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ORIGINAL ARTICLE

Evaluation of oxidative status in patients with chronic periodontitis and polycystic ovary syndrome: A cross-sectional study

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Abstract

Background: In patients with polycystic ovary syndrome (PCOS), chronic periodontitis (CP) contributed to increased oxidative stress (OS), owing to an increase in serum and salivary 8-hydroxy-2′-deoxyguanosine (8-OHdG) and malondialdehyde (MDA) levels and a decrease in serum total antioxidant status (TAS) levels. The aim of the present study is to investigate salivary and serum 8-OHdG and MDA levels as well as total antioxidant status (TAS) in females with CP and PCOS compared with healthy females.

Methods: Four groups, each consisting of 22 individuals, were: 1) women with both PCOS and CP (PCOSCP); 2) systemically healthy women with CP; 3) periodontally healthy women with PCOS (PCOSPH); and 4) periodontally and systemically healthy women (PH). Demographic and clinical periodontal parameters were measured. Oxidative parameters were evaluated in serum and salivary samples.

Results: Salivary 8-OHdG levels in the PCOSCP and CP groups were statistically higher than those in both the PCOSPH and the PH groups ($P < 0.05$). There was no statistical difference between the PCOSCP, CP, and PCOSPH groups with regard to salivary MDA and TAS levels ($P > 0.05$). Highest serum 8-OHdG and MDA levels and lowest serum TAS levels were seen in the PCOSCP group ($P < 0.05$). Serum 8-OHdG and MDA levels in the PCOSPH group were higher than those in both systemically healthy groups (PH and CP) ($P < 0.05$). Salivary TAS levels were highest ($P < 0.05$) in the PH group. There was no statistical difference between the CP and PCOSPH groups, but serum TAS levels were lower than those in the PH group ($P < 0.05$).

Conclusions: CP, which led to an increase in serum and salivary 8-OHdG and MDA levels and a decrease in serum TAS levels in patients with PCOS, contributed to increased OS. This effect was more prominent in serum levels than in salivary levels.

KEYWORDS

Chronic periodontitis, malondialdehyde, oxidative stress, polycystic ovary syndrome

Chronic periodontitis (CP) is described as a destructive inflammatory disorder induced by bacterial products and resulting in attachment loss (AL) and alveolar bone destruction.[1] When immune response is stimulated by periodontopathic bacteria, reactive oxygen species (ROS) are released by host cells. Excessive ROS production in

polymorphonuclear leukocytes is one of the pathologic pathways of periodontal inflammation and can cause oxidative stress (OS) and affect periodontal tissues by causing damage to biologic molecules, including lipids, proteins, and DNA.[2] Periodontal disease has been implicated as a potential risk factor for the onset and development of systemic diseases such as cardiovascular diseases (CVDs),[3] rheumatoid arthritis,[4] and diabetes mellitus (DM).[5]

Polycystic ovary syndrome (PCOS), which affects ≤ 15% of females, is the most common endocrine disorder in women and is characterized by chronic low-grade inflammation and increased OS. PCOS carries the risk of CVDs, insulin-dependent DM, dyslipidemia, endothelial dysfunction, and visceral obesity.[6] Thus, PCOS is considered to be a metabolic syndrome.

ROS production and antioxidant defense systems are typically in equilibrium. When this equilibrium shifts toward an increase in ROS production, OS can potentially damage the affected organism.[7] Both free radicals and ROS can attack nucleic acids via oxidation, resulting in DNA damage. Originating from specific enzymatic cleavage after the 8-hydroxylation of guanine, 8-hydroxy-2′-deoxyguanosine (OHdG) is the most common stable product of oxidative DNA damage in the nucleus.[8] Increased ROS production leads to lipid peroxidation via formation of malondialdehyde (MDA) and damages cell-membrane lipids.[7] Total antioxidant status (TAS), which is sensitive to changes in the degree of OS, combines concentrations of various individual antioxidants and reflects potential synergistic and antagonistic interactions between antioxidants.[9]

A number of studies have indicated a possible relationship between PCOS and periodontal inflammation.[10–13] Dursun et al.[13] suggested that local/periodontal oxidant status appears to be affected in patients with PCOS but not in healthy young women. Despite common risk factors, including OS, the relationship between CP and PCOS remains unclear. There has been no study on the possible effects of PCOS and CP on OS in both serum and saliva. Therefore, the aim of the present study is to evaluate serum and saliva levels of 8-OHdG, MDA, and TAS in non-obese women with CP and PCOS.

