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## ORIGINAL RESEARCH ARTICLE

# Oral and periodontal assessment at the first trimester of pregnancy: The PERISCOPE longitudinal study

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## Abstract

**Introduction:** Periodontal diseases (gingivitis and periodontitis) are chronic non-communicable inflammatory diseases. The risk of developing gingivitis and periodontitis increases during pregnancy. Also, periodontitis increases the risk of developing adverse pregnancy outcomes such as preterm birth and preeclampsia. Early diagnosis of adverse pregnancy outcomes is essential and periodontitis could be an early sign to take into consideration.

**Material and methods:** We conducted a longitudinal observational study (PERISCOPE study: CNIL, no. 1967084 v 0; CER, no. 01-0416) on 121 pregnant women in the first trimester to determine their oral and periodontal health status. We explored the relations between oral and periodontal health status and sociodemographic and behavior characteristics, as well as their course and outcome of pregnancy.

**Results:** A total of 47.1% of the women had periodontitis, of which only 66.7% presented clinical manifestations associated with the disease such as gingival bleeding. These women had a poorer oral and periodontal health, and a higher body mass index, and more of them developed gestational diabetes during the course of pregnancy. The remaining 33.3% showed only discreet and isolated inflammatory signs and, unless

**Abbreviations:** APO, adverse pregnancy outcomes; BMI, body mass index; CPI, Community Periodontal Index; DMFT, decayed-missing-filled teeth; GB, gingival bleeding; PI, plaque index.

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thoroughly examined, would have gone undiagnosed for periodontitis. Interestingly these women were more often primiparous, still active professionally and had had a recent oral examination.

**Conclusions:** The PERISCOPE study is one of the few studies that reports the oral and periodontal health status of pregnant women in the first trimester. Furthermore, the results highlight the need for early oral and periodontal assessment and treatment, even in the absence of exterior clinical signs, in order to prevent periodontal disease aggravation and also, by reducing low grade systemic inflammation, possibly adverse pregnancy outcomes.

#### KEYWORDS

adverse pregnancy outcomes, early diagnosis, gingival bleeding, periodontitis

## 1 | INTRODUCTION

Periodontal diseases (gingivitis and periodontitis) are chronic inflammatory non-communicable diseases and are considered the 11th most prevalent disease in the world.<sup>1</sup> Gingivitis, a mild form of periodontal inflammation, and periodontitis have respectively reversible and irreversible consequences on tissues surrounding teeth. Severe periodontitis affects 20% of the world population, leading ultimately to tooth loss and thus impairing oral and general quality of life of patients.<sup>2</sup> During pregnancy, physiological, immunological and hormonal modifications occur in women, increasing their susceptibility to infections including oral and periodontal diseases.<sup>3,4</sup> Gingivitis causes redness, swelling and in some cases gingival tenderness and profuse bleeding, which tends to increase during pregnancy.<sup>5</sup> Changes in levels of estrogen and progesterone also have an effect on the composition of the oral microbiota, compatible with the development of periodontitis.<sup>6</sup> Periodontal diseases are also considered established or potential risk factors in numerous systemic diseases and conditions such as the course of pregnancy.<sup>7,8</sup> Periodontitis may increase the risk of adverse pregnancy outcomes (APO) including preterm birth, preeclampsia, gestational diabetes, low birthweight and intrauterine growth retardation.<sup>9,10</sup> Furthermore, maternal periodontal conditions seem to be associated with stillbirth and perinatal death.<sup>11,12</sup> Two biological mechanisms supporting this association between periodontal diseases and APO have been proposed, one through systemic dissemination of periodontal pathogens that could cross the placenta into the amniotic fluid and fetal circulation, the other through inflammatory mediators such as interleukin-6 (IL-6), IL-8 and tumor necrosis factor alpha (TNF- $\alpha$ ) produced during periodontal inflammation that could, by entering the systemic circulation, induce an acute inflammatory response affecting the fetus and placenta.<sup>13,14</sup> Finally, the placenta harbors a unique microbiome structured by the history of infections during pregnancy and shares similarities with the woman's oral microbiome.<sup>15</sup> Recent studies have shown that both placental and oral microbiomes may play a role in periodontitis-associated APO.<sup>16</sup> *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, Gram-negative anaerobes, commonly found in periodontitis, have been shown to be able to translocate to the fetal-placental unit<sup>17,18</sup> and are associated with APO such as

#### Key message

Periodontitis can affect the course and outcome of pregnancy by increasing the risk of adverse pregnancy outcomes. Beware of periodontitis in pregnant women presenting discreet and isolated inflammatory signs.

preeclampsia, early-onset neonatal morbidity, sepsis and stillbirth.<sup>16,19,20</sup> The relation between APO and the oral and periodontal status of pregnant women is widely studied because it can affect the quality of life of women and the course and outcome of pregnancy.<sup>21,22</sup> The onset of APOs, such as preeclampsia, occurs at a subclinical stage during the first trimester, thus early diagnosis and risk factor control is essential.<sup>23</sup> Our hypothesis is that the presence of periodontal disease might be an early diagnostic sign to take into consideration for APO (such as preeclampsia). However, little is known about the oral and periodontal status in the first trimester of pregnancy, as most studies are conducted during the second trimester or after delivery.

The main objective of the PERISCOPE study was to determine the oral and periodontal health status of pregnant women in the first trimester. The secondary aims were to explore the relation between the oral and periodontal health status with sociodemographic and behavior characteristics.

