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Dentistry Section

Estimation of Salivary Advanced Glycation End Products in Polycystic Ovarian Syndrome Patients with and without Chronic Periodontitis: A Cross-sectional Study

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ABSTRACT

Introduction: Polycystic Ovarian Syndrome (PCOS), formerly known as Stein-Leventhal syndrome, is a common hormonal disorder associated with chronic low-grade inflammation, oxidative burden and insulin resistance. Many studies have reported that PCOS negatively impacts periodontal health, resulting in the worsening of chronic periodontitis. Chronic periodontitis, an inflammatory condition, is one of the most prevalent oral diseases affecting the supporting tissues of the teeth. Oxidative burden plays a crucial role in the pathophysiology of both conditions.

Aim: To evaluate and compare the salivary levels of Advanced Glycation End products (AGEs), which are markers of oxidative stress, in patients with PCOS, both with and without chronic periodontitis.

Materials and Methods: A cross-sectional study was conducted at the Department of Periodontology, Sri Ramachandra Dental College and Hospital, Chennai, Tamil Nadu, India between July 2023 and January 2024, with 48 women aged 18-35 years, divided into four groups: healthy controls (H+H), systemically healthy with periodontitis (H+P), PCOS with a healthy periodontium (PCOS+H) and PCOS with periodontitis (PCOS+P). Periodontal clinical parameters, including Oral Hygiene Index Simplified (OHI-S), Probing Pocket Depth (PPD), Clinical Attachment Loss (CAL), Bleeding On Probing (BOP) and Periodontal Inflamed Surface Area (PISA), were recorded. Salivary AGEs levels were measured using an Enzyme-linked Immunoassay (ELISA) kit. Statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) software.

Results: The PCOS+P group exhibited the highest levels of salivary AGEs (72.28±4.76 pg/mL) and clinical parameters, followed by the H+P (63.46±9.87 pg/mL) and PCOS+H (62.87±6.91 pg/mL) groups. A significant correlation was observed between the PISA scores and AGE levels for all groups, with a moderately positive correlation for the PCOS+H group ($r=0.765$, $p<0.01$). There was no significant difference ($p=1.000$) in AGE levels between the H+P and PCOS+H groups, suggesting independent contributions of each condition to systemic AGE levels.

Conclusion: Salivary AGE levels were markedly elevated in patients with both PCOS and chronic periodontitis, suggesting a synergistic effect. The present study also highlights that PCOS and periodontitis independently contribute to oxidative stress, even in the absence of the other. These findings support the use of salivary AGEs as potential biomarkers of periodontal inflammation in patients with PCOS.

Keywords: Biomarkers, Hormonal disorder, Oxidative stress, Salivary biomarkers

INTRODUCTION

Polycystic Ovarian Syndrome (PCOS), formerly known as Stein-Leventhal syndrome [1], is a prominent heterogeneous condition affecting women of reproductive age, with a pooled prevalence of 5.8% in 2022 [2], according to the National Institutes of Health (NIH) criteria [3] and 11.34% in 2022 [2] based on the Rotterdam criteria [4] in the Indian population. PCOS is a multifactorial condition marked by clinical and biochemical features, including menstrual cycle irregularities such as oligomenorrhoea or amenorrhoea, hyperandrogenism and the presence of polycystic ovaries evidenced in ultrasound scans.

In addition to reproductive implications, PCOS is frequently associated with chronic low-grade inflammation, oxidative stress and insulin resistance—factors that are also involved in the etiology of periodontitis [5]. Periodontal disease is a widespread immunoinflammatory condition of the oral cavity that causes inflammation of the supporting tissues of the tooth, leading to alveolar bone resorption and, ultimately, tooth loss. The paradigm shift in the etiology and pathogenesis of periodontal disease asserts that periodontopathic microorganisms primarily initiate periodontitis, while the abnormal host response is crucial to the disease's progression [6].

Evidence based on various studies [7-9] shows that periodontal disease has been linked to diabetes, cardiovascular disease and other systemic conditions. Recently, a significant association has been established between periodontal disease and PCOS, suggesting shared mechanisms and bidirectional influences between these conditions [10].

Multiple systematic reviews and meta-analyses have consistently highlighted a positive bidirectional interplay between PCOS and periodontal diseases [11-15]. Dursun E et al., (2011) first documented a possible relationship between these two conditions [16]. According to a meta-analysis in 2020, women with PCOS have a 28% higher likelihood of developing periodontitis, whereas periodontal disease increases the risk of developing PCOS by 46% [11]. Hormonal imbalances and metabolic disturbances associated with PCOS may alter the composition of the oral microbiota [17,18] and increase the host's vulnerability to periodontal diseases. Moreover, both conditions share environmental and genetic predispositions as risk factors [10].