1 | MATERIALS AND METHODS

1.1 | Patient selection

The study protocol was approved by the ethics committee of the Medicine Faculty, Ataturk University, Erzurum, Turkey. All participants were recruited from the Department of Obstetrics and Gynecology, School of Medicine, Ataturk University, from May 2013 to May 2015. All individuals were informed about the aim and methods of the study, and written informed consent forms were prepared according to the principles of the Helsinki Declaration and obtained before clinical periodontal examinations and saliva and serum sampling.

Sample size was specified by using a power analysis of the serum 8-OHdG, which had the greatest variation among all the groups (PCOSCP, CP, PCOSPH, and PH). To detect a significant difference at an effect size of 0.61 and power level of 80% with a 95% confidence level, at least 18 patients were required for each group.[14] In this study, 22 participants were included in each group to allow for dropouts.

Of the 109 individuals examined for this cross-sectional comparative study, 94 were eligible and met the inclusion criteria; six participants declined to take part. Thus, the total study population comprised age- and body mass index (BMI)-matched, non-obese women (88 females; 44 females [aged 19 to 40 years] newly diagnosed with PCOS who had not started any medical treatment for the syndrome; and 44 systemically healthy females [aged 20 to 38 years] upon routine medical examination). These individuals were categorized into four groups, each consisting of 22 participants: 1) PCOS participants with CP (PCOSCP); 2) systemically healthy participants with CP; 3) PCOS participants who were periodontally healthy (PCOSPH); and 4) the control group, composed of systemically and periodontally healthy participants (PH).

Based on the 2003 Rotterdam criteria, PCOS was diagnosed according to the presence of at least two of the following: 1) oligomenorrhea and/or anovulation; 2) hyperandrogenism (clinical and biochemical); and 3) polycystic ovaries detected on ultrasound examination.[6] Systemically healthy participants were matched for BMI and had regular menstrual cycles but no clinical or biochemical signs of hyperandrogenism; polycystic ovaries were excluded via ultrasound.

All anthropometric measurements and dental examinations were performed by the same physician (ES) on the day blood specimens were obtained. All individuals included in the study met the following criteria: 1) they had never been smokers; 2) were not pregnant at the time of the study; and 3) had no history of systemic disease other than PCOS. It was also a requirement that they had not taken medication within the previous 3 months, including antibiotics, oral contraceptive agents, steroid hormones or associated preparations, hypertensive medications, and insulin-sensitizing drugs because these medications may affect metabolic criteria.[6] None of the individuals had a history of periodontal therapy in the previous 6 months.

BMI, waist circumference (WC), and waist-hip ratio (WHR) were measured as previously described.[15] Normal weight was defined as a BMI of ≥ 18.5 and < 25 kg/m^2, and overweight/obesity was defined as a BMI of ≥25 (kg/m^2). Glycated hemoglobin (HbA1c) and 75-g, 2-hour oral glucose tolerance tests (OGTT-2h) were performed.[16] Females who had a BMI of ≥ 25 kg/m^2, HbA1c ≥6.5%,

or OGTT-2h ≥200 mg/dL were excluded from the study. Confounding factors such as Cushing syndrome, non-classic congenital adrenal hyperplasia, hyperprolactinemia, thyroid dysfunction, and androgen-secreting tumors have a clinical presentation similar to PCOS. To establish the diagnosis of PCOS, these disorders were also excluded.[6]

This study was registered at ClinicalTrials.gov in November 2016 (registration number: NCT02954120).

1.2 | Dental examination

Six sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual) on each tooth, excluding third molars, were assessed for dental variables. Periodontal parameters were measured clinically via probing depth (PD), clinical AL, gingival index (GI),[17] bleeding on probing (BOP),[18] and plaque index (PI)[19] using a periodontal probe.* PD was measured as the distance between the free gingival margin and the base of the pocket. Clinical AL was determined by measuring the distance from the cemento-enamel junction to the base of the pocket. Patients with severe generalized CP were included in the study. CP was defined as one or more interproximal sites with a PD ≥5 mm as well as one or more interproximal sites with clinical AL ≥6 mm, not on the same tooth.[20] In the control group, periodontal health was defined as a PD of ≤3 mm, no clinical AL, and BOP in ≤25% of teeth.[21] All participants had ≥20 natural teeth.

