	48.4	492	44.4		273	44.0	
Yes	565	51.6	615	55.6		347	56.0	
High quantity of plaque ^a					0.59			0.90
No	354	32.4	351	31.7		207	33.4	
Yes	740	67.6	756	68.3		413	66.6	
High quantity of calculus ^b					0.05			0.24
No	843	77.1	808	73.0		461	74.3	
Yes	251	22.9	299	27.0		159	25.7	
Periodontitis					0.14			0.68
No	858	78.4	830	75.0		478	77.1	
Localized	118	10.8	129	11.6		75	12.1	
Generalized	118	10.8	148	13.4		67	10.8	
Last visit to the dentist					0.86			0.89
<1 year before pregnancy	813	74.4	817	74.3		456	74.5	
≥1 year before pregnancy	279	25.6	282	25.7		156	25.5	

*Calculated using logistic regression models (Wald Chi² test), pre-term birth (PTB) compared to controls (adjusted for dental examiner).
 **Calculated using logistic regression models (Wald Chi² test), spontaneous PTB or PPROM compared to controls (adjusted for dental examiner).

^aAt least one site with visible plaque on at least one tooth.

^bAt least one site with calculus covering more than one third of the exposed tooth surface of at least one tooth.

probably lead to under-estimation of the associations. Second, the initial sample size was calculated according to the primary aim of the study, resulting in lack of power for the present analysis. Finally, the addition of social characteristics to the multivariate analysis resulted in a decrease of the association between tooth decay and pre-term birth. Considering social characteristics as independent confounders was a matter of debate since dental caries could also be considered as an intermediate factor between distal risk factors of pre-term birth (i.e. poor access to care, poor socio-economic status or other social characteristics) and pre-term birth. For this reason, the model proposed in the adjustment strategy may be over-adjusted, explaining the loss of significance. We may therefore assume that the observed associations might be under-estimated. We studied the relationship between dental caries and pre-term birth after controlling for well-known pre-term birth risk factors, social characteristics, periodontitis and dental examiner inter-variability. However, previous pre-term delivery was not considered. Adjusting or stratifying for an obstetric history that may result from the exposure considered (dental caries) may be problematic in an aetiological approach [21].

Epidemiological investigations of the link between dental caries and adverse pregnancy outcomes are

scarce and report conflicting results. Unlike the present work, previous reports on the topic provided data from studies assessing the link between periodontal disease and pre-term birth, without specific analyses focused on dental caries [13,22–24]. Our crude results are in agreement with two previous reports providing some evidence for a link between presence of dental caries and pre-term birth [13,14]. Other reports giving an analysis of the association between adverse birth outcomes and a quantitative measure of dental caries (mean number of decayed, missing or filled teeth) failed to find a significant association [12,14,22–24]. This could be explained by the lifelong cumulative nature of the DMF indices (DMFT and DMFS), which may be considered inadequate for the time frame of pregnancy. In our study, the DMFS score was significantly higher among pre-term birth cases than among controls. We assigned the maximum possible value for the ‘M’ component of DMFS index for a given missing tooth (i.e. 4 for missing canines or incisors and 5 for missing premolars or molars). This over-estimation of the individual’s past caries experience could explain the observed difference between groups [25].

Although there is little information in the literature to support a pathophysiological association between

Table III. Maternal characteristics of controls, PTB cases and spontaneous PTB/PPROM cases.

	Controls (n = 1094)		PTB cases (n = 1107)			Spontaneous PTB/PPROM cases (n = 620)		
	n	%	n	%	p-value*	n	%	p-value**
Age	1094		1107		0.14	620		0.16
18–24 years	148	13.5	173	15.6		107	17.3	
25–29 years	331	30.3	307	27.7		169	27.3	
30–34 years	375	34.3	354	32.0		205	33.0	
≥35 years	240	21.9	273	24.7		139	22.4	
Parity	1093		1106		0.17	619		0.11
Primiparous	569	52.1	608	55.0		272	56.1	
Multiparous	524	47.1	498	45.0		347	43.9	
Smoking status	1091		1105		0.004	619		0.05
Non-smoker	843	77.3	796	72.0		454	73.3	
Stopped smoking during pregnancy	141	12.9	152	13.8		81	13.1	
Smoker during pregnancy	107	9.8	157	14.2		84	13.6	
BMI before pregnancy ^a	1082		1078		0.003	606		0.12
<18.5	92	8.5	116	10.8		71	11.7	
18.5–24.9	761	70.3	679	63.0		406	67.0	
25.0–29.9	151	14.0	176	16.3		78	12.9	
≥30	78	7.2	107	9.9		51	8.4	
Nationality	1091		1105		0.001	619		0.002
French	892	81.8	842	76.2		468	75.6	
Other	199	18.2	263	23.8		151	24.4	
Marital status	1094		1106		0.001	619		0.006
Married couple	627	57.3	564	51.0		317	51.2	
Unmarried couple	395	36.1	421	38.1		238	38.5	
Living alone	72	6.6	121	10.9		64	10.3	
Educational level	1093		1103		0.001	618		0.001
Compulsory education only	232	21.2	307	27.8		170	27.5	
Sixth form	192	17.6	245	22.2		141	22.8	
University	669	61.2	551	50.0		307	49.7	
Employment during pregnancy	1092		1103		0.03	617		0.03
Yes	764	70.0	722	65.5		401	65.0	
No	328	30.0	381	34.5		216	35.0	

*Chi² test, preterm birth compared to controls.

