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Correlation Between Periodontal Health Status with Some Salivary Inflammatory Biomarkers in Pregnant and Lactating Women

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ABSTRACT

Background and Objectives: Periodontal health may be influenced by the hormonal and immunological shifts that occur during pregnancy and lactation. This study aimed to assess and compare the periodontal status and salivary concentrations of matrix metalloproteinase 8 (MMP-8) and tumor necrosis factor-alpha (TNF-α) among pregnant, post-partum lactating, and non-pregnant/non-lactating (control) women.

Methods: A case-control study was performed on 90 systemically healthy women, with an average age ranging from 25-35 years, equally divided into pregnant, postpartum lactating, and control groups. Clinical periodontal parameters, including bleeding on probing (BOP), gingival index (GI), probing pocket depth (PPD), and plaque index (PI), were examined, and salivary levels of MMP-8 and TNF-α were assessed via enzyme-linked immunosorbent assay (ELISA).

Results: The mean level of GI, BOP, PPD, MMP-8, and TNF-α were significantly elevated in pregnant women, followed by lactating and control groups, with significant differences between each two groups and among the three groups ($P < 0.001$), except for non-significant differences between lactating and control groups regarding MMP-8 ($P = 1.000$). All the correlations between clinical and inflammatory biomarkers were weak and non-significant (rho < 0.4), whereas a significant negative correlation was found between GI and MMP-8 in the pregnant group (rho = -0.544, p = 0.002).

Conclusion: Pregnancy is associated with increased gingival inflammation and biochemical inflammatory markers, indicating a heightened risk for periodontal disease. Lactating women displayed intermediate changes, emphasizing the need for periodontal monitoring and preventive care throughout the peripartum period.

Keywords: Pregnancy, Periodontal Diseases, Matrix Metalloproteinase 8, Tumor Necrosis Factor-alpha

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INTRODUCTION

Periodontal disease (PD) is a complex infectious condition resulting from the proliferation of pathogenic microorganisms on dental surfaces, which ultimately causes deterioration of the supporting structures.[1] It affects 20-50% of individuals globally, with an increasing burden.[2] PD is associated with several systemic conditions that particularly affect women's health, such as Alzheimer's disease, autoimmune disorders, osteoporosis, cardiovascular disease, infertility, and negative pregnancy outcomes.[3] Previous research has demonstrated a clear association between women's dental health and total systemic wellness, especially during physiological phases such as pregnancy, lactation, and menopause, which can influence immune response and hormonal balance.[4] These stages impact both maternal and child health; for example, maternal periodontal health during pregnancy can influence fetal enamel formation and elevate the risk of early childhood caries.[5] Additionally, researchers reported that maternal gingival inflammation during lactation modifies human milk composition, thereby affecting the infant's gut microbiome and overall well-being.[6]

Pregnancy and lactation are marked by significant hormonal, immune, and metabolic changes, these changes can influence the host response to bacterial plaque, leading to increased susceptibility to gingival inflammation and periodontal disease even in individuals with previously healthy periodontal status.[7] Pregnancy-induced elevations in estrogen and progesterone can enhance vascular permeability and immune reactivity, resulting in pregnancy gingivitis, marked by erythema, edema, and bleeding on probing, even in the presence of minimal plaque accumulation.[8] Although these symptoms typically resolve postpartum, some women may continue to experience periodontal breakdown during lactation, as this period is characterized by hormonal adjustments, including reductions in estrogen and progesterone and increases in prolactin, alongside behavioral changes such as diminished attention to oral hygiene due to caregiving responsibilities, even though many inflammatory symptoms typically resolve post-childbirth.[9] Research indicates that although postpartum periodontal health improves, it may not fully revert to preconception levels.[10]