1.3 | Collection of serum and saliva samples

All samples were obtained in the morning after overnight fasting during the early follicular phase (second to fifth days) of spontaneous or progesterone-induced menstrual cycle.

1.3.1 | Saliva sampling

Before clinical periodontal measurements were taken, participants were asked not to drink (except water) or chew gum and then to keep their mouth open for 5 minutes; unstimulated saliva samples were collected by expectoration into polypropylene tubes. Approximately 5 mL of whole saliva was collected and centrifuged† for 10 minutes at 1,000 × rpm at 4°C to remove cell debris. Supernatant was stored in 500 μL aliquots at −80°C until the biochemical analyses were performed.

1.3.2 | Serum sampling

Ten milliliters of venous blood was taken from the antecubital vein by the standard venipuncture method. To obtain serum, blood samples were collected in tubes‡ and centrifuged for 5 minutes at 3,500 × rpm at 4°C. Serum samples were transferred to 500-μL aliquots and stored at −80°C until the biochemical analyses were performed.

1.4 | Measurement of MDA levels, 8-OHdG levels, and TAS

To determine serum and salivary 8-OHdG levels, high-sensitivity 8-OHdG enzyme-linked immunosorbent assay kits§ were used.

Serum and salivary MDA levels in the clinical samples were measured by the method of Ohkawa et al.[22] This method is based on spectrophotometric determination of the complex formed by the reaction of MDA with thiobarbituric acid.

Serum and salivary TAS were measured spectrophotometrically using assay kits.¶ The assay was based on the principle that 2.2′-azino-di-[3-ethylbenzothiazoline sulphonate] (ABTS) may be incubated with peroxidase and hydrogen peroxide to produce the radical cation ABTS.[23]

1.5 | Statistical analyses

All statistical data analyses were performed using software.#,‖ A Kolmogorov–Smirnov test was used to evaluate the normality of the data distribution. Demographic, clinical, and laboratory parameters were found to be non-normally distributed. Statistical comparisons between groups were assessed by the Kruskal–Wallis and Mann–Whitney *U* tests. The Spearman correlation test was used to detect correlations. Statistical significance was considered to be $P < 0.05$.

2 | RESULTS

2.1 | Clinical and demographic findings

The demographic features and clinical periodontal measurements of the patients are summarized in Tables 1 and 2. There were no significant differences between the groups in ages, BMI score, OGTT-2h scores, or HbA1c scores among the groups ($P > 0.05$). In comparing the CP groups with the periodontally healthy groups, all clinical periodontal

* Williams periodontal probe, Hu-Friedy, Chicago, IL.

† Vacuette, Greiner Bio-One, Kremsmünster, Austria.

‡ BD Vacutainer SST II Advance Tube, Becton Dickinson, Franklin Lakes, NJ.

§ Product NWK-8-OHDG-02, Northwest Life Science Specialties, Vancouver, WA.

¶ Randox assay kits (Cat No. NX2331 and NX2332), Randox Laboratories, Crumlin, U.K.

SPSS for Windows, v.17, SPSS, Chicago, IL.

‖ Excel, Microsoft, Redmond, WA.

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TABLE 1 Demographic parameters of all groups (n = 88)

	PCOSCP (n = 22)	CP (n = 22)	PCOSPH (n = 22)	PH Control Group (n = 22)
Age	28.61 ± 4.455	28.23 ± 4.317	27.64 ± 4.001	27.78 ± 3.944
BMI (kg/m^2)	22.437 ± 2.805	22.664 ± 1.819	22.498 ± 2.018	21.063 ± 2.144
WC (cm)	78.31 ± 2.114	79.98 ± 2.412	80.13 ± 2.178	81.34 ± 2.286
WHR	0.73 ± 0.042	0.74 ± 0.057	0.72 ± 0.065	0.76 ± 0.459
OGTT-2h (mg/dL)	107.8 ± 8.275	94.845 ± 9.269	100.2 ± 10.837	91 ± 13.008
HbA1c (%)	4.7 ± 0.417	4.5 ± 0.461	4.8 ± 0.389	4.6 ± 0.318

Values are presented as mean ± SD.