## 2 | MATERIAL AND METHODS

We followed the STROBE statement guidelines for reporting observational studies.<sup>24</sup>

### 2.1 | Study design and settings

PERISCOPE is a single-center longitudinal study ancillary to the DROP (Dépistage du Risque Obstétrical au Premier trimestre

– Obstetrical Risk Screening at the first trimester) study. DROP is a screening protocol for trisomy 21 and early detection of preeclampsia and evaluation of its preventive treatment with low-dose aspirin. According to the French National Conference on Obstetrical and Fetal Sonography and French Health Care recommendations, first trimester sonography must be conducted between 11+0 and 13+6 weeks of amenorrhea<sup>25,26</sup>. Thus, the DROP study was offered to all women presenting themselves for the first trimester sonography (between 11+0 and 13+6 weeks of amenorrhea) in the prenatal diagnosis department of the Paule de Viguier Hospital in Toulouse's Public Teaching Hospital (CHU de Toulouse, France). The PERISCOPE study was conducted in the prenatal diagnosis department by three trained, qualified and calibrated investigators (CT, IT and EB). The inclusion was offered between January 2017 and June 2018 to all pregnant woman included in the DROP study who met the eligibility criteria of PERISCOPE. The course of the pregnancy, the delivery and the child's characteristics were recorded after delivery. All participants agreed to an interview and an oral examination performed at the time of this first trimester sonography visit. Moreover, all participants received a customized report of the dental examination and personalized advice, and were referred to a dental practitioner if treatment was needed.

## 2.2 | Participants

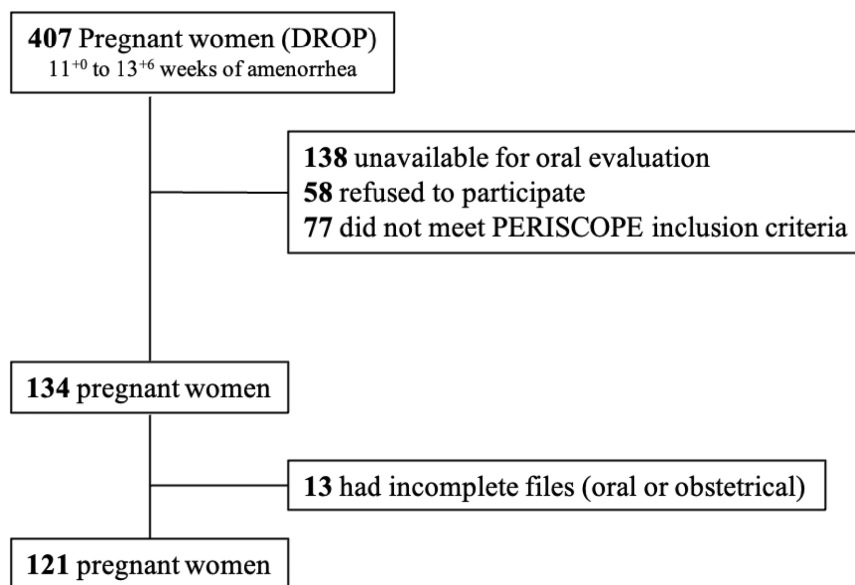
The women included in the PERISCOPE study must be of legal age ( $\geq 18$  years old), have at least six natural teeth and have signed a non-objection form to participate in the study. The non-inclusion criteria was comprised of women receiving anticoagulant treatment on the day of the 1st trimester sonography and/or presenting medium or high risk of infective endocarditis. According to the current recommendations of the Agence Nationale de Sécurité du Médicament, when performing instrumentation at the level of the gingiva, the degree of individual risk of infective endocarditis should be taken

into account and, if present, preventive antibiotic therapy should be prescribed.<sup>27</sup> From the 407 women included in DROP, 134 (32.9%) pregnant women were included in the PERISCOPE study; 33.9% were not evaluated because they were unavailable and did not have time to participate in it, 14.2% were informed but refused to participate in the study and 18.9% were not included because they did not meet with PERISCOPE inclusion criteria (Figure 1).

## 2.3 | Variables and data measurements

Before the oral examination, women provided information about: age, parity (primiparous or multiparous), nationality, socioprofessional status, working status during pregnancy, matrimonial status, height and weight for body mass index calculation ( $BMI \leq 25 \text{ kg/m}^2$ ,  $25 \text{ kg/m}^2 < BMI < 30 \text{ kg/m}^2$ ,  $BMI \geq 30 \text{ kg/m}^2$ ) and smoking status (non-smoker, former smoker who stopped during pregnancy, and smoker during pregnancy). The last dental visit was recorded (oral exam  $\leq 1$  year, oral exam  $> 1$  year).

Complete oral and periodontal examinations were then carried out. Prior to the onset of the study, the investigators were trained in periodontal charting and oral and periodontal health assessment (plaque index, gingival bleeding [GB], periodontal probing) with the overall inter-rater Cohen's Kappa coefficient value of 0.9 for periodontal pocket depth assessment.<sup>28</sup> They also verified that they used the exact same protocol when conducting a clinical examination. Oral status was assessed on all teeth present by counting the number of decayed, missing and filled teeth, excluding wisdom teeth (maximum 28 teeth). The Decay-Missing-Filled-Teeth (DMFT) index, validated by the World Health Organization, was calculated from 0 to 28,<sup>29</sup> dichotomized as follows: 0 (all teeth were healthy) vs  $\geq 1$  (at least one tooth was decayed, missing or filled). Oral hygiene was measured by the Plaque Index (PI), which determines the percentage of teeth with plaque for each woman.<sup>30</sup> Oral hygiene was then considered good if the PI was  $< 10\%$  and insufficient if the PI was



**FIGURE 1** Flow chart of the PERISCOPE longitudinal study. DROP, Dépistage du Risque Obstetrical au Premier trimestre (Obstetrical Risk Screening at the first trimester) study.