**Chi² test, spontaneous PTB or preterm premature rupture of membranes compared to controls.

^aBody Mass Index (kg/m²) before pregnancy.

dental caries and pre-term birth, some hypotheses may be suggested. Two recent studies have emphasized the complexity of the link between oral bacteria, other than periodontal pathogens, and pregnancy outcomes [11,12]. Dental caries is the result of the metabolic activities of bacteria in dental biofilms [26]. Oral streptococcal species (i.e. *Streptococcus mutans*, *S. sanguinis*, *S. oralis*, *S. mitis* and *S. sobrinus*) are known to play an important role in the development of dental caries [26]. These streptococcal bacteria belong to the *Streptococcus viridans* group, a group

of bacteria that also have the potential to cause endocarditis if they end up in the bloodstream, particularly in subjects with damaged heart valves [27]. Rabe et al. [28] have suggested that the subchorionic fibrin of the placenta, like the platelet-fibrin deposits on heart valves, may be susceptible to infection by the dextran-producing viridans group streptococcal species and it is recognized that infection of the placenta (histological chorioamnionitis) is a major cause of spontaneous pre-term birth [4]. In a study involving 48 women with elective caesarean section, *Streptococcus* spp. were

Table IV. Risk factors for PTB and spontaneous PTB/PPROM^a.

	PTB		Spontaneous PTB/PPROM	
	aOR ^b	95% CI ^c	aOR ^b	95% CI ^c
Tooth decay				
Yes	1.10	0.91–1.32	1.14	0.91–1.42
No	1.00		1.00	
Age				
18–24 years	1.00		1.00	
25–29 years	1.02	0.76–1.38	0.92	0.66–1.30
30–34 years	1.15	0.85–1.56	1.11	0.78–1.58
≥35 years	1.32	0.95–1.82	1.14	0.78–1.67
Parity				
Primiparous	1.24	1.03–1.51	1.28	1.02–1.60
Multiparous	1.00		1.00	
Smoking status				
Non-smoker	1.00		1.00	
Stopped smoking during pregnancy	1.15	0.88–1.49	1.05	0.77–1.44
Smoker during pregnancy	1.41	1.06–1.88	1.33	0.95–1.86
BMI before pregnancy ^d				
<18.5	1.36	1.00–1.84	1.40	0.99–1.97
18.5–24.9	1.00		1.00	
25.0–29.9	1.20	0.93–1.54	0.88	0.64–1.19
≥30	1.42	1.03–1.96	1.11	0.76–1.64
Periodontitis				
No	1.00		1.00	
Localized	1.09	0.82–1.45	1.12	0.81–1.55
Generalized	1.12	0.84–1.47	0.82	0.59–1.17
Nationality				
French	1.00		1.00	
Other	1.23	0.96–1.57	1.31	0.98–1.73
Marital status				
Married couple	1.00		1.00	
Unmarried couple	1.11	0.92–1.35	1.11	0.88–1.39
Living alone	1.54	1.10–2.18	1.32	0.88–1.97
Educational level				
Compulsory education only	1.38	1.09–1.76	1.40	1.06–1.87
Sixth form	1.46	1.15–1.85	1.54	1.17–2.04
University	1.00		1.00	
Employment during pregnancy				
Yes	1.00		1.00	
No	0.98	0.79–1.21	1.00	0.78–1.28

^aLogistic regression model adjusted for dental examiner and all factors reported in the table.

^bAdjusted Odds Ratio.

^c95% Confidence Interval of the aOR.

^dBody Mass Index (kg/m²) before pregnancy.

found in the amniotic fluid of 20 women and in the dental plaque of all the women [29]. It has been suggested that *Streptococcus* spp. found in the amniotic fluid may have an oral origin. In one case report,

intra-amniotic *Streptococcus mutans* were identified and successfully eradicated in a woman at 25 weeks gestation with threatened pre-term labour and a short cervix [30].

Another pathway by which oral bacteria could lead to intra-uterine infection is the ascending route. The first stage of ascending intrauterine infection consists of a change in the vaginal microbial flora, followed by an infection of the decidua, leading to the microbial invasion of the amniotic cavity (with or without rupture of the membranes) [19]. Presence of viridans group streptococcal species in the vaginal microflora has been associated with an increased risk of intra-amniotic infection [31]. However, it is still unclear whether the presence of viridans streptococci in the vaginal microflora could be the result of a self-transmission from mouth to vagina or from the mouth of the sexual partner as previously reported [32] or whether there is a host predisposition to streptococcal flora in both locations. This underlines the need for further research to enhance the understanding of microbiological associations between oral and vaginal flora.

In conclusion, this study failed to demonstrate a significant association between tooth decay and pre-term birth. However, possible under-estimation of this association, as well as putative pathophysiological mechanisms, suggest that further studies conducted on the link between oral diseases and adverse pregnancy outcomes should not only consider periodontal disease as a potential risk factor, but also dental caries and its related micro-organisms.

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Appendix: The EPIPAP (EPIdeMiological study on the relation between Periodontitis and Adverse Pregnancy outcomes) study group

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