One of the key proinflammatory molecules found at higher levels in both PCOS and periodontitis is AGEs, which are a diverse family of bioactive molecules produced endogenously via the non enzymatic glycation of proteins and lipids through a multistep chemical process called the Maillard reaction [19]. In addition, exogenous AGEs, known as glycotoxins, are present in a diet high in cooked fast food [19]. The binding of AGEs to their corresponding receptors (RAGE) activates downstream signaling pathways, leading to an increase in proinflammatory cytokines and tissue destruction [20].

Recent systematic reviews have reported an increase in AGE deposition and RAGE activation in both normoglycaemic and hyperglycaemic patients with chronic periodontitis [21,22]. However, to the best of the authors knowledge, no study has explored salivary AGEs levels in periodontitis patients suffering from PCOS. Therefore, The present study aimed to estimate and compare the salivary levels of AGE products in healthy individuals and in patients with PCOS and periodontitis.

MATERIALS AND METHODS

Study population: The present cross-sectional study was conducted at the Department of Periodontology, Sri Ramachandra Dental College and Hospital, Chennai, Tamil Nadu, India, conducted between July 2023 and January 2024, received ethical clearance (CSP/23/JUL/131/585) from the Institutional Review Board of of the study Institute.

Sample size calculation: A total of 48 age-matched participants, divided equally into four groups (12 per group), were included based on a sample size calculation (N=48) performed using G*Power software, which indicated a statistical power of 80.3% and a significance level of α=0.05. A total of 48 individuals were selected from an initially assessed 75 South Indian patients at the outpatient departments of obstetrics and gynaecology and periodontology at Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India. All patients provided written informed consent prior to enrollment in the study.

Inclusion and Exclusion criteria: The inclusion criteria were as follows: i) age range of 18-35 years; ii) no history of smoking; iii) not pregnant; iv) no other systemic diseases; v) not under any antimicrobial or anti-inflammatory therapy in the previous three months; and vi) no history of periodontal therapy in the previous six months. The exclusion criteria included patients under 18 years of age, those currently under any antimicrobial or anti-inflammatory therapy, a history of non surgical or surgical periodontal therapy in the previous six months, the presence of systemic diseases other than PCOS, a habit of tobacco chewing or cigarette smoking and immunocompromised patients.

Study Procedure

The Rotterdam Criteria (2003) was used by a single gynaecologist to diagnose PCOS based on the presence of at least two of the following symptoms: i) oligomenorrhoea and/or anovulation; ii) hyperandrogenism (clinical and biochemical); or iii) polycystic ovaries detected on ultrasound examination [4]. Individuals without systemic diseases or periodontal problems comprised the control group.

Patients who met the inclusion criteria were classified into the following four groups: Group I - Systemically and Periodontally Healthy Group (H+H, n=12), Group II - Systemically Healthy with Periodontitis (H+P, n=12), Group III - PCOS with Healthy Periodontium (PCOS+H, n=12) and Group IV - PCOS with Periodontitis (PCOS+P, n=12).

Periodontal screening and evaluation: Patients were screened by a single trained examiner using an University of North Carolina (UNC) 15 probe (PCP UNC 15, Hu Friedy Manufacturing Co., Chicago, IL, USA), which was inserted parallel to the long axis of the tooth with gentle apical pressure at six sites of each tooth. Periodontal evaluation included the assessment of [23] OHI-S, PPD, CAL and BOP, expressed as a percentage of total sites [24,25]. The diagnosis of periodontitis was established according to the Page and Eke 2012 criteria [26].

Biochemical analysis: After periodontal measurements, 1.0-1.5 ml of unstimulated whole saliva was collected into sterile, graduated Eppendorf tubes using the passive drooling method [27]. Saliva samples contaminated with blood were discarded. The samples were centrifuged at 1000 g for 20 minutes and stored at -20°C until further analysis. AGEs were determined using a Human AGEs ELISA kit (Abbkine, Inc., China). This ELISA kit employs a two-site sandwich method to quantify AGEs. Antibody-coated microplates were used to immobilise AGEs from the samples and unbound materials were washed away. An Horseradish Peroxidase (HRP)-conjugated detection antibody was added. After further washing to remove unbound reagents, a chromogen solution was introduced, producing a colour proportional to the AGEs concentration. The reaction was stopped and the resulting colour intensity was measured to determine the AGEs levels.

STATISTICAL ANALYSIS

All statistical analyses were performed using IBM SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). Data were summarised as means and standard deviations. Intergroup comparisons of clinical parameters and AGEs levels were performed using one-way analysis of variance. Tukey's post-hoc test and post-hoc Bonferroni test were used to conduct multiple pair-wise comparisons of clinical parameters and salivary AGEs levels, respectively. A p-value of ≤0.05 was considered statistically significant and a p-value of ≤0.001 was considered highly statistically significant.