Saliva is widely acknowledged as a diagnostic fluid that is non-invasive, revealing both local and general inflammatory responses.[11] Biomarkers were recognized as vital indications of periodontal inflammation and tissue destruction.[12,13] MMP-8, primarily released by neutrophils, degrades type I collagen and shows elevated levels during pregnancy.[14] Similarly, TNF-α is a central inflammatory cytokine found in increased concentrations in pregnant women with PD.[15,16]

While several studies have examined periodontal changes during pregnancy,[4,17] few have orderly compared these changes across different physiological stages of pregnancy, postpartum lactation, and non-pregnant/non-lactating states, particularly with the use of salivary biomarkers as diagnostic tools. Therefore, the objective of this research was to evaluate and contrast clinical periodontal and salivary levels of inflammatory biomarkers (MMP-8 and TNF-α) among pregnant, postpartum lactating, and non-pregnant non-lactating (control) women groups, to improve the knowledge of the influence of reproductive phases on periodontal inflammation.

METHODS

Study Design and Setting

A case-control study was carried out in Erbil, Kurdistan Region- Iraq, between October 2024 and April 2025. Pregnant participants were recruited from individuals attending the Maternity Teaching Hospital and Tarin Health Center for routine antenatal care, while post-partum lactating participants were selected from mothers presenting for infant vaccination. The study was approved by the Scientific Ethics Committee of the College of Dentistry - Hawler Medical University (Ethical approval No: 2425056) before the conduction of the study.

Study Population

Ninety systemically healthy women with the mean ages of 29.3± 5.3 years were categorized into three groups: the first group comprised thirty non-pregnant/non-lactating married women and was considered as control group; the second group included thirty pregnant women in their second trimester (approximately 13–26 weeks of gestation); and the third group involved thirty breastfeeding mothers within the first six months postpartum. All participants met the following inclusion criteria of being female, with an age

ranging from 25–35 years, systemically healthy, and having at least 20 teeth. In addition, healthy periodontium was included in the control group (GI ≤ 0.6, BOP ≤ 10%, PPD ≤ 3 mm, and CAL=0). Participants were excluded if they had any chronic systemic disease (e.g., diabetes mellitus, cardiovascular disease, autoimmune disorders) or other conditions affecting periodontal health, a history of periodontal therapy within the previous six months, used antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs, or immunosuppressants in the last three months. Demographic details, such as age, occupation, socioeconomic status, as well as oral hygiene habits including brushing frequency and use of adjuncts (mouthwash, floss), were recorded in a questionnaire sheet. Each participant provided informed written consent to sign before the conduction of the study, following the discussion of detailed information regarding the study's objectives and methodologies.

Sample Collection

The participants were directed to refrain from eating for a minimum of 30 minutes before saliva collection. Unstimulated saliva samples were obtained around 9:00 am and 11:00 am, before clinical periodontal examination. Saliva was obtained through the passive drooling technique. Participants were positioned upright with their heads slightly tilted forward, allowing saliva to passively accumulate and drip into a sterilized disposable container. The collection of salivary samples was continued for approximately 2–5 minutes, until a minimum volume of 5 mL was obtained. Saliva samples underwent centrifugation for a duration of 10 minutes at 6000 rpm to get a clean supernatant. The clarified supernatants were aliquoted into sterile microcentrifuge tubes (Sarstedt, Nümbrecht, Germany) and immediately placed on ice. Within one hour of collection, the aliquots were transferred and preserved at -20°C for further examination of MMP-8 and TNF-α using ELISA kits.

MMP-8 and TNF-α analysis

MMP-8 and TNF-α were quantified in saliva using ELISA kits Human MMP-8 ELISA Kit and Human TNF-α ELISA Kit, Sunlong Biotech, China, according to the manufacturer's instructions. For both assays, microplates pre-coated with specific monoclonal antibodies were used. Subsequent to the addition of samples and standards, incubation with either an HRP-conjugated antibody (for TNF-α) or a biotin-labeled detection antibody and streptavidin-HRP (for MMP-8) was done. After washing, tetramethylbenzidine (TMB) substrate was added, colour development proportional to analyte concentration was measured at 450 nm following the addition of the reagent.

