

# Impact of Polycystic Ovary Syndrome on Periodontal Status of Women of Adolescent and Adult Age Groups: A Cross-Sectional Study

Swati Jaglan<sup>a</sup> Shikha Tewari<sup>a</sup> Savita Rani Singhal<sup>b</sup> Rajinder Kumar Sharma<sup>a</sup>

<sup>a</sup>Department of Periodontics, Post Graduate Institute of Dental Sciences, Pandit Bhagwat Dayal Sharma University of Health Sciences, Rohtak, India; <sup>b</sup>Department of Obstetrics and Gynecology, Post Graduate Institute of Medical Sciences, Pandit Bhagwat Dayal Sharma University of Health Sciences, Rohtak, India

## Highlights of the Study

- High levels of serum high-sensitivity C-reactive protein and periodontal inflammation were observed in adolescents with polycystic ovary syndrome (PCOS), similar to adult females with PCOS.
- Initiation of periodontal inflammation and destruction in adolescents with PCOS may present a risk for progression of periodontal disease if not treated at an early age.
- Periodontal tissue destruction was significantly higher in adults with PCOS compared to adolescents with PCOS.

## Keywords

Body mass index · Hirsutism · Hyperandrogenism · Polycystic ovary syndrome

## Abstract

**Objective:** Polycystic ovary syndrome (PCOS) is identified as the most common endocrine disorder in reproductive-aged women, and symptoms of PCOS appear during the early pubertal age. There is a gap in knowledge in recognizing the status of gingival inflammation/periodontal destruction and high-sensitivity C-reactive protein levels (hsCRP) in adolescents versus adults with PCOS. This study aimed to observe the impact of PCOS on periodontal status and systemic inflammation in adolescents and compared them with adults with PCOS. **Methods:** A total of 100 newly diagnosed female subjects with PCOS were

enrolled into two groups: adolescents (11–19 years,  $n = 50$ ) and adult females (20–40 years,  $n = 50$ ). Periodontal parameters, anthropometric parameters, PCOS phenotype, hirsutism score, and serum hsCRP levels were recorded. **Results:** High levels of mean hsCRP, gingival index, and bleeding on probing % were observed in adolescent and adult PCOS groups, though nonsignificant between the groups ( $p > 0.05$ ). Significantly more sites with probing pocket depth 3–4 mm, higher mean clinical attachment level (CAL) and sites with CAL 1–2 mm, and high frequency of patients ( $n = 11$ ) with periodontitis (stage 1) were observed in adults with PCOS compared to adolescents ( $p \leq 0.05$ ). Similar and predominant prevalence of PCOS phenotype A (66%) and moderate hirsutism (46% adolescents vs. 58% adults) were observed in both groups. **Conclusion:** Similar levels of hsCRP and periodontal inflammation were found in adolescents and

adults with PCOS. More periodontal tissue destruction was observed in adults with PCOS as compared to adolescents with PCOS.

© 2024 The Author(s).  
Published by S. Karger AG, Basel

## Introduction

Polycystic ovary syndrome (PCOS) is a common, complex disease affecting women of reproductive age worldwide [1]. Prevalence rate of adult females with PCOS is reported as 2.2–26% in Western countries [2], while prevalence of adolescent girls having PCOS is 9.13–36% in India [3].

In PCOS, imbalance in the production of estrogen and androgen is caused by decreased aromatase activity and elevated levels of gonadotropin-releasing hormone [4]. This rhythm of gonadotropin-releasing hormone levels is linked with hyperandrogenism, and increased ovarian volume [5], and the whole reproductive axis is switched on in adolescent females with PCOS [6]. Chronic anovulation in PCOS leads to a hyperandrogenic state, and increased levels of sex steroid hormones alter the periodontal tissue response, reducing the resistance of the epithelial barrier permitting bacteria to colonize rapidly in the gingival tissue [6]. Wendland et al. [7] investigated the association between subgingival microbes and gingival health and reported unfavorable microorganisms were not associated with PCOS in adolescents and found similar gingival inflammation and bleeding sites in healthy adolescents. In another study, Wendland et al. [8] demonstrated that adolescents with PCOS had higher levels of the inflammatory cytokines IL-1 $\beta$ , IL-6, and TNF- $\alpha$ , with similar levels of gingival inflammation and bleeding sites compared to healthy controls. The association of higher gingival inflammation with PCOS and its link with low-grade systemic inflammation, a possible pathophysiological mechanism, demonstrates a relationship between PCOS and periodontal diseases [9, 10]. Considering the hormonal changes and persistent low-grade systemic inflammation in females with PCOS, it is hypothesized that PCOS may influence the gingival/periodontal status and systemic inflammation in adolescents. Periodontitis is characterized by microbe-associated, host-mediated inflammation that results in loss of periodontal attachment [11]. Age is also present as a risk factor and associated with the severity of periodontal diseases in middle aged and elderly individuals [12]. Poor oral hygiene is a major risk factor as it may

manifest severe periodontal inflammation/destruction due to the cumulative effect of bacterial plaque on periodontal tissues. The impact of PCOS on periodontal inflammation has been observed in females with PCOS in a wide age range of 17–43 years [13]; more periodontal destruction was observed in young adults with PCOS [13–16]. Activation of low-grade systemic inflammation in adolescents with PCOS may influence the periodontium in early life [8]. Therefore, it is important to identify gingival inflammation/periodontal destruction in adolescents so that preventive measures can be implemented for the gingival/periodontal diseases, to halt the further progression of disease into periodontitis. Evaluation of gingival inflammation or periodontal diseases along with serological markers of low-grade inflammation in narrow age cohorts of PCOS females is also needed as PCOS affects women and its manifestations change throughout life from early pubertal years to the postmenopausal period [17]. Studies demonstrating the correlation of low-grade systemic inflammation with periodontal parameters are lacking in adolescent PCOS females.