≥10%. Gingival inflammation characterized by GB was assessed by intrasulcular gingival irritation with a PCP UNC-15 periodontal probe (HuFriedy, Henry Schein, Alfortville, France). The GB index was determined as the percentage of teeth presenting GB.<sup>30</sup> It is known that pregnancy can induce physiological changes at the gingival level resulting in isolated GB spots upon probing. Also, a patient is considered to be able to maintain good oral hygiene after initial periodontal therapy if GB is <20%.<sup>31</sup> Thus, for this study, we dichotomized the GB index as follows: “minimal GB”, corresponding to GB <20%, if the inflammation was considered minimal and isolated, and “profuse GB”, corresponding to GB ≥20%, if the inflammation was considered important and profuse. Concerning the periodontal status, according to the World Health Organization recommendations for epidemiological studies,<sup>32</sup> the periodontal charting was partially carried on 10 teeth (six measurements per tooth): all first and second molars, one upper central incisor and one lower central incisor (teeth numbers: 17, 16, 11, 26, 27, 47, 46, 31, 36 and 37). The charting was performed with a constant pressure periodontal probe Florida Probe® to minimize intra- and interobserver bias related to the different probing pressures. Periodontal status recorded the criteria commonly used in epidemiological studies, probing depth and clinical attachment loss.<sup>33,34</sup> Probing depth was measured as the distance (in millimeters) from the gingival margin to the bottom of the periodontal pocket.<sup>34</sup> Clinical attachment loss was measured as the distance (in millimeters) from the cemento-enamel junction of the tooth to the bottom of the periodontal pocket.<sup>34</sup> The examiners (CT, IT, EB) were calibrated and standardized by an expert periodontist (SLD). Finally, periodontal status was defined by the Community Periodontal Index (CPI), which assesses periodontal care needs according to previously measured probing depth, GB and PI. CPI varies from 0 to 4. Periodontal status was dichotomized as follows: a CPI between 0 and 2 corresponded to “no periodontitis”, while a CPI of 3 or 4 corresponded to “periodontitis”, as it reflects the presence of periodontal lesions or pockets.<sup>32</sup>

Finally, variables concerning the course of the pregnancy, the delivery and newborn birthweight and gestational age were extracted from medical records after delivery. Data recorded for the course of the pregnancy were the presence of gestational diabetes, iron supplementation (ie given in cases of anemia or which could be considered a proxy of anemia), infectious episode and type if applicable (defined by the antibiotic intake during pregnancy), pregnancy complications (including at least one of the following: preeclampsia, intrauterine growth retardation, obstetric hemorrhage, premature rupture of the membrane, risk of preterm delivery). Onset of labor (spontaneous, induced or planned cesarean delivery), mode of delivery (spontaneous or cesarean section), gestational age at delivery and neonatal birthweight were also recorded.

## 2.4 | Statistical analyses

Statistical analyses were performed on 121 women with a complete file with follow-up from inclusion to delivery (Figure 1). Cohen's Kappa statistics coefficient was used to calibrate the investigators

for periodontal disease.<sup>28</sup> After being described by their mean and standard deviation, some quantitative variables were categorized to facilitate the interpretation and understanding of the results, despite a loss of statistical power. The sociodemographic, oral, pregnancy and delivery data are presented in the form of numbers with the corresponding proportions. First, the characteristics of women with minimal GB and with profuse GB were compared. Secondly, given that gestational gingivitis is a common but not systematic oral complication described during pregnancy, we chose to further explore the characteristics of the women according to the two GB groups (minimal and profuse GB) and then explored the characteristics of the women in each group of GB according to the presence or absence of periodontitis. Comparisons between the two groups were performed with Student *t*-tests (under the double hypothesis of normal distribution values and variances in equality) or non-parametric Mann-Whitney Wilcoxon tests for quantitative variables. Fisher tests were applied for qualitative variables. The database was created using Microsoft EXCEL 2010 and statistical analyses were performed using STATA 13.0. Next, we performed an exploratory data analysis using principal component analysis (PCA) to best identify which parameters characterized the two groups of women with periodontitis, those with profuse GB and those with minimal GB.<sup>35,36</sup>

The number of women needed was not calculated due to the main descriptive objective to determine the oral and periodontal health status of pregnant women in the first trimester. Statistical analyses were conducted with a level of significance of 5%.

## 2.5 | Ethics statement

In accordance with French law, the study was approved by the French Data Protection Authority: it was approved by the *Commission Nationale de l'Informatique et des Libertés* (CNIL, no. 1967084 v 0, June 7, 2016) and the *Comité d'Ethique pour la Recherche hospitalière* (CER; no. 01-0416, April 12, 2016).

## 3 | RESULTS

Table 1 gives the description of the sample of the 121 women (90.0% of the 134 women included in PERISCOPE analyzed). The remaining 10% had a miscarriage, terminated their pregnancy or did not receive a complete oral exam because they were either phobic of the dentist or hyperalgetic, and thus were not included in the final analysis. The mean age of the 121 women was 31.0 years ( $\pm 3.7$  years); 62.8% were between 25 and 34 years old. 69.4% were of French nationality, 95.0% were married or living as a couple. Only 18.2% had no professional qualifications or were unemployed at the time of their pregnancy, and slightly over half of them (55.4%) were working at the end of the first trimester. In all, 52.9% were primiparous.