RESULTS

The study included 48 patients, with 12 women in each of the four groups: PCOS+P, PCOS+H, H+P and H+H. The demographic data and clinical parameters is shown in [Table/Fig-1]. Statistical analysis revealed no significant difference in the age of the patients among the groups (p=0.498), indicating proper age matching. However, the clinical parameters, including OHI-S, BOP, PPD, CAL and PISA, were highly statistically significant (p<0.001) among all the groups, with the highest scores recorded for the PCOS+P group. The mean probing depth was highest in the PCOS+P group (3.43±0.47 mm), followed by the H+P (2.75±0.49 mm) and PCOS+H (1.94±0.20 mm) groups. Furthermore, the mean PISA value was highest in the PCOS+P group (372.42±50.68 mm^2), followed by H+P, PCOS+H and the least in the H+H group. Multiple pair-wise comparisons of all clinical parameters [Table/Fig-2] using Tukey's post-hoc test revealed high statistical significance for the PCOS+P group compared to the other groups (p<0.001). PPD and CAL were significantly elevated in

Variables	Groups	Mean±SD	95% CI for mean		p-value
			Lower	Upper	
Age (in years)	H+H (I)	25.46±3.33	23.45	27.48	0.498
	H+P (II)	27.31±4.44	24.62	29.99	
	PCOS+H (III)	26.40±4.03	23.89	28.92	
	PCOS+P (IV)	26.92±4.61	24.14	29.71	
OHI-S	H+H (I)	0.7077±0.23260	0.5671	0.8483	<0.001
	H+P (II)	1.4308±0.27804	1.2627	1.5988	
	PCOS+H (III)	1.2538±0.32046	1.0602	1.4475	
	PCOS+P (IV)	1.8231±0.41864	1.5701	2.0761	
BOP (%)	H+H (I)	4.6923±0.99454	4.0913	5.2933	0.0001
	H+P (II)	26.6246±5.54490	23.2739	29.9754	
	PCOS+H (III)	32.4377±3.25823	30.4688	34.4066	
	PCOS+P (IV)	44.6862±4.67620	41.8604	47.5120	

PPD (mm)	H+H (I)	1.5292±0.23193	1.3891	1.6694	0.0001
	H+P (II)	2.7546±0.49335	2.4565	3.0527	
	PCOS+H (III)	1.9400±0.20170	1.8181	2.0619	
	PCOS+P (IV)	3.4323±0.47872	3.1430	3.7216	
CAL (mm)	H+H (I)	0.0000±0.00000	0.0000	0.0000	0.0001
	H+P (II)	2.7052±0.77115	2.2392	3.1712	
	PCOS+H (III)	0.0000±0.00000	0.0000	0.0000	
	PCOS+P (IV)	4.1178±0.38302	3.8863	4.3492	
PISA (mm²)	H+H (I)	53.0231±4.11849	50.5343	55.5119	0.0001
	H+P (II)	245.7154±20.43982	233.3637	258.0670	
	PCOS+H (III)	90.8615±21.05131	78.1404	103.5827	
	PCOS+P (IV)	372.4238±50.68373	341.7960	403.0517	

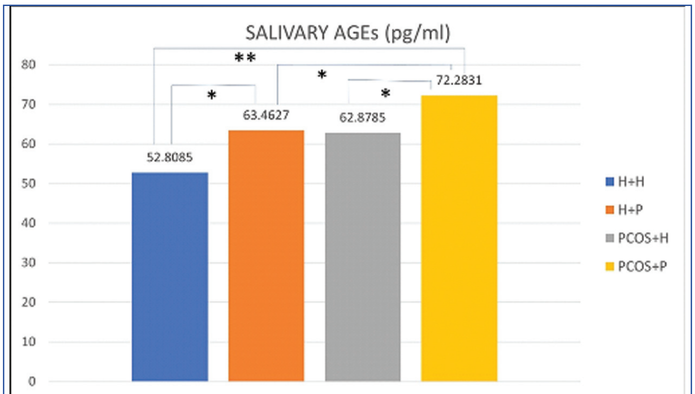
[Table/Fig-1]: Demographic and clinical parameters in each group.
One-way Analysis of Variance (ANOVA) test; OHI-S: Oral hygiene index-simplified; BOP: Bleeding on probing; PPD: Probing pocket depth; CAL: Clinical attachment loss; PISA: Periodontal inflamed surface area. p-value ≤ 0.05- statistically significant; p-value ≤ 0.01-high statistical significance.