TABLE 2 Clinical periodontal parameters of all groups (n = 88)

	PCOSCP (n = 22)	CP (n = 22)	PCOSPH (n = 22)	PH Control Group (n = 22)
PD (mm)	4.14 ± 0.355*	4.11 ± 0.301*	1.34 ± 0.297	1.33 ± 0.165
Clinical AL (mm)	4.51 ± 0.387*	4.48 ± 0.444*	1.84 ± 0.325	1.66 ± 0.216
GI	1.89 ± 0.190*	1.96 ± 0.201*	0.08 ± 0.036	0.06 ± 0.025
BOP (%)	88.33 ± 4.998*	87.37 ± 5.376*	0.07 ± 0.044	0.07 ± 0.036
PI	2.39 ± 0.167*	2.41 ± 0.178*	0.04 ± 0.031	0.04 ± 0.020

Values are presented as mean ± SD.

*$P < 0.05$; statistically significant difference.

TABLE 3 Salivary and serum 8-OHdG, MDA, and TAS levels (n = 88)

	PCOSCP (n = 22)	CP (n = 22)	PCOSPH (n = 22)	PH Control Group (n = 22)
Salivary 8-OHdG (ng/mL)	0.411 ± 0.074^b	0.384 ± 0.053^b	0.232 ± 0.044^a	0.225 ± 0.056^a
Salivary MDA (μmol/L)	6.130 ± 2.691^b	5.578 ± 1.989^b	5.786 ± 2.106^b	3.965 ± 1.477^a
Salivary TAS (mmol/L)	1.170 ± 0.668^b	1.150 ± 0.514^b	1.116 ± 0.743^b	1.647 ± 0.619^a
Serum 8-OHdG (ng/mL)	3.68 ± 0.686^d	2.177 ± 0.629^b	2.972 ± 0.527^c	1.461 ± 0.429^a
Serum MDA (μmol/L)	4.289 ± 1.376^d	2.023 ± 1.166^b	3.146 ± 2.533^c	1.364 ± 0.953^a
Serum TAS (mmol/L)	0.784 ± 0.419^c	1.039 ± 0.422^b	1.08 ± 0.473^b	1.603 ± 0.351^a

Values are presented mean ± SD. Values with different letters within the same row are statistically different ($P < 0.05$). Same letters within the same row indicate no significant difference.

parameters were found to be significantly higher in the CP groups ($P < 0.001$) (Table 2).

2.2 | Laboratory findings

Table 3 shows the mean 8-OHdG, MDA, and TAS levels in the serum and saliva of the four groups.

2.3 | 8-OHdG levels

Salivary 8-OHdG levels in both CP groups (PCOSCP and CP) were statistically higher than those in both periodontally healthy groups (PCOSPH and PH) ($P < 0.05$) Salivary 8-OHdG levels were similar in the periodontally healthy groups. Salivary 8-OHdG levels in the PCOSCP group were higher than those in the CP group; however, this difference was not statistically significant ($P > 0.05$).

The serum 8-OHdG levels were statistically significantly different in all groups, and serum 8-OHdG levels in both CP groups and the PCOSPH group were statistically significantly higher than those in the control group (PH) ($P < 0.05$). Serum 8-OHdG levels in the PCOSCP group were statistically higher than those in both the CP and PCOSPH groups ($P < 0.05$). Moreover, 8-OHdG levels in the PCOSPH group were statistically higher than those in the CP group ($P < 0.05$).

2.4 | MDA levels

Saliva MDA levels in the control group were statistically significantly lower than those in other groups ($P < 0.05$). However, there was no statistical difference in the mean salivary MDA levels between the PCOSCP, CP, and PCOSPH groups ($P > 0.05$).

The serum MDA levels were statistically significantly different in all the groups, and serum MDA levels in both PCOS groups (PCOSCP and PCOSPH) were higher than those in both systemically healthy groups. Serum MDA levels in the PCOSCP group were statistically higher than those in both the CP and PCOSPH groups ($P < 0.05$). Moreover, serum MDA levels in the PCOSPH group were statistically higher than those in the CP group ($P < 0.05$).