Concerning their general health and behaviors, mean body mass index (BMI) was 25.0 ( $\pm 5.9$ ), 62.0% were considered normal weight with a BMI before pregnancy  $\leq 25 \text{ kg/m}^2$  and 38.0% were considered

**TABLE 1** General sociodemographic, oral and pregnancy characteristics and outcomes of the women included in PERISCOPE and the course and outcomes of pregnancy.

Characteristics, n (%)	121 (100)
Age	
<25 years	15 (12.4)
25–34 years	76 (62.8)
≥35 years	30 (24.8)
French nationality	84 (69.4)
Matrimonial status (married or living as a couple)	115 (95.0)
Socioprofessional status	
Agricultural workers	1 (0.8)
Craftsmen, traders and entrepreneurs	11 (9.1)
Managers and higher intellectual professions	11 (9.1)
Intermediate occupations	33 (27.2)
Employees	36 (29.8)
Worker	7 (5.8)
Retiree	0
Other /unemployed	22 (18.2)
Working status during pregnancy (working during pregnancy)	67 (55.4)
Primiparous	64 (52.9)
Body mass index (BMI) before pregnancy	
≤25 kg/m <sup>2</sup>	75 (62.0)
25 < BMI < 30 kg/m <sup>2</sup>	29 (24.0)
≥30 kg/m <sup>2</sup>	17 (14.0)
Smoking status	
Non-smoker	91 (75.2)
Stopped smoking during pregnancy	23 (19.0)
Smoker during pregnancy	7 (5.8)
Oral exam <1 year	71 (58.7)
Decayed-Missing- Filled Teeth (DMFT ≥1)	106 (87.6)
Periodontitis (CPI 3–4)	57 (47.1)
With profuse Gingival Bleeding (GB ≥20%)	67 (55.4)
Oral hygiene (Plaque index ≥ 10%)	63 (52.1)
Onset of labor	
Spontaneous	69 (57.0)
Induced	42 (34.7)
Cesarean	10 (8.3)
Pregnancy complications <sup>a</sup>	41 (33.9)
Gestational diabetes	20 (16.5)
Iron supplementation	56 (46.3)
Infectious episode during pregnancy	27 (22.3)
Type of infection	
Vaginal	14 (51.9)
Urinary	5 (18.5)
Other	8 (29.6)

(Continues)

**TABLE 1** (Continued)

Characteristics, n (%)	121 (100)
Mode of delivery	
Vaginal	106 (87.6)
Cesarean section	15 (12.4)
Gestational age at delivery ≥37 weeks	112 (92.6)
Birthweight ≥2500 g	112 (92.6)

<sup>a</sup>Pregnancy complications include at least one of these criteria: intrauterine growth retardation, obstetric hemorrhage, premature rupture of the membrane, risk of preterm delivery, preeclampsia.

overweight or obese (BMI > 25 kg/m<sup>2</sup>). Among the 121 women, only seven (5.8%) declared that they were still active smokers; the others were either non-smokers (75.2%) or former smokers (19.0%) who had stopped smoking at the onset of their pregnancy.

As far as their oral health was concerned, 58.7% had been to the dentist less than a year ago. Mean DMFT was 5.4 (±4.7), 87.6% had at least 1 DMFT ≥1, and 47.1% had periodontitis; 55.4% also displayed profuse GB and 52.1% of them had insufficient oral hygiene.

The onset of labor was spontaneous for 69 women (57.0%), whereas 42 women (34.7%) had to have induced labor. A total of 41 women (33.9%) had pregnancy complications such as preeclampsia, premature rupture of the membrane, intrauterine growth retardation, obstetric hemorrhage or risk of preterm delivery, and 20 (16.5%) developed gestational diabetes. Also, 56 (46.3%) needed iron supplementation and probably suffered from anemia and 27 (22.3%) presented with an infectious episode during their pregnancy. The vast majority of the women gave birth at or after 37 weeks of amenorrhea (92.6%). Most of the children were delivered vaginally (87.6%) and weighed ≥2500 g (92.5%).

The results reported in [Table 2](#) compare general, oral and pregnancy outcome characteristics of women with minimal (44.6%) or profuse (55.4%) GB. Women with minimal GB were significantly more often working during pregnancy (66.7%) compared with those with profuse GB (47.0%;  $p = 0.04$ ); in contrast, 23.9% of the women with profuse GB had no professional qualifications or were unemployed at the time of their pregnancy, compared with 11.1% with minimal GB. Women with minimal GB were more often primiparous (63.0%) compared with those with profuse GB (44.8%). The oral hygiene (PI) seemed better in the group of women with minimal GB than women with profuse GB (20.4% vs 77.5%,  $p < 0.001$ ). Interestingly, 19 women (35.2%) with minimal GB vs 56.7% with profuse GB suffered from periodontitis ( $p = 0.02$ ). Finally, when comparing both groups as far as pregnancy course and outcomes, women with profuse GB developed significantly more gestational diabetes (23.9%) than did those without isolated and minimal bleeding (7.4%;  $p = 0.02$ ). No other significant differences were found between the two groups.

[Table 3](#) shows, for both groups of women with minimal and with profuse GB, the characteristics according to the absence or presence of periodontitis.

**TABLE 2** General sociodemographic, oral and pregnancy characteristics and outcomes of women with minimal and with profuse gingival bleeding (GB).