Parameters	(I) Group	(J) Group	Mean Difference (I-J)	p-value
OHI-S	H+H (I)	H+P (II)	0.72308*	<0.001
		PCOS+H (III)	0.54615*	<0.001
		PCOS+P (IV)	1.11538*	<0.001
	H+P (II)	H+H (I)	0.72308*	<0.001
		PCOS+H (III)	0.17692	0.499
		PCOS+P (IV)	0.39231*	0.015
	PCOS+H (III)	H+H (I)	0.54615*	<0.001
		H+P (II)	0.17692	0.499
		PCOS+P (IV)	0.56923*	<0.001
	PCOS+P (IV)	H+H (I)	1.11538*	<0.001
		H+P (II)	0.39231*	0.015
		PCOS+H (III)	0.56923*	<0.001
BOP (%)	H+H (I)	H+P (II)	-21.93231*	0.0001
		PCOS+H (III)	-27.74538*	0.0001
		PCOS+P (IV)	-39.99385*	0.0001
	H+P (II)	H+H (I)	21.93231*	0.0001
		PCOS+H (III)	-5.81308*	0.003
		PCOS+P (IV)	-18.06154*	0.0001
	PCOS+H (III)	H+H (I)	27.74538*	0.0001
		H+P (II)	5.81308*	0.003
		PCOS+P (IV)	-12.24846*	0.0001
	PCOS+P (IV)	H+H (I)	39.99385*	0.0001
		H+P (II)	18.06154*	0.0001
		PCOS+H (III)	12.24846*	0.0001
PPD (mm)	H+H (I)	H+P (II)	-1.22538*	0.0001
		PCOS+H (III)	-0.41077*	0.037
		PCOS+P (IV)	-1.90308*	0.0001
	H+P (II)	H+H (I)	1.22538*	0.0001
		PCOS+H (III)	0.81462*	0.0001
		PCOS+P (IV)	-0.67769*	0.0001
	PCOS+H (III)	H+H (I)	0.41077*	0.037
		H+P (II)	-0.81462*	0.0001
		PCOS+P (IV)	-1.49231*	0.0001
	PCOS+P (IV)	H+H (I)	1.90308*	0.0001
		H+P (II)	0.67769*	0.0001
		PCOS+H (III)	1.49231*	0.0001
CAL (mm)	H+H (I)	H+P (II)	-2.70515*	0.0001
		PCOS+H (III)	0.00000	1.000
		PCOS+P (IV)	-4.11777*	0.0001
	H+P (II)	H+H (I)	2.70515*	0.0001
		PCOS+H (III)	2.70515*	0.0001
		PCOS+P (IV)	-1.41262*	0.0001
	PCOS+H (III)	H+H (I)	0.00000	1.000
		H+P (II)	-2.70515*	0.0001
		PCOS+P (IV)	-4.11777*	0.0001
	PCOS+P (IV)	H+H (I)	4.11777*	0.0001
		H+P (II)	1.41262*	0.0001
		PCOS+H (III)	4.11777*	0.0001
PISA (mm²)	H+H (I)	H+P (II)	-192.69231*	0.0001
		PCOS+H (III)	-37.83846*	0.010
		PCOS+P (IV)	-319.40077*	0.0001
	H+P (II)	H+H (I)	192.69231*	0.0001
		PCOS+H (III)	154.85385*	0.0001
		PCOS+P (IV)	-126.70846*	0.0001
	PCOS+H (III)	H+H (I)	37.83846*	0.010
		H+P (II)	-154.85385*	0.0001
		PCOS+P (IV)	-281.56231*	0.0001
	PCOS+P (IV)	H+H (I)	319.40077*	0.0001
		H+P (II)	126.70846*	0.0001
		PCOS+H (III)	281.56231*	0.0001

[Table/Fig-2]: Multiple pair-wise comparison of clinical parameters using Tukey's post-hoc test.
OHI-S: Oral hygiene index-simplified; BOP: Bleeding on probing; PPD: Probing pocket depth; CAL: Clinical attachment loss; PISA: Periodontal inflamed surface area. p-value≤0.05- statistically significant; p-value≤0.01-high statistical significance.

the PCOS+P group, especially when compared to healthy individuals and non-periodontitis groups (p<0.001). Interestingly, the PCOS+H group had significantly higher BOP% (p=0.003) and PISA (p=0.010) scores than healthy controls (H+H), suggesting that PCOS may independently contribute to a low-grade systemic inflammatory status even in the absence of periodontal disease.