2.5 | TAS levels

Salivary TAS levels in the control group were statistically significantly higher than those in the other groups ($P < 0.05$). Although salivary TAS levels in the PCOSCP group were higher than those in the CP group, and salivary TAS levels in the CP group were higher than those in the PCOSPH group, there were no statistically significant differences in salivary TAS levels between the PCOSCP, CP, and PCOSPH groups ($P > 0.05$).

Serum TAS levels in both CP groups were statistically lower than those in the control group ($P < 0.05$). There were no statistically significant differences in serum TAS levels between the CP and PCOSPH groups ($P > 0.05$). The lowest serum TAS level was observed in the PCOSCP group.

Comparisons of salivary and serum 8-OHdG, MDA, and TAS levels between the groups are shown in Figure 1.

2.6 | Correlations

Salivary 8-OHdG levels had statistically significant positive correlations with all clinical periodontal parameters ($P < 0.01$). Serum 8-OHdG levels also had statistically significantly positive correlations with all clinical periodontal parameters except for clinical AL.

There was no statistically significantly correlation between salivary MDA levels and clinical AL, but statistically significant correlations between salivary MDA levels and other clinical parameters were observed ($P < 0.05$). Serum MDA levels did not show any correlation with PI and BOP, but statistically significantly positive correlations were observed between serum MDA levels and other clinical parameters ($P < 0.05$).

Salivary TAS levels exhibited no correlation with PI, BOP, and clinical AL, but statistically significant negative correlations were observed between salivary TAS levels and other clinical parameters ($P < 0.05$). Serum TAS levels showed statistically significant negative correlations with all clinical parameters ($P < 0.05$) (Table 4).