Characteristics, n (%)	With minimal GB 54 (44.6)	With profuse GB 67 (55.4)	p Value
<b>Age</b>			
<25 years	8 (14.8)	7 (10.4)	0.68
25–34 years	32 (59.3)	44 (65.7)	
≥35 years	14 (25.9)	16 (23.9)	
Nationality French	43 (79.6)	41 (61.2)	<b>0.03</b>
Matrimonial status (married or living as a couple)	52 (96.3)	63 (94.0)	0.69
<b>Socio-professional category</b>			
Farmer	1 (1.8)	0	0.19
Craftsmen, trader and entrepreneur	6 (11.1)	5 (7.4)	
Manager and higher intellectual profession	7 (13.0)	4 (6.0)	
Intermediate occupation	18 (33.3)	15 (22.4)	
Employee	13 (24.1)	23 (34.3)	
Worker	3 (5.6)	4 (6.0)	
Retiree	0	0	
Other /unemployed	6 (11.1)	16 (23.9)	
Active worker (working during pregnancy)	36 (66.7)	31 (47.0)	<b>0.04*</b>
Primiparous	34 (63.0)	30 (44.8)	0.06
<b>BMI before pregnancy</b>			
≤25 kg/m <sup>2</sup>	38 (70.4)	39 (58.2)	0.47
25 < BMI < 30 kg/m <sup>2</sup>	11 (20.4)	16 (23.9)	
≥30 kg/m <sup>2</sup>	5 (9.2)	12 (17.9)	
<b>Smoking status</b>			
Non-smoker	42 (77.8)	49 (73.1)	0.89
Stopped smoking during pregnancy	9 (16.7)	14 (20.9)	
Smoker during pregnancy	3 (5.5)	4 (6.0)	
Oral exam <1 year	36 (66.7)	35 (52.7)	0.13
Decayed-Missing-Filled Teeth (DMFT ≥1)	47 (87.0)	59 (88.1)	>0.99
Oral hygiene (Plaque index ≥10%)	11 (20.4)	52 (77.5)	<b>&lt;0.001**</b>
Periodontitis (CPI 3–4)	19 (35.2)	38 (56.7)	<b>0.02*</b>
Gestational diabetes	4 (7.4)	16 (23.9)	<b>0.02*</b>
Iron supplementation	26 (48.1)	30 (44.8)	0.71
Infectious episode during pregnancy	49 (90.7)	65 (97.0)	0.19
Pregnancy complications <sup>a</sup>	18 (33.3)	23 (34.3)	>0.99
<b>Onset of labor</b>			
Spontaneous	33 (61.1)	36 (53.7)	0.75
Induced	17 (31.5)	25 (37.3)	
Cesarean	4 (7.4)	6 (9.0)	
<b>Mode of delivery</b>			
Vaginal	49 (90.7)	57 (85.1)	0.41
Cesarean	5 (9.3)	10 (14.9)	
Gestational age at delivery ≥37 weeks	51 (94.4)	61 (91.0)	0.73
Birthweight ≥2500 g	52 (96.3)	60 (89.5)	0.42

<sup>a</sup>Pregnancy complications include at least one of these criteria: intrauterine growth retardation, obstetric hemorrhage, premature rupture of the membrane, risk of preterm delivery, preeclampsia.

\* $p < 0.05$ ; \*\* $p < 0.001$ .

**TABLE 3** General sociodemographic, oral and pregnancy characteristics and outcomes of the women presenting with minimal and profuse gingival bleeding (GB) according to their periodontal status (with or without periodontitis).

Characteristics, n (%)	With minimal GB 54 (44.6)		p Value	With profuse GB 67 (55.4)		p Value
	No periodontitis	Periodontitis		No periodontitis	Periodontitis	
Age						
<25 years	5 (14.3)	3 (15.8%)	0.31	6 (20.7)	1 (2.6)	0.05*
25–34 years	23 (65.7)	9 (47.4)		18 (62.1)	26 (68.4)	
≥35 years	7 (20.0)	7 (36.8)		5 (17.2)	11 (29.0)	
Nationality French	28 (80.0)	15 (78.9)	>0.99	18 (62.1)	23 (60.5)	>0.99
Matrimonial status (married or living as a couple)	34 (97.1)	18 (94.7)	>0.99	28 (96.5)	35 (92.1)	0.62
Active worker (working during pregnancy)	23 (65.7)	13 (68.4)	>0.99	15 (53.6)	16 (42.1)	0.45
Primiparous	22 (62.9)	12 (63.2)	>0.99	16 (55.2)	14 (36.8)	0.14
BMI before pregnancy						
≤25 kg/m <sup>2</sup>	26 (74.3)	12 (63.2)	0.52	20 (69.0)	19 (50.0)	0.06
25 < BMI < 30 kg/m <sup>2</sup>	6 (17.1)	5 (26.3)		5 (17.2)	11 (28.9)	
≥30 kg/m <sup>2</sup>	3 (8.6)	2 (10.5)		4 (13.8)	8 (21.1)	
Smoking status						
Non-smoker	28 (80.0)	14 (73.7)	0.86	23 (79.3)	26 (68.4)	0.61
Stopped smoking during pregnancy	5 (14.3)	4 (21.0)		5 (17.2)	9 (23.7)	
Smoker during pregnancy	2 (5.7)	1 (5.3)		1 (3.5)	3 (7.9)	
Oral exam <1 year	25 (71.4)	11 (57.9)	0.37	13 (44.8)	22 (57.9)	0.33
Decayed missing and filled Teeth (DMFT ≥ 1)	30 (85.7)	17 (89.5)	>0.99	23 (79.3)	36 (94.7)	0.06
Oral hygiene (Plaque index ≥ 10%)	4 (11.4)	7 (36.8)	0.03*	20 (69.0)	32 (84.2)	0.15
Gestational diabetes	3 (8.6)	1 (5.3)	>0.99	4 (13.8)	12 (31.6)	0.14
Iron supplementation	13 (37.1)	13 (68.4)	0.04*	10 (34.5)	20 (52.6)	0.21
Infectious episode during pregnancy	6 (17.1)	3 (15.8)	>0.99	10 (34.5)	8 (21.0)	0.27
Pregnancy complications <sup>a</sup>	12 (34.3)	6 (31.6)	>0.99	12 (41.4)	11 (28.9)	0.31
Gestational age at delivery ≥ 37 weeks	2 (5.7)	1 (5.3)	>0.99	3 (10.3)	3 (7.9)	>0.99
Birthweight ≥ 2500 g	34 (97.1)	18 (94.7)	0.58	24 (82.76)	36 (94.7)	0.24