The intergroup comparison of the mean salivary AGEs values for all the study participants is shown in [Table/Fig-3]. with the highest values found in the PCOS+P group (72.28±4.76 pg/mL), followed by the H+P group (63.46±9.87 pg/mL), the PCOS+H group (62.87±6.91 pg/mL) and the lowest values in the healthy controls (52.80±7.01 pg/mL). Multiple pair-wise comparisons of AGEs levels [Table/Fig-4] revealed that AGEs levels were highly statistically significant (p<0.0001) in the PCOS+P group compared to the healthy controls, with no significant difference between the PCOS+H and H+P groups (p=1.000). A significant positive correlation was found between PISA and salivary AGEs values across all groups



[Table/Fig-3]: Intergroup comparison of salivary Advanced Glycation End products (AGEs) levels in women with established PCOS and control subjects.
**represents p-value ≤ 0.01- High statistical significance and *represents p-value ≤ 0.05- presence of statistical significance

(I) Group	(J) Group	Mean difference (I-J)	p-value
H+H (I)	H+P (II)	-10.65423*	0.003
	PCOS+H (III)	-10.07000*	0.006
	PCOS+P (IV)	-19.47462*	0.000
H+P (II)	H+H (I)	10.65423*	0.003
	PCOS+H (III)	0.58423	1.000
	PCOS+P (IV)	-8.82038*	0.022
PCOS+H (III)	H+H (I)	10.07000*	0.006
	H+P (II)	-0.58423	1.000
	PCOS+P (IV)	-9.40462*	0.013
PCOS+P (IV)	H+H (I)	19.47462*	0.000
	H+P (II)	8.82038*	.022
	PCOS+H (III)	9.40462*	.013

[Table/Fig-4]: Multiple pair-wise comparison of AGEs levels using post-hoc Bonferroni's test.
p-value ≤ 0.05- statistically significant; p-value ≤ 0.01-high statistical significance

[Table/Fig-5]. Groups H+H, H+P and PCOS+H showed moderately positive correlations with r-values of 0.724, 0.717 and 0.765 and p-values of 0.005, 0.006 and 0.002, respectively, while Group IV showed a weak positive correlation (r=0.599, p=0.030). All correlations were statistically significant (p<0.05), suggesting a consistent association between the extent of inflamed periodontal tissue and the concentration of salivary AGEs.

Parameters correlated		Group-I H+H	Group-II H+P	Group-III PCOS+H	Group-IV PCOS+P
PISA vs AGES	Pearson's Correlation coefficient (r)	0.724**	0.717**	0.765**	0.599*
	p-value	0.005	0.006	0.002	0.030
	Significance	Significant	Significant	Significant	Significant
	Strength of correlation	Moderate positive	Moderate positive	Moderate positive	Weak positive

[Table/Fig-5]: Correlation between PISA and salivary AGEs levels in different groups.
**represents p-value ≤ 0.01- High statistical significance and *represents p-value ≤ 0.05- presence of statistical significance

DISCUSSION

The PCOS is a predominant hormonal condition affecting females in their reproductive years. In addition to exhibiting a wide range of clinical symptoms, patients with PCOS typically demonstrate low-grade chronic inflammation, which predisposes them to a higher likelihood of developing obesity, diabetes, dyslipidemia, cardiovascular disease and endometrial cancer [28]. Emerging evidence suggests that there is a bidirectional link between PCOS and periodontitis. An imbalance in sex hormones, low-grade inflammation, disruption of immune function and oxidative stress in PCOS deteriorate the periodontal microenvironment, while the presence of periodontal disease exacerbates low-grade inflammation, oxidative stress and insulin resistance, consequently increasing the risk of PCOS [10].

The present study is the first to evaluate the concentration of salivary AGEs in patients with PCOS associated with periodontitis in comparison to healthy controls. The results highlighted that clinical periodontal parameters and salivary AGEs levels were highest in the group with PCOS and periodontitis. Moreover, The present study implies that the concomitant presence of periodontitis with PCOS may have a synergistic effect on the elevation of salivary AGEs.

The study population was adjusted for age (p=0.498) as it could be a potential confounding factor. Compared to healthy controls, patients with PCOS had significantly higher gingival bleeding scores in terms of the percentage of BOP. These findings align with those of Dursun E et al., who reported increased gingival inflammation in the PCOS group compared to healthy women [16]. Possible endocrinological causes of this phenomenon include elevated levels of testosterone, epiandrostenedione, luteinising hormone and estrogen. It is well established that higher levels of estrogen decrease keratinisation, increase the proliferation of vascular endothelial cells and promote the growth of periodontal pathogens, particularly Prevotella intermedia, leading to increased gingival inflammation in women with PCOS [29].

Previous reports by Porwal S et al. and Rahiminejad ME et al., demonstrated that individuals with PCOS exhibited greater pocket depth and CAL [30,31]. A similar trend was observed in the present study, where PPD and CAL were significantly higher in the PCOS with periodontitis group (p<0.001). This could be attributed to PCOS contributing to exaggerated chronic low-grade inflammation [10].