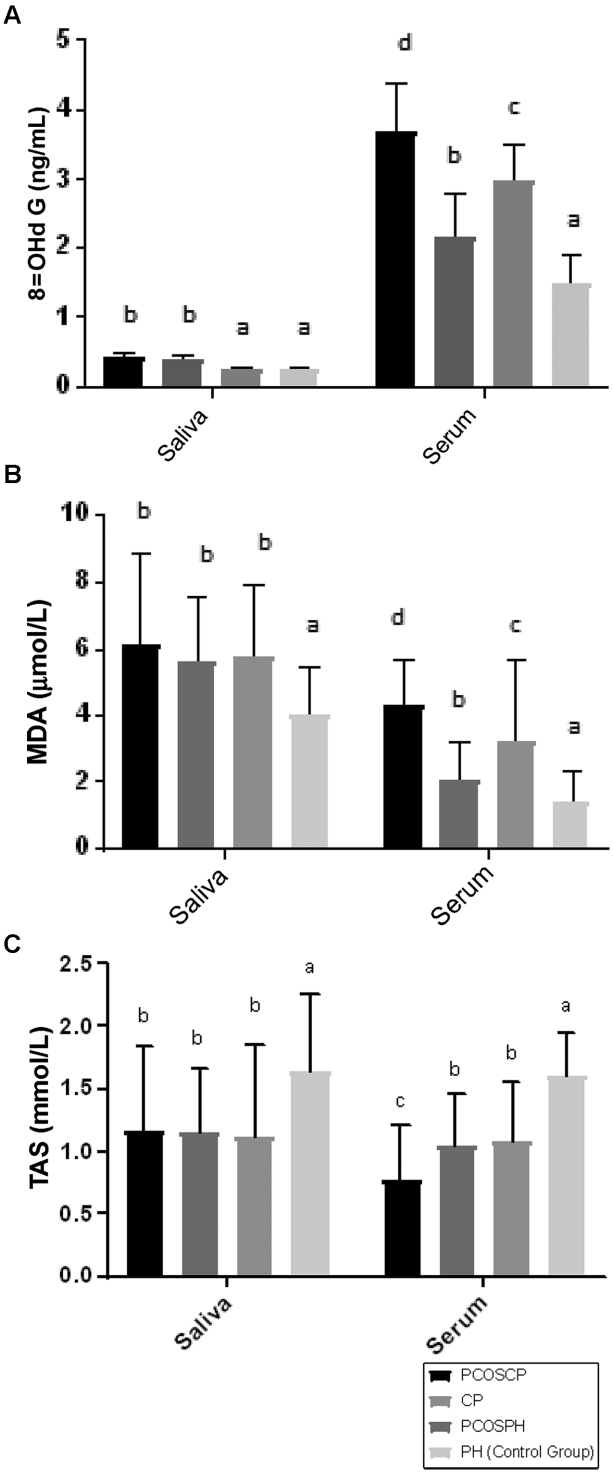

FIGURE 1 The comparisons of salivary and serum 8-OHdG (A), MDA (B), and TAS (C) levels between groups. Different lowercase letters indicate values that are statistically different ($P < 0.05$)

3 | DISCUSSION

To the best of the authors' knowledge, this is the first study to analyze the relationship between PCOS and CP using the 8-OHdG, MDA, and TAS parameters. Results of the study show that both PCOS and CP can generate an increase in OS, either alone or through synergistic interaction. To the best of the authors' knowledge, this is also the first report to hypothesize that periodontitis and PCOS may be linked through systemic and local OS responses.

BMI, WC, WHR, age, smoking status, alcohol consumption, and systemic diseases could have potentially affected the data and its interpretation. Using WHR and WC along with BMI better predicts adiposity, which may affect oxidative status.[24] Age and BMI were matching variables, and WHR

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TABLE 4 Correlations among periodontal clinical measurements and laboratory parameters

	GI		PI		BOP		PD		Clinical AL	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Serum 8-OHdG	0.305[a]	0.004	0.289[a]	0.006	0.265[b]	0.013	0.356[a]	0.001	0.184	0.09
Serum MDA	0.277[a]	0.009	0.140	0.19	0.111	0.30	0.285[a]	0.007	0.304[a]	0.004
Serum TAS	−0.411[a]	<0.001	−0.340[a]	0.001	−0.308[a]	0.004	−0.463[a]	<0.001	−0.305[a]	0.004
Salivary 8-OHdG	0.574[a]	<0.001	0.555[a]	<0.001	0.563[a]	<0.001	0.719[a]	<0.001	0.601[a]	<0.001
Salivary MDA	0.262[b]	0.03	0.270[b]	0.02	0.285[b]	0.014	0.274[b]	0.02	0.202	0.09
Salivary TAS	−0.242[b]	0.02	−0.118	0.27	−0.137	0.20	−0.237[b]	0.03	−0.108	0.32

r = Spearman correlation coefficient.

[a]Correlation is significant at the 0.01 level (2-tailed).

[b]Correlation is significant at the 0.05 level (2-tailed).

and WC values were not statistically significantly different between the groups. OGTT-2h and HbA1c values differ statistically significantly between the groups.

OS in PCOS, a metabolic syndrome, is significantly increased compared with levels in healthy individuals.[25–28] On the other hand, increased ROS production and reduced antioxidant capacity due to inflammatory activity reportedly play an important role in the pathogenesis of CP.[2,29,30] Similarly, OS is reported to play an important role in the interaction mechanisms between CP and systemic diseases such as CVD,[3] rheumatoid arthritis,[4] and DM.[5] For these reasons, it is deduced that OS may have a role in the possible interaction between CP and PCOS.[13]

Only a few studies have evaluated the relationship between PCOS and periodontal diseases, all of which found that individuals with PCOS seem to be more prone to gingival inflammation. This may be related to the role of chronic systemic inflammation in the pathophysiology of both PCOS and periodontal disease.[10–13,31–33]

Specific lipid peroxidation and oxidative degradation products, such as MDA and 8-OHdG, are widely used to evaluate OS levels. Furthermore, separate evaluations of enzymatic or non-enzymatic antioxidant levels do not adequately reflect antioxidant effectiveness. TAS reflects the effectiveness not only of known antioxidants, but also of antioxidants that have not yet been discovered.[34,35]

Although there are many studies in which local and systemic 8-OHdG,[14,30,36,37] MDA,[26,28,29,38,39] and TAS[39–43] levels have been researched in systemically healthy individuals with periodontitis, the study by Dursun et al.[13] is the only one to have evaluated PCOS and CP. In that study, periodontitis and periodontal health were not differentiated. Only myeloperoxidase levels were evaluated, but the assessment of a single antioxidant does not reflect total antioxidant capacity.