<sup>a</sup>Pregnancy complications include at least one of these criteria: intrauterine growth retardation, obstetric hemorrhage, premature rupture of the membrane, risk of preterm delivery, preeclampsia.

\* $p < 0.05$ .

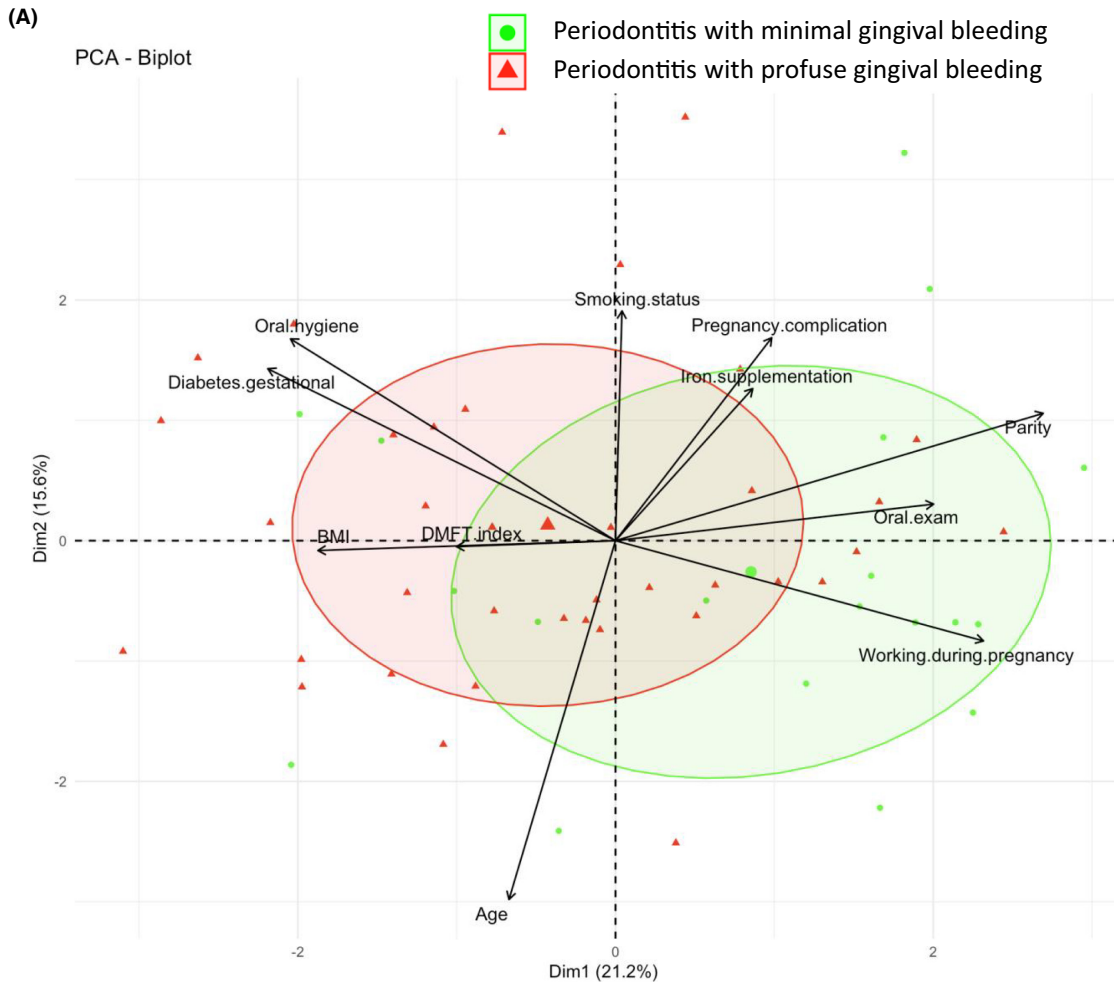
Among the 54 women with minimal GB, 19 (35.2%) suffered from periodontitis. Women without periodontitis had a better oral hygiene than those with periodontitis (88.6% vs 63.2%,  $p = 0.03$ ). As far as their general health was concerned, women with periodontitis needed more iron supplementation during pregnancy compared with those without periodontitis (68.4% vs 37.1%,  $p = 0.04$ ).