The PISA index measures the inflamed periodontal tissue. The results of the study by Dharuman S et al. and Joseph RA et al., were confirmed in the present study, where PISA scores were significantly higher in the PCOS with periodontitis group than in systemically healthy patients with periodontitis [28,32]. Proinflammatory mediators such as IL-6, IL-1, IL-10, IL-8, Tumour Necrosis Factor (TNF)α, High-sensitivity C-reactive Protein (HsCRP) and Granulocyte Colony-Stimulating Factor (GCSF) are elevated in patients with PCOS due to reduced estrogen levels. These proinflammatory cytokines activate neutrophils to release collagenases like Matrix Metalloproteinase-9 (MMP-9) and Myeloperoxidase (MPO) [33], breaking down the connective tissue of the periodontium, which leads to CAL [34-36].

Takeda M et al., concluded in 2006 that serum AGEs are potential biomarkers for assessing the impact of oxidative stress on periodontal disease progression [37]. AGEs are endogenously synthesised through glycoxidation reactions known as browning or Maillard reactions, in which non enzymatic reactions occur between the carbonyl groups of carbohydrates and the free amino groups of proteins, nucleic acids, or lipids. The research group of Diamanti–Kandarakis E et al., observed elevated levels of serum AGEs in age- and weight-matched women with PCOS for the first time [38,39]. Similarly, in the present study, the levels of salivary glycation end products were highest among the PCOS with periodontitis group (72.28±4.76 pg/mL) due to the cumulative effects of both PCOS and periodontitis. The AGEs levels were comparable, with no significant difference (p=1.0) between the two groups: patients with PCOS and a healthy periodontium (62.87±6.91 pg/mL) and systemically healthy patients with periodontitis (63.46±9.87 pg/mL). This suggests that both conditions independently contribute to the elevation of systemic AGE levels.

In the PCOS group, elevated AGE levels can be attributed to low-grade systemic inflammation and insulin resistance, which are hallmark features of this syndrome. Conversely, the systemically Healthy with Periodontitis (H+P) group exhibited elevated AGE levels, likely due to the two mechanisms proposed by Chopra A et al., in their systematic review in 2022 [21]. First, *Tannerella forsythia* and *Porphyromonas gingivalis*, commonly referred to as red complex bacteria involved in the pathogenesis of periodontal disease, are known to produce methylglyoxal synthase, an enzyme that catalyses the formation of methylglyoxal. In gingival connective tissue, methylglyoxal binds to arginine and lysine residues to form AGEs [40]. Second, it has been established that inflammatory periodontal tissues act as "foci of chronic infection" and create an "inflammatory milieu," generating proinflammatory cytokines such as TNF-α, IL-6, IL-17 and free radicals. This, in turn, increases the production of C-reactive Protein (CRP), which contributes to the systemic inflammatory burden and AGE formation [5]. These results highlight the shared pathways of inflammation and oxidative stress in PCOS and periodontitis, even in the absence of overt systemic disease in some patients.

Interestingly, these AGE products positively correlated with the periodontal inflammatory surface area score, signifying that the severity of periodontal disease increases with higher salivary AGEs levels. This finding does not concur with that of Thomas JT et al., who found a negative correlation between PISA and salivary AGEs. This discrepancy may be due to differences in systemic conditions, as their study included older diabetic individuals, while the present study involved non diabetic younger PCOS patients [20]. This indicates that young women with PCOS may be more susceptible to periodontal disease. Therefore, PCOS may be a significant risk factor for the development and progression of periodontal disease.

Limitation(s)

An important limitation of the study is the reliance on salivary biomarkers, as Gingival Crevicular Fluid (GCF) would have provided a more site-specific representation of periodontal inflammation. Moreover, exploring the scope of PCOS phenotypes would yield more insights into the link between the two diseases and a longitudinal follow-up could offer insights into the progression and causal relationship between PCOS and periodontal disease.

CONCLUSION(S)

The present study demonstrates that salivary AGE products were highest in women with both PCOS and periodontitis, indicating a cumulative effect of systemic and local inflammation. PCOS may increase susceptibility to periodontal destruction through shared oxidative and inflammatory mechanisms. Therefore, increased salivary AGE products may represent one of the plausible biological mechanisms linking both conditions. Treating PCOS will also help reduce periodontal inflammation, thereby improving periodontal health. Thus, it can be concluded that salivary AGEs levels could be used as potential biomarkers to assess periodontal destruction in patients with PCOS. However, long-term clinical studies with interventions are required to confirm this association and evaluate the efficacy of salivary AGEs as non-invasive biomarkers in the diagnosis of PCOS.

REFERENCES

[1] Azziz R. Polycystic ovary syndrome: What's in a name? J Clin Endocrinol Metab. 2014;99(4):1142-45.