The majority of published data about oxidative DNA damage reported higher 8-OHdG levels in the saliva of patients with periodontitis.[30,36,37] Similarly, in the present study, the salivary 8-OHdG levels in both CP groups were statistically higher than those in both periodontally healthy groups, and salivary 8-OHdG levels were similar in the periodontally healthy groups. Also, no statistically significant difference was detected between the CP groups. Even salivary 8-OHdG levels in the PCOSCP group were higher than those in the CP group; however, this difference was not statistically significant. These results suggest that PCOS either does not affect salivary 8-OHdG levels or that this effect is not detectable.

Scarce data exist regarding the effect of CP on serum 8-OHdG levels.[44–46] Two studies reported that there were no significant differences between periodontally healthy and CP individuals in terms of serum 8-OHdG levels.[44,45] However, in a ligature-induced rat periodontitis model, serum 8-OHdG levels were reported to be higher than in periodontally healthy groups.[46] The present study indicates that serum 8-OHdG levels in both the CP groups and the PCOSPH group were statistically significantly higher than those in the control group. Serum 8-OHdG levels in the PCOSCP group were statistically higher than those in both the CP and PCOSPH groups. Moreover, 8-OHdG levels in the PCOSPH group were statistically higher than those in the CP group. Both PCOS and CP increase serum 8-OHdG levels, and the co-occurrence of these two diseases causes a synergistic effect on serum 8-OHdG levels.

On the other hand, only three studies have investigated the serum 8-OHdG levels of individuals with PCOS.[14,47,48] The results of these studies contradict one another. Hamurcu et al.[47] suggested that there was no difference between the groups, while Sova et al.[14] reported statistically significantly decreased serum 8-OHdG levels in participants. The results of the present study, which find that serum 8-OHdG levels in both PCOS groups are higher than those in both systemically healthy groups, are in line with Gao et al.[48] The discrepancy between the results of the cited studies may be explained by methodologic differences or the variable systemic and periodontal status of the PCOSCP, CP, and PCOSPH groups. According to the results of the present study, PCOS itself seems to be more effective in enhancing serum 8-OHdG levels than CP alone. We think that this may be due to the fact that the systemic and metabolic effects of PCOS are more prominent than CP. In addition, CP seems to have a contributory effect on serum 8-OHdG levels in patients with PCOS. This may

be explained by the synergistic effect of these two diseases or the propensity of these patients to develop inflammation. Furthermore, it may be suggested that enhanced oxidative DNA damage plays a role in the interaction between the two diseases.

MDA is a widely used biomarker for OS. Several studies have focused on comparing MDA levels in the saliva of patients with periodontitis with those of periodontally healthy controls.[29,30,34,49,50] These studies, with one exception,[50] showed either a significant increase in salivary MDA levels in patients with periodontitis compared with periodontally healthy controls or a significant correlation between salivary MDA levels and clinical periodontal parameters.[29,30,34,49] The present investigation confirms the results of previous studies, finding that salivary MDA levels in both CP groups were statistically significantly higher than those in the control group.

Some studies have evaluated serum MDA levels to assess OS levels in patients with PCOS, but there have been no studies of salivary MDA levels in such patients. The results of the present study indicate that both PCOS and CP cause an increase in salivary MDA levels, but there were no statistically significant differences between the PCOSCP, CP, and PCOSPH groups in this regard. According to these results, CP and PCOS alone seem to have an enhancing effect on salivary MDA levels, yet these increases did not result in a synergistic effect in patients with PCOSCP. This situation may be explained by other factors, such as dietary habits or difficulties in the homogenization of the PCOS criteria, which may have a greater effect on salivary biochemical markers.