Among the 67 women with profuse GB, 38 (56.7%) suffered from periodontitis. Compared with those without periodontitis, women with periodontitis were more often ≥35 years old (29.0%,  $p = 0.05$ ), multiparous (63.2%,  $p = 0.14$ ) and overweight or obese (28.9% and

21.1%, respectively,  $p = 0.06$ ). Women with periodontitis more frequently had DMFT ≥ 1 (94.7% vs 79.3%,  $p = 0.06$ ) and insufficient oral hygiene (84.2% vs 69.0%,  $p = 0.15$ ). From a medical point of view, 31.6% of women with profuse GB and periodontitis developed gestational diabetes compared with those with profuse GB and no periodontitis (13.8%,  $p = 0.14$ ).

Finally, to explore the relation between the sociodemographic and medical parameters of the women with periodontitis, we performed a multivariate analysis by PCA (Figure 2A). The PCA showed that parameters such as oral hygiene, BMI, gestational diabetes, DMFT index, pregnancy complications, iron supplementation,





(B)

Characteristics, n (%)	Periodontitis (n=57)	
	With minimal gingival bleeding 19 (33.3)	With profuse gingival bleeding 38 (66.7)
Age (years)	32.0±6.1	32.0±4.2
Working status during pregnancy (working during pregnancy), n (%)	13 (22.8)	16 (28.1)
Primiparous, n (%)	12 (21.0)	14 (24.6)
BMI before pregnancy (kg/m <sup>2</sup> )	24.5±4.6	26.5±7.5
Smoking status, n (%)		
Non-smoker	14 (24.6)	26 (45.6)
Stopped smoking during pregnancy	4 (7.0)	9 (15.8)
Smoker during pregnancy	1 (1.7)	3 (5.3)
Oral Exam <1 year, n (%)	11 (19.3)	22 (38.6)
Decayed Missing and Filled Teeth (DMFT)	4.1±3.4	7.3±5.9
Oral hygiene (Plaque index ≥10%), n (%)	7 (12.3)	32 (56.1)
Gestational diabetes, n (%)	1 (1.7)	12 (21.0)
Iron supplementation, n (%)	13 (22.8)	20 (35.1)
Pregnancy complications*, n (%)	6 (10.5)	11 (19.3)

FIGURE 2 Association between periodontitis and gingival bleeding. (A) Principal component analysis (PCA) to explore the relations between periodontitis and the importance of gingival bleeding (minimal or profuse). (B) Clinical, behavior and sociodemographic characteristics of women with periodontitis.

parity, oral exam and working during pregnancy seem to have an influence on periodontitis. When visualizing the PCA biplot, two sample groups seem to emerge, separated by the first dimension, which is highly correlated with the variables: oral exam, working during pregnancy, BMI and DMFT Index. Figure 2B presents the different characteristics evaluated according to the importance (minimal or profuse) of GB among the patients with periodontitis.

Insufficient oral hygiene, BMI >25 kg/m<sup>2</sup> and presence of gestational diabetes seem to be particularly associated with a group of women with profuse GB, whereas primiparity, oral exam and working during pregnancy seem to be associated with a group of women with minimal GB. However, age, smoking status, pregnancy complication and iron supplementation were highly correlated with the second axis and seemed to influence both groups equally.

## 4 | DISCUSSION

We examined the oral and periodontal health of pregnant women in the first trimester and the course and outcome of their pregnancies. The main finding was that almost half of the women (47.1%) were affected by periodontitis and 55.4% presented profuse GB. However, more than a third (35.2%) of the 54 pregnant women with minimal GB had periodontitis which would probably not have been diagnosed, as they did not present exterior signs of periodontal disease such as profuse GB. Even though periodontal disease assessment was done using the CPI index, which consists of a partial mouth screening and thus potential underestimation of periodontal disease, studies have shown that the risk is reduced.<sup>37</sup> When comparing the different groups of women with periodontitis, those with minimal and with profuse GB, two different profiles seemed to emerge. The first profile was characterized by the presence of profuse GB and was associated with poor oral health as assessed by the DMFT score and plaque index and a higher BMI before pregnancy, and a greater tendency to develop gestational diabetes. The second profile was characterized by isolated and minimal GB, and was associated with good oral hygiene, primiparity, a recent oral examination (<1 year) and maintaining professional activity.

The strength of our longitudinal study lies in the fact that only few studies describe such a complete oral and periodontal health status of pregnant women in the first trimester.<sup>38</sup> Also, even though this study was conducted in a public hospital, it is fairly similar in terms of sociodemographic characteristics and pregnancy course and outcomes to the French national perinatal epidemiological representative survey.<sup>39</sup>

The major limitations in our work are the small sample size of 121 pregnant women and insufficient statistical power. This limited number of participants is partly due to the population selection criteria because the PERISCOPE study was an ancillary study of DROP. Overall, the data on 29.7% (121 women) of the 407 DROP patients who agreed to participate, were included in PERISCOPE and analyzed. The others were not included for different reasons: 14.2%

refused to participate and some women declared that they had just visited their dentist and did not sign the non-opposition consent form. Also, oral examination of the women was conducted in the first trimester when they came for a full checkup and sonography. The duration of this first trimester appointment was sometimes incompatible with adding an oral health exam. Finally, some women were not included in the study due to communication difficulties or because they did not meet PERISCOPE inclusion criteria.