[2] Bharali MD, Rajendran R, Goswami J, Singal K, Rajendran V. Prevalence of polycystic ovarian syndrome in india: A systematic review and meta-analysis. Cureus. 2022;14(12):e32351.

[3] Zawadzki JK, Dunaif A. Diagnostic criteria for polycystic ovary syndrome: Towards a rational approach In: Dunaif A, Givens JR, Haseltine FP, Merriam GR, eds. Polycystic ovary syndrome. Polycystic ovary syndrome; 1992:377-84.

[4] Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41-47.

[5] Tanguturi SC, Nagarakanti S. Polycystic ovary syndrome and periodontal disease: Underlying links-a review. Indian J Endocrinol Metab. 2018;22(2):267-73.

[6] Bartold PM, Van Dyke TE. Periodontitis: A host-mediated disruption of microbial homeostasis. Unlearning learned concepts. Periodontol 2000. 2013;62(1):203-17.

[7] Sanz M, Ceriello A, Buysschaert M, Chapple I, Demmer RT, Graziani F, et al. Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. J Clin Periodontol. 2018;45(2):138-49.

[8] Herrera D, Sanz M, Shapira L, Brotons C, Chapple I, Frese T, et al. Association between periodontal diseases and cardiovascular diseases, diabetes and respiratory diseases: Consensus report of the Joint Workshop by the European Federation of Periodontology (EFP) and the European arm of the World Organization of Family Doctors (WONCA Europe). J Clin Periodontol. 2023;50(6):819-41.

[9] Sanz M, Marco Del Castillo A, Jepsen S, Gonzalez-Juanatey JR, 'Aiuto FD, Bouchard P, et al. Periodontitis and cardiovascular diseases: Consensus report. J Clin Periodontol. 2020;47(3):268-88.

[10] Dou Y, Xin J, Zhou P, Tang J, Xie H, Fan W, et al. Bidirectional association between polycystic ovary syndrome and periodontal diseases. Front Endocrinol (Lausanne). 2023;14:1008675.

[11] Machado V, Escalda C, Proença L, Mendes JJ, Botelho J. Is there a bidirectional association between polycystic ovarian syndrome and periodontitis? A systematic review and meta-analysis. J Clin Med. 2020;9(6):1961.

[12] Bitonti V, Perri T, Cigni L, Familiari D, Vazzana G, Franco R. The association between periodontal disease and polycystic ovary syndrome: A systematic review and meta-analysis. Dent J (Basel). 2025;13(5):188.

[13] Farook F, Ng K, MNM N, Koh W, Teoh WY. Association of periodontal disease and polycystic ovarian syndrome: A systematic review and meta-analysis with trial sequential analysis. Open Dent J. 2019;13(1).

[14] Kellesarian SV, Malignaggi VR, Kellesarian TV, Al-Kheraif AA, Alwageet MM, Malmstrom H, et al. Association between periodontal disease and polycystic ovary syndrome: A systematic review. Int J Impot Res. 2017;29(3):89-95.

[15] Márquez-Arrico CF, Silvestre-Rangil J, Gutiérrez-Castillo L, Martinez-Herrera M, Silvestre FJ, Rocha M. Association between periodontal diseases and polycystic ovary syndrome: A systematic review. J Clin Med. 2020;9(5):1586.

[16] Dursun E, Akalın FA, Güncü GN, Çınar N, Aksoy DY, Tözüm TF, et al. Periodontal disease in polycystic ovary syndrome. Fertil Steril. 2011;95(1):320-23

[17] Lindheim L, Bashir M, Münzker J, Trummer C, Zachhuber V, Pieber TR, et al. The salivary microbiome in Polycystic Ovary Syndrome (PCOS) and its association with disease-related parameters: A pilot study. Front Microbiol. 2016;7:1270.

[18] Akcalı A, Bostanci N, Özçaka Ö, Öztürk-Ceyhan B, Gümüş P, Buduneli N, et al. Association between polycystic ovary syndrome, oral microbiota and systemic antibody responses. PLoS One. 2014;9(9):e108074.

[19] Garg D, Merhi Z. Advanced glycation end products: Link between diet and ovulatory dysfunction in PCOS? Nutrients. 2015;7(12):10129-44.

[20] Thomas JT, Joseph B, Varghese S, Kamalasanan Vijayakumari B, Sorsa T, et al. Salivary advanced glycated end products, their receptors and aMMP-8 in periodontitis patients with varying glycemic levels: A cross-sectional study. J Periodontol. 2024:01-13.

[21] Chopra A, Jayasinghe TN, Eberhard J. Are inflamed periodontal tissues endogenous source of Advanced Glycation End-Products (AGEs) in individuals with and without diabetes mellitus? a systematic review. Biomolecules. 2022;12(5):642.