Clinical Periodontal Examination

Following salivary sample collection, all participants underwent a comprehensive clinical periodontal examination by single trained examiners. Clinical parameters were assessed at four sites for each tooth with the exception of third molar, three locations for buccal (mesiobuccal / Labial, mid buccal /labial, disto buccal /Labial) and one site for lingual (mid palatal/lingual) using a straight dental explorer for PI and manual Williams periodontal probe (Hu-Friedy, Chicago, IL, USA) for GI, BOP and PPD. The evaluated variables included plaque index,18 gingival index,19, bleeding on probing,20 and probing pocket depth.21

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS, version 26). The Shapiro-Wilk test was used to evaluate normality; non-parametric tests were employed when necessary. The Chi-square test evaluated the proportions of the groups. The Kruskal-Wallis test evaluated mean rankings across the three groups, using Bonferroni post-hoc analysis for pairwise comparisons. The Mann-Whitney test compared two groups. Spearman's rho evaluated correlations. A p-value of ≤ 0.05 was deemed statistically significant.

RESULTS

Clinical Periodontal Parameters in the Studied Groups.

The GI means, median, and mean rank (2.20, 2.23, and 75.5, respectively) of the pregnant women were significantly higher than post-partum lactating group (1.42, 1.47, and 45.5, respectively), and those were significantly higher than the non-pregnant/non-lactating group. All the p-values were highly significant ($p < 0.001$). For PI, the means, median, and mean rank (1.62, 1.59, and 49.67, respectively) of the pregnant women were non significantly higher than the post-partum lactating group (1.56, 1.53, and 47.52, respectively), and those were not significantly higher than the non-pregnant/non-lactating

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group (1.32,1.43, and 39.32, respectively). The differences among the three groups in regard to PI were non-significant (P = 0.269). For BOP, the highest mean percentage of BOP was found among the pregnant group (47.7%), which was significantly higher than that of the lactating group (27.2%) and significantly higher than that of the control group (6.3%). This can be applied to the medians and mean ranks ($p < 0.001$). The same pattern can be observed regarding the PPD, where the highest mean values of PPD were found among pregnant women (4.61mm), followed by the lactating group (4.22mm) and control group (2.00mm), with significant differences among the three groups ($p < 0.001$) as shown in Table 1.

Table 1. Clinical periodontal parameters among pregnant, postpartum lactation and non-pregnant/non-lactating (control) groups

Biomarkers/ Groups	Mean	± SD	Median	Mean Rank	P*	Groups	P**
GI							
A. Control	0.44	0.11	0.44	15.50		AXB	<0.001
B. Pregnant	2.20	0.19	2.23	75.50	< 0.001	AXC	< 0.001
C. Lactating	1.42	0.25	1.47	45.50		BXC	< 0.001
PI							
A. Control	1.32	0.69	1.43	39.32		AXB	
B. Pregnant	1.62	0.78	1.59	49.67	0.269	AXC	N/A
C. Lactating	1.56	0.82	1.53	47.52		BXC	
BOP (%)							
A. Control	6.3	1.9	6.0	16.23		AXB	< 0.001
B. Pregnant	47.7	2.6	48.0	75.50	< 0.001	AXC	< 0.001
C. Lactating	27.2	6.4	27.0	44.77		BXC	< 0.001
PPD (mm)							
A. Control	2.00	0.40	1.95	15.50		AXB	< 0.001
B. Pregnant	4.61	0.16	4.60	74.65	< 0.001	AXC	< 0.001
C. Lactating	4.22	0.14	4.20	46.35		BXC	< 0.001

*Calculated by the Kruskal-Wallis test. **Calculated by Bonferroni post-hoc test.