Given the profound hormonal, microbiota, immune and clinical perturbations during pregnancy, it is expected that these modifications can affect the periodontium and that, conversely, chronic periodontal infection can disturb the course and outcome of pregnancy.<sup>3,40</sup> The percentage of pregnant women with periodontitis varies significantly in the literature from 0.6% to 47.0% and seems to depend on sociodemographic and environmental factors, but also on the stage of pregnancy.<sup>41-45</sup> GB is usually associated with an increased PI in the first trimester of pregnancy compared with the second and third trimesters, and some authors have suggested that it could come from vomiting and the difficulties maintaining good oral hygiene.<sup>46,47</sup> However, gingival symptoms may be aggravated during pregnancy independently of the PI due to a higher susceptibility of the periodontium to pregnancy-related hormones, thus increasing the risk of developing periodontal disease (ie gingivitis and periodontitis).<sup>5,40</sup>

Even though the number of participants included in our study is low and does not give the analysis sufficient statistical power, it still seems to show a tendency for two different profiles of pregnant women, ie those with minimal and with profuse GB. When correlating the results of PCA and sample distribution, two groups with periodontitis seem to emerge: the first with profuse GB associated with the already known periodontal risk factors – poor oral health (characterized by higher DMFT index and plaque index), a higher BMI and risk of developing gestational diabetes – and the other with minimal GB associated with good oral hygiene, primiparity, recent oral examination (<1 year) and maintaining a professional activity. Two main biological mechanisms link periodontal diseases and APO. Both can affect the fetal-placental unit either directly, through oral microbiota dissemination via the bloodstream or the genitourinary tract, or indirectly, by the inflammatory mediators produced in response to periodontopathogens that increase systemic low-grade inflammation.<sup>9,48</sup> Another factor of importance to consider, even if it affected both groups equally, is the iron supplementation medication during the course of pregnancy, considered as a proxy for anemia. Anemia is a leading cause of APOs<sup>49</sup> and chronic periodontitis can also result in anemia. Iron deficiency may also affect the periodontium by disturbing the host defense by producing reactive oxygen species.<sup>50</sup> Women with iron deficiency seem to have more severe periodontitis, especially non-smoking women, who correspond to the majority of the participants of PERISCOPE.<sup>51,52</sup> due to the lack of exterior clinical signs regularly associated with periodontitis; in the group of women with isolated and minimal GB, periodontal disease would remain undiagnosed without thorough periodontal and oral health examination. These preliminary results

need to be confirmed in a larger population in which not only oral and periodontal health status is clinically assessed but also biological samples of saliva and periodontal crevicular fluid could be analyzed. Also, it would be interesting to evaluate nutritional behavior changes in this particular population, since they can also affect oral and general health.<sup>53-55</sup> This additional information could confirm the two groups that tended to emerge from our study even though the number of participants was low and some analyses were non-significant.

Dental care, especially preventive and restorative dentistry, can be provided to pregnant women safely, even if many dentists are still reluctant to do so.<sup>56</sup> Unfortunately, the awareness of non-dental healthcare professionals concerning oral complications associated with pregnancy seems insufficient.<sup>57</sup> In addition, many pregnant women still consider GB a common oral manifestation and do not seek professional care when confronted with it, leading to delayed diagnosis and treatment.<sup>58,59</sup> As far as periodontal treatment is considered, there is insufficient evidence that it reduces APOs when administered usually during the second and third trimester of pregnancy, as, due the different study designs and timing of intervention during pregnancy, it is often considered too late for periodontal treatment and healing.<sup>60-63</sup> Given that APOs are usually diagnosed in the second trimester and that periodontal inflammation and oral complications increase in the course of pregnancy, early diagnosis seems essential.<sup>64</sup> Based on pathophysiology, the lack of evidence should not undermine the hypothesis that early periodontal diagnosis and treatment during the first trimester or even prior to conception could play a role in effectively reducing conception difficulties and obstetrical complications as well as progression and aggravation of periodontal.<sup>65,66</sup>

As previously suggested, these findings further highlight the importance of preconception preventive oral assessment and healthcare.<sup>67-69</sup> As gynecologists still rarely refer their patients to the oral health professional in the preconception period,<sup>70</sup> several countries have included oral health consultations in their pregnant women healthcare programs. In France, since 2013, national healthcare insurance provides a free preventive oral check-up during the fourth month of pregnancy and, in Canada, it is recommended at the start of pregnancy and even before. Also, simplified tools have been developed for non-oral health professionals, such as the Maternal Oral Screening (MOS) tool, and have been proven efficient in identifying poor oral health.<sup>71</sup>

## 5 | CONCLUSION

GB, periodontal diseases as well as caries are non-communicable, preventable and treatable diseases. Left undiagnosed they can have multiple consequences on oral and general health as well as impact wellbeing and quality of life of pregnant women. Simple oral manifestations like GB should not be ignored during pregnancy and should lead to immediate oral health check-up. However, as shown in our study, pregnant women who do not

complain of such signs should also undergo preventive oral examination. For that matter, behavioral and educational counseling on oral health during pregnancy has proven to be efficient in preventing and improving periodontal health status.<sup>72</sup> Finally, since periodontal diseases can be responsible for low-grade systemic inflammation, future studies should focus on the importance and impact, even during preconception, of early oral and periodontal biological and clinical assessment, treatment and the course and outcome of pregnancy.

## AUTHOR CONTRIBUTIONS

Charlotte Thomas contributed in carrying out the oral exams, analyzing and writing up of the work. Inessa Timofeeva and Elyes Bouchoucha contributed in planning and carrying out the oral exams. Thibault Canceill, Camille Champion and Catherine Arnaud contributed in analyzing and writing up of the work. Marion Groussolles contributed in planning the study. Christophe Vayssière contributed in planning and writing up of the work. Cathy Nabet and Sara Laurencin-Dalieux contributed in the conception, planning, analyzing and writing up of the work. All authors accept responsibility for the paper as published.

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## CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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