[22] Thomas JT, Joseph B, Sorsa T, Mauramo M, Anil S, Waltimo T. Expression of advanced glycation end products and their receptors in diabetic periodontitis patients. Oral Dis. 2024;30(5):2784-96.

[23] Greene JC, Vermillion JR. The simplified oral hygiene index. J Am Dent Assoc. 1964;68:07-13.

[24] Lang NP, Joss A, Orsanic T, Gusberti FA, Siegrist BE. Bleeding on probing. A predictor for the progression of periodontal disease? J Clin Periodontol. 1986;13(6):590-96.

[25] Nesse W, Abbas F, van der Ploeg I, Spijkervet FK, Dijkstra PU, Vissink A. Periodontal inflamed surface area: Quantifying inflammatory burden. J Clin Periodontol. 2008;35(8):668-73.

[26] Eke PI, Page RC, Wei L, Thornton-Evans G, Genco RJ. Update of the case definitions for population-based surveillance of periodontitis. J Periodontol. 2012;83(12):1449-54.

[27] Priya KY, Prathibha KM. Methods of collection of saliva-a review. Int J Oral Health Dent. 2017;3(3):149-53.

[28] Dharuman S, Kumar SA, Balaji SK, Vishwanath U, Parameshwari RP, Santhanakrishnan M. Evaluation of levels of advanced oxidative protein products in patients with polycystic ovary syndrome with and without chronic periodontitis: A cross-sectional study. Int J Fertil Steril. 2022;16(1):55.

[29] Pavankumar S, Yellarthi PK, Jn S, Boyapati R, Damera TK, G NVK. Evaluation of periodontal status in women with polycystic ovary syndrome versus healthy women: A cross-sectional study. J Yeungnam Med Sci. 2023;40(Suppl):S17-S22.

[30] Porwal S, Tewari S, Sharma RK, Singhal SR, Narula SC. Periodontal status and high-sensitivity C-reactive protein levels in polycystic ovary syndrome with and without medical treatment. J Periodontol. 2014;85(10):1380-89.

[31] Rahiminejad ME, Moaddab A, Zaryoun H, Rabiee S, Moaddab A, Khodadoustan A. Comparison of prevalence of periodontal disease in women with polycystic ovary syndrome and healthy controls. Dent Res J (Isfahan). 2015;12(6):507-12.

[32] Joseph RA, Ajitkumar S, Balaji SK, Santhanakrishnan M. Evaluation of microbial profile in patients with polycystic ovary syndrome and periodontal disease: A case control study. Int J Fertil Steril. 2023;17(4):248-25.

[33] Akcalı A, Bostanci N, Özçaka Ö, Gümüş P, Öztürk-Ceyhan B, Tervahartiala T, et al. Gingival inflammation and salivary or serum granulocyte-secreted enzymes in patients with polycystic ovary syndrome. J Periodontol. 2017;88(11):1145-52.

[34] Massler M. Oral manifestations during the female climacteric (the postmenopausal syndrome). Oral Surg Oral Med Oral Pathol. 1951;4(10):1234-43.

[35] Jafri Z, Bhardwaj A, Sawai M, Sultan N. Influence of female sex hormones on periodontium: A case series. J Nat Sci Biol Med. 2015;6(Suppl 1):S146-S149.

[36] Deepti, Tewari S, Narula SC, Singhal SR, Sharma RK. Effect of non-surgical periodontal therapy along with myo-inositol on high-sensitivity C-reactive protein and insulin resistance in women with polycystic ovary syndrome and chronic periodontitis: A randomized controlled trial. J Periodontol. 2017;88(10):999-1011.

[37] Takeda M, Ojima M, Yoshioka H, Inaba H, Kogo M, Shizukuishi S, et al. Relationship of serum advanced glycation end products with deterioration of periodontitis in type 2 diabetes patients. J Periodontol. 2006;77(1):15-20.

[38] Diamanti-Kandarakis E, Katsikis I, Piperi C, Kandaraki E, Piouka A, Papavassiliou AG, et al. Increased serum advanced glycation end-products is a distinct finding in lean women with polycystic ovary syndrome (PCOS). Clin Endocrinol (Oxf) [Internet]. 2008;69(4):634-41.

[39] Diamanti-Kandarakis E, Piperi C, Kalofoutis A, Creatsas G. Increased levels of serum advanced glycation end-products in women with polycystic ovary syndrome. Clin Endocrinol (Oxf). 2005;62(1):37-43.

[40] Kashket S, Maiden MFJ, Haffajee AD, Kashket ER. Accumulation of methylglyoxal in the gingival crevicular fluid of chronic periodontitis patients. J Clin Periodontol. 2003;30(4):364-67.

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