Inflammatory biomarkers in the studied groups

The mean salivary level of salivary TNF-α in the pregnant women (1.22pg/ml) was significantly higher than postpartum lactation (1.03 pg/ml) and control (0.66 pg/ml) groups ($p < 0.001$). All the differences between the groups were significant ($P < 0.001$). Nearly the same pattern can be applied for the MMP-8, where the highest mean values were significantly found among the pregnant group (1.38 pg/ml), followed by post-partum lactation and control groups (1.03 pg/ml), with significant differences among the three groups ($P< 0.001$), as presented in Table 2.

Table 2. Inflammatory biomarkers in pregnant, non-pregnant/non-lactating (control) and post-partum lactating women groups

Biomarkers/Groups	Mean	± SD	Median	Mean Rank	P*	Groups	P**
TNF-α							
A. Non-pregnant/non-lactating	0.66	0.44	0.87	23.28		AXB	< 0.001
B. Pregnant	1.24	0.23	1.20	66.98	< 0.001	AXC	0.002
C. Lactating	1.03	0.21	1.06	46.23		BXC	0.006
MMP-8							
A. Non-pregnant/non-lactating	1.11	0.15	1.10	35.10		AXB	< 0.001
B. Pregnant	1.38	0.24	1.32	65.10	< 0.001	AXC	1.000
C. Lactating	1.11	0.16	1.09	36.30		BXC	< 0.001

*Calculated by the Kruskal-Wallis test. **Calculated by Bonferroni post-hoc test.

Correlation between the clinical and the inflammatory biomarkers

Table 3 shows that all the rho correlation coefficient values were less than 0.4, indicating weak correlations; in addition that they were not significant, except for the correlation between GI and MMP 8 in the pregnant groups, where there was a significant negative correlation (rho = -0.544, p = 0.002) as presented in Figure 1.

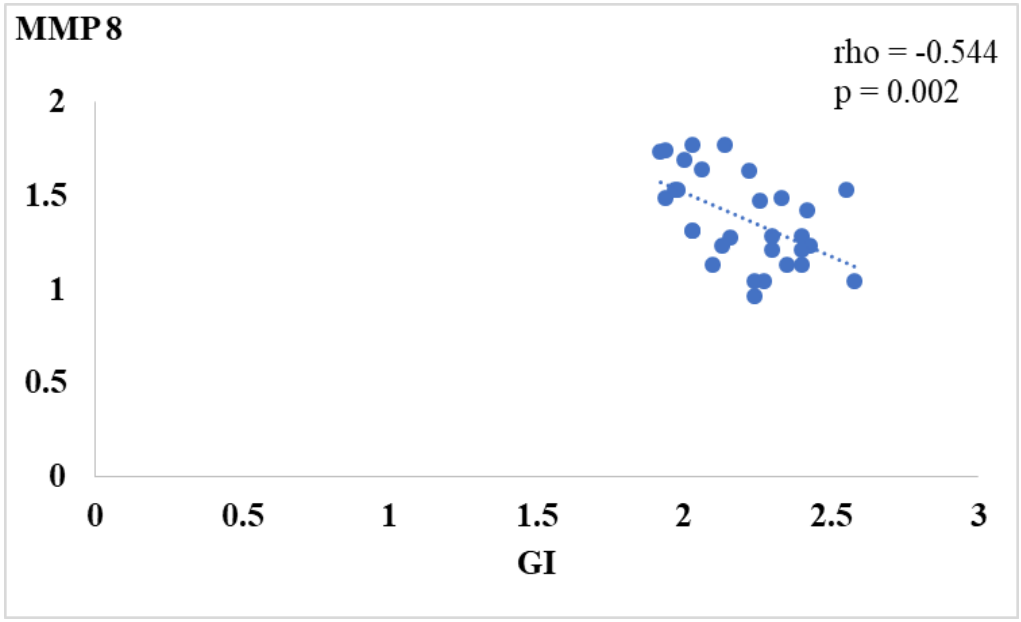

Figure 1. Correlation between MMP-8 and GI among pregnant women

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Table 3. Correlation between the clinical and the inflammatory biomarkers in the three groups