Although some studies have reported that CP does not affect serum MDA levels,[29,34,45,50] the present results revealed that periodontitis increases serum MDA levels, a finding in line with one study.[39] The discrepancy between these studies may be due to the variability of the study groups in which hyperlipidemia, pre-eclampsia, PCOS, and CP occur. Several studies reported that serum MDA levels could serve as proof of the existence of higher OS in women with PCOS than in systemically healthy women.[26,28,48] Consistent with these studies, the results of the present study reveal that serum MDA levels in both PCOS groups are higher than those in both systemically healthy groups. Moreover, serum MDA levels in the PCOSPH group are statistically higher than those in the CP group. The highest serum MDA levels were seen in the PCOSCP group. It is shown that both CP and PCOS contribute to increased OS, but PCOS seems to be more effective in enhancing serum MDA levels than CP. These results suggest that, although PCOS has a predominant effect, both PCOS and CP increase systemic lipid peroxidation, and the co-occurrence of these two diseases causes a synergistic effect on serum MDA levels.

Some studies[39,41,42] reported that salivary TAS levels of individuals with CP were significantly lower than those of healthy individuals; however, Su et al.[38] found an increase in salivary TAS levels in patients with periodontitis. Salivary TAS levels in both CP groups were statistically significantly lower than those in the PH group. The discrepancy in the results may be attributable to the variety of disease activities or the various study designs used. There has not yet been a study evaluating PCOS and salivary TAS levels. In the present study, the PH group is statistically higher in terms of salivary TAS levels than the other groups. There is no difference between salivary TAS levels in patients with CP, PCOS, or both of these diseases. According to the present study, although salivary TAS levels in the PCOSPH group are lower than those in the PCOSCP group, the salivary TAS levels are not statistically different between the PCOSCP, CP, and PCOSPH groups. Therefore, it can be said that both PCOS and CP caused a decrease in salivary TAS levels, but that CP had no effect or a minimum effect on the salivary TAS levels of individuals with PCOS or vice versa.

Many studies[39,40,43] have reported that the serum TAS levels of individuals with CP were significantly lower than those of healthy individuals. Similarly, in the present study, serum TAS levels in both CP groups were statistically lower than those in the control group. On the other hand, a few studies[15,25,27] have evaluated serum TAS levels in women with PCOS. Two of these studies[15,25] reported that there was no difference in the serum TAS levels of systemically healthy individuals when compared with individuals with PCOS, whereas another study[27] reported a statistically significant decrease. In line with this study, serum TAS levels in both PCOS groups in the present study were lower than those in the control group. There were no statistically significant differences between the CP and PCOSPH groups, but both CP and PCOS contributed to serum TAS levels. Both PCOS and CP decreased local and systemic TAS levels, and this decrease was larger in individuals with both periodontitis and PCOS via synergistic interaction.

Only two studies have assessed the correlation between periodontal inflammation and inflammatory cytokines in individuals with PCOS, and both of these studies reported a positive correlation between periodontal clinical parameters and inflammatory cytokines.[11,12] Correlation between OS and clinical periodontal parameters in individuals with PCOS has been evaluated in only one study,[13] which found significant positive correlations among the serum and gingival crevicular fluid myeloperoxidase and nitricoxide levels and clinical periodontal parameters.[13] Data from correlation tests in the present study show that PI and BOP did not correlate with serum MDA or saliva TAS levels and that CAL did not correlate with serum 8-OHdG, saliva MDA, or saliva TAS levels. Statistically significant correlations were observed among all the other clinical and laboratory parameters. Because of this heterogeneity in correlation results, further studies are recommended to understand the interaction between PCOS and CP.

Large sample sizes are needed to minimize the effects of interactions in such complex diseases, and the relatively small sample size of the present study is a major limitation. Other limitations of this study with the potential to affect oxidant/antioxidant status included the cross-sectional design, the diversity of the Rotterdam criteria, and the differences within and among groups in participants' diets.

4 | CONCLUSIONS

In summary, CP, which led to an increase in serum and salivary 8-OHdG and MDA levels and a decrease in serum TAS levels in patients with PCOS, caused an additional increase in OS. CP had a more prominent effect on increased serum-related OS in patients with PCOS but did not have a prominent effect on increased salivary OS. Similarly, PCOS caused an additional increase in serum levels of 8-OHdG and MDA and an additional decrease in serum levels of TAS in patients with CP.

Longitudinal, prospective studies in larger populations would be useful to reveal the relationship between periodontitis and PCOS more clearly, taking into consideration the mechanisms triggered by OS.

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