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Relation of salivary antioxidant status and cytokine levels to clinical parameters of oral health in pregnant women with diabetes

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ABSTRACT

Objective: Both pregnancy and diabetes are thought to predispose to the impairment of oral health. As saliva contributes to oral homeostasis, we have characterised its properties and flow rate in pregnant women with or without diabetes.

Design: Unstimulated whole mixed saliva was collected from 63 women in the first trimester of pregnancy and analysed for the concentration of selected antioxidants, cytokines, and growth factors.

Results: Pregnant women with diabetes were found to have markedly increased indexes of caries activity, plaque formation, gingival and periodontal status, as well as increased salivary antioxidant capacity and pro-inflammatory cytokine levels. These changes were more pronounced in patients with long-term disease and systemic diabetic complications, but only partly correlated with the level of blood glycated haemoglobin. Of the cytokines examined, salivary VEGF and HGF concentrations in diabetic pregnant women correlated in a positive and negative manner, respectively, with the prevalence of caries. Moreover, VEGF levels in this group correlated inversely with the probing depth and clinical attachment levels. All such associations did not occur in healthy individuals. In contrast, the salivary pH and flow rate correlated inversely with several parameters of caries and plaque formation irrespectively of whether the pregnant women were diabetic or not.

Conclusions: Diabetes in pregnant women significantly changes saliva properties, which may contribute to accelerated deterioration of the oral status in this population.

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Abbreviations: API, approximal plaque index; CAL, clinical attachment level; DM, diabetes mellitus; DMF-T, caries prevalence index (decayed, missing, and filled teeth); DMF-S, caries prevalence index (decayed, missing, and filled surfaces); GI, gingival index; G-CSF, granulocyte-colony stimulating factor; GROα, growth related oncogene α; HbA_{c1}, glycated haemoglobin; HGF, hepatocyte growth factor; IL, interleukin; IL-6sR, interleukin-6 soluble receptor; MCP-1, monocyte chemoattractant protein-1; PL-I, plaque index; PD, probing depth; SBI, sulcus bleeding index; SDF-1, stromal-derived factor-1; sICAM-1, soluble intercellular adhesion molecule-1; SOD, superoxide dismutase; TNFα, tumour necrosis factor α; TNF-R, tumour necrosis factor receptor; VEGF, vascular endothelial cell growth factor.

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1. Introduction

Pregnancy-associated physiological changes are thought to predispose to the impairment of oral health. The most frequent alterations have been reported to occur in the gingiva and saliva and included an increased prevalence and severity of gingivitis, and a decrease in salivary pH and its buffering capacity (see Ref. 1 for review). These changes are partly attributed to sex hormone-mediated effects on the vasculature in the gingival tissue and salivary glands. Clinical signs of gingivitis may appear as early as in the 2nd month of pregnancy whilst the salivary pH decreases towards late pregnancy. The impact of pregnancy on dental health is less clear. It is feared, however, that pregnancy may increase the risk of caries development by increasing or modifying the gingival and cariogenic flora, and by decreasing salivary pH.[1]

Also diabetes mellitus is linked with increased incidence of several oral conditions, including periodontal disease, salivary gland dysfunction, stomatitis, glossitis, and possibly dental caries (reviewed in Ref. 2,3). The mechanism by which diabetes promotes these abnormalities is probably multifactorial and most likely related to increased oxidative stress, compromised host defence, chronic systemic inflammation, vasculopathy, and impaired salivary secretion.

All the above alterations may have a cumulative effect in pregnancy associated with diabetes. Therefore pregnant diabetic women may be at increased risk of accelerated deterioration of oral health. However, only few studies assessed the oral status of this population. And, indeed, they detected an increased incidence of periodontal disease[4–6] and dental caries[7] in pregnant diabetics.

The antioxidant capacity of saliva contributes largely to the protection of teeth and oral mucosa against oxidative stress.[8] In this respect, it has been demonstrated that both pregnancy and periodontitis may decrease the antioxidant capacity of saliva and gingival crevicular fluid.[9,10] In addition to maintaining oral homeostasis, saliva has recently been gaining increasing attention as a diagnostic fluid.[11,12] As a result, several salivary components have been proposed to serve as biomarkers for monitoring both periodontal and systemic disease.[13–16] Interestingly, a recent proteomic analysis identified many potential targets in the saliva from patients with diabetes.[17]

In the present study we have characterised the antioxidant system and cytokine levels in saliva from pregnant women with or without diabetes. We have sought to verify the hypothesis that differences in the properties of saliva may correspond to the parameters of oral health in these patients.

2. Methods

2.1. Patients

Sixty-three women aged 20–30 years in the first trimester of pregnancy were examined. Thirty-three women were healthy and 30 women had diabetes that was classified according to White (Table 1). The classification is based on the duration of diabetes and the presence of severe diabetic complications. Class A refers to diabetes that began during pregnancy, whilst classes B, C, and D correspond to diabetes that existed before pregnancy and lasted for <10 years, 10–19 years, and >20 years, respectively. Other classes indicate the occurrence of diabetic retinopathy (R), nephropathy (F) or the combination thereof (R/F).

The study was reviewed and approved by the local ethics committee (decision no. 1189/06) and all participants gave their written informed consent. None of the women recruited smoked or received iron supplementation.

Table 1 – Basic haematologic and oral health parameters in pregnant women with and without diabetes. The data are presented as medians (and interquartile ranges). Asterisks represent significant differences compared with the controls. The hash sign represents a significant difference compared to the group ABC.

	Controls ($n = 33$)	Group ABC ($n = 13$)	Group DFR ($n = 17$)	Anova p-value	Test power
The White classification	–	A-2; B-5; C-6	D-6; R-8; RF-3		
Basic haematology					
Haemoglobin (mM)	8.4 (7.7–9.2)	7.8 (7.3–8.4)	7.7 (7.0–8.1)*	0.0095	80%
Haemoglobin A_{1c} (%)	n.d.	7.2 (6.2–8.1)	8.8 (8.1–9.4)$^{\#}$		
Haematocrit (%)	39 (38–44)	37 (34–40)*	37 (33–39)**	0.0019	80%
Erythrocytes ($\times 10^6/\mu l$)	4.30 (4.15–4.70)	4.32 (3.96–4.54)	4.12 (3.90–4.19)**	0.0039	70%
Leukocytes ($\times 10^3/\mu l$)	7.40 (6.75–8.80)	10.00 (7.35–13.05)*	9.90 (8.20–12.15)**	0.0010	95%
Platelets ($\times 10^3/\mu l$)	225 (198–293)	246 (178–289)	260 (216–317)	0.2253	–
Oral health parameters					
DMF-T	11 (7–19)	14 (8–17)	16 (12–23)*	0.0221	95%
DMF-S	15 (10–25)	32 (13–49)	35 (18–55)**	0.0010	95%
PL-I	0.50 (0.40–0.92)	1.00 (0.63–1.35)	1.33 (1.07–1.63)***	0.0004	50%
API (%)	40 (30–55)	70 (58–84)**	77 (70–90)***	0.0001	95%
SBI (%)	50 (37–66)	65 (47–73)	65 (56–76)*	0.0354	95%
GI	0.96 (0.60–1.35)	1.50 (0.80–1.90)	1.70 (0.85–2.00)*	0.0227	90%
PD (mm)	3.0 (2.5–3.6)	3.0 (2.6–4.0)	3.3 (2.8–3.8)	0.5557	–
CAL (mm)	1.8 (1.3–1.9)	4.7 (3.3–5.8)***	4.5 (3.6–5.1)***	0.0001	95%

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
$^{\#}$ $p < 0.05$.