Groups	Variable Y	Variable X	rho	P-value
Control	GI	TNF-α	0.161	0.395
	GI	MMP-8	-0.100	0.597
	PI	TNF-α	0.261	0.163
	PI	MMP-8	0.022	0.906
	BOP %	TNF-α	-0.215	0.254
	BOP %	MMP-8	0.071	0.709
	PPD (mm)	TNF-α	-0.106	0.578
	PPD (mm)	MMP-8	0.313	0.092
Pregnant	GI	TNF-α	0.124	0.514
	GI	MMP-8	-0.544	0.002
	PI	TNF-α	0.323	0.082
	PI	MMP-8	-0.148	0.434
	BOP	TNF-α	0.099	0.603
	BOP	MMP 8	-0.264	0.159
	PPD	TNF-α	-0.017	0.927
	PPD	MMP-8	-0.134	0.481
Lactating	GI	TNF-α	0.069	0.718
	GI	MMP-8	-0.053	0.782
	PI	TNF-α	0.195	0.301
	PI	MMP-8	-0.012	0.952
	BOP	TNF-α	0.260	0.165
	BOP	MMP-8	0.123	0.516
	PPD	TNF-α	0.068	0.719
	PPD	MMP-8	-0.237	0.208

DISCUSSION

Pregnancy and lactation represent unique physiological states marked by substantial metabolic, hormonal, inflammatory, immunological, and nutritional adaptations.[22] Considering the rising incidence of PD in females throughout reproductive phases and the necessity to focus efforts to address this matter, this case-control study investigated periodontal health status throughout clinical periodontal examination and inflammatory biomarker (TNF-α and MMP-8) assessment among pregnant women (in the second trimester), postpartum lactating, and non-pregnant/non-lactating (control) women.

In the current study, pregnant women demonstrated the highest mean values of GI, BOP, and PPD as compared to both post-partum lactating and control groups ($p < 0.001$). This may be due to the hormonal fluctuations during pregnancy that exacerbated gingival inflammation, vascular permeability, and susceptibility to plaque accumulation.[23,24] Similarly, numerous studies reported a higher rate of severe gingivitis occurring throughout pregnancy.[25-27]

In the current study, post-partum lactating women still exhibited periodontal inflammation more than the control group, although less than that noticed in the pregnant group. This may be due to the persistent hormonal influences on periodontal tissue after delivery. Consistent with previous studies reported persistent hormonal effects were reported during early lactation.[28-31] Several studies reported that although gingival inflammation typically improves postpartum, several periodontal markers might stay high in comparison to baseline levels.[17,32,33] These findings suggest that the hormonal milieu during lactation may still influence periodontal tissues, albeit to a lesser extent than during pregnancy.

Regarding GI and BOP, the present study revealed notable variations in GI & BOP among the examined groups, with the pregnant group showing the highest percentage, followed by the postpartum lactating and control groups. Statistically significant differences were observed in all pairwise comparisons. The elevated gingival inflammation during gestation may be attributed to hormonal, immunological, and microbial alterations.[34,35] This finding is consistent with numerous studies reporting significant increases in GI and BOP throughout gestation. [36,37]

In contrast, there was no significant difference in the mean values of PI between and among the three groups ($p = 0.269$), implying similar levels of plaque accumulation observed in the three groups. This finding aligned with previous studies suggested that increased periodontal inflammation during pregnancy and postpartum lactation may not be solely attributed to local factors such as plaque, but systemic variables, especially hormonal shifts, may have a more substantial impact on periodontal health during these phases.[27,38]

Similarly to GI and BOP results, PPD mean values were greatest among the pregnant women, closely followed by postpartum lactating, and control groups ($p < 0.001$), with significant differences between the three groups. Numerous studies have regularly demonstrated that increased levels of PPD in pregnant women. However, this increase was not typically linked to significant clinical attachment loss, implying that the periodontal alterations occurring during pregnancy are predominantly reversible.[39,40] Pregnancy alone does not cause true periodontal pockets in healthy gums; it can worsen existing conditions, potentially leading to or deepening true periodontal pockets.[41] Previous studies reported a significant improvement in gingival health and a reduction in PPD following childbirth.[17,42,43] The present findings revealed that the deepening of periodontal pockets is most likely false pockets caused by gingival inflammation and edema, rather than actual periodontal breakdown.

Biochemically, salivary mean levels of MMP-8 and TNF-α were considerably increased in pregnant women in comparison to both postpartum lactating and control groups ($p < 0.001$). This may be attributed to pregnancy-induced hormonal changes that increase the gingival inflammatory reaction to plaque biofilm and immune activation, resulting in an upregulation of both TNF-α and MMP-8. Consistent with their role as markers of inflammation and periodontal destruction.[44-46] Studies reported elevated MMP-8 and -9 levels of pregnant women as compared to controls,[47] and elevated salivary TNF-α levels in pregnant women with PD in comparison to individuals with a normal periodontal tissue.[48] However, a notable decrease in the average levels of

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both biomarkers was observed in postpartum lactating women as compared to pregnancy, but remained higher than the control group, indicating a partial return but not full recovery of periodontal health.[49,50] Reduction in inflammatory cytokines postpartum might be associated with decreased progesterone levels.[17] A study reported that postpartum women showed elevated MMP-8 values in healthy periodontal and diseased sites, whereas non-pregnant women exhibited increased MM-8 levels only in inflamed pocket sites. The study revealed that in the absence of pregnancy, MMP-8 remains a site-specific marker of periodontal inflammation, while its elevation in healthy sites during pregnancy or lactation might be reflected in hormonal modulation of the inflammatory response.[51]

The correlations between clinical parameters and inflammatory biomarkers were generally weak and statistically non-significant, with the exception of the significant negative correlation between GI and MMP-8 in pregnant women. This can be associated with complex hormone and immunological adaptations during pregnancy that elevate inflammatory biomarkers, regardless of the severity of local periodontal inflammation. The modified immune response, influenced by elevated estrogen and progesterone levels, may affect neutrophil and macrophage function, resulting in an altered inflammatory biomarker that does not directly correlate with clinical manifestations. The variability in salivary composition during pregnancy may further diminish these correlations. Supporting this finding, a systematic review revealed minimal variation in cytokine levels among individuals carrying a child without or with PD, suggesting a potentially modified inflammation reaction during pregnancy.[9] These outcomes highlight the significance of considering physiological changes during pregnancy and lactation in evaluating periodontal health. It is essential to emphasize the necessity for additional research to clarify the mechanisms that underlie these associations.

This study's potential limitations include a very small sample size and the unwillingness of specific individuals to participate, which may impact the generalizability of the results. Furthermore, unmeasured confounding factors such as nutrition, stress, and genetic predisposition could have influenced both periodontal health status and biomarker levels. Variability in salivary composition due to hormonal fluctuations, hydration, and diurnal changes may also have impacted the precision of biomarker measurements.

CONCLUSION

The current study demonstrated that pregnancy significantly exacerbated periodontal inflammation, as evidenced by elevated clinical periodontal variables and salivary concentrations of MMP-8 & TNF-α in comparison to both lactating and non-pregnant women. However, lactating women had intermediate results, indicating a reduction in inflammatory markers following childbirth. The findings support the effects of hormonal and immunological changes throughout pregnancy and early breastfeeding on periodontal health, emphasizing the importance of increased periodontal screening and preventative care throughout these reproductive periods. Additional longitudinal research is required to examine the fundamental processes and repercussions.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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