The aim of the present study was to assess the periodontal status and systemic inflammation in newly diagnosed adolescents with PCOS compared to adult females with PCOS who had not started medical treatment for the syndrome. The primary objective of the study was to assess periodontal inflammation and destruction, serum levels of high-sensitivity C-reactive protein (hsCRP), and anthropometric parameters in newly diagnosed adolescents and adults with PCOS. The secondary objectives of this study were to explore the association of anthropometric parameters, age, periodontal parameters, and serum levels of hsCRP in newly diagnosed adolescents and adults with PCOS and to estimate the PCOS phenotype, hirsutism score, and periodontal phenotype in newly diagnosed adolescents and adults with PCOS.

## Subjects and Methods

This cross-sectional study was conducted between November 2021 and June 2022 at the Department of Periodontology, Post Graduate Institute of Dental Sciences, Rohtak, India, in joint collaboration with the Department of Obstetrics and Gynecology, Post Graduate Institute of Medical Sciences (PGIMS), Rohtak. Approval for the study was obtained from the Institutional Review Board, Pandit Bhagwat Dayal Sharma University of Health Sciences, Rohtak.

### Study Design

A total of 100 female patients with PCOS were recruited from the outpatient Department of Obstetrics and Gynecology, PGIMS, Rohtak. Newly diagnosed females with PCOS who had not started medication for the syndrome were enrolled into two groups: (1)

adolescent (age range 11–19 years) and (2) adults (age range 20–40 years) as positive controls, with 50 individuals in each group based on inclusion and exclusion criteria. Diagnosis of PCOS females was according to Rotterdam criteria [18], including any two out of the following three abnormalities: (1) clinical and/or biochemical hyperandrogenism; (2) chronic anovulation; and (3) polycystic ovaries on ultrasound. The inclusion of adolescent females with PCOS was according to having an onset of menarche from at least 3 years and reported to our department with issues related to menstrual cycle and hyperandrogenism. Exclusion criteria were patients with a history of thyroid disease, androgen hormone-related tumors, and hyperprolactinemia, patients with chronic renal failure, nephrotic syndrome, established diabetes mellitus (type 1 or 2), active neoplasm involving any body part within the past 5 years, and any significant cardiovascular disease were also excluded. Patients with formerly/currently consumed tobacco/alcohol, systemic antibiotic intake within the previous 3 months, received periodontal therapy in the previous 6 months, pregnant and lactating females, and taking oral contraceptive pills were also not considered in the study. Systemic diseases or conditions were ruled out by taking detailed medical histories, consulting with physicians, and conducting laboratory investigations. Socioeconomic status and oral hygiene habits were also recorded.

#### *Data Collection: Anthropometric Parameters*

Waist circumference (WC) was recorded, by measuring at the middle point, between the inferior margin of the lowest palpable rib and the uppermost aspect of the iliac crest (in centimeters) [19]. Hip circumference was recorded by taking measurements around the broad portion of the buttocks and calculating the waist-hip ratio [19]. Body mass index (BMI) was recorded by calculating: body mass (weight of the body) divided by the square height (expressed in units of kg/m<sup>2</sup>).

#### *Serological Markers of Systemic Inflammation*

Serum hsCRP levels estimation was done by a particle-enhanced immune-turbidimetric assay (C-Reactive Protein (Latex) High-Sensitivity Assay, Roche Diagnostics, Indianapolis, IN) with high-sensitivity procedure in an auto-analyzer (KoneLab Clinical Chemistry Analyzer, Thermo Fisher Scientific, Waltham, MA, USA). The immune complex turbidity was measured at 546 nm, with the lower noticeable limit 0.15 mg/L.

#### *Periodontal Parameters*

Periodontal parameters were recorded by a single experienced examiner (S.J.) using a periodontal probe (PCP-UNC, Hu-Friedy, Chicago, IL, USA) on each tooth, excluding third molars. Four sites of a tooth were recorded (mesiobuccal, mid-buccal, distobuccal, and mid-lingual/palatal) for gingival index (GI) [20] and plaque index (PI) [21]. Bleeding on probing (BOP%), probing pocket depth (PPD), and clinical attachment level (CAL) were registered at six sites (mesiobuccal, mid-buccal, distobuccal, mesiolingual/palatal, mid-lingual/palatal, and distolingual/palatal) per tooth. PPD sites were further segregated into PPD = 3–4 mm and PPD > 4 mm, while sites with CAL were segregated into CAL = 1–2 mm, 3–4 mm, and ≥ 5 mm. BOP was recorded dichotomously: 0 denotes absence and 1 denotes the presence of Bleeding on probing. Individuals with gingival health, gingivitis, and periodontitis were diagnosed according to the case-definition criteria of the 2017 World Workshop classification of periodontal disease and conditions [11, 22].

Gingival thickness (GT) was measured using an endodontic k file (Dentsply M Access K-file Number-20) and a digital vernier caliper (zhart vernier caliper Digital 150 mm/6-inches LCD Display, India). Keratinized tissue width (KTW) was measured as a distance from the marginal gingiva to the mucogingival junction. These parameters were recorded on the selected teeth: central incisor, canine, and second premolar (CI, C, and PM) of the first quadrants of the maxillary arch and the third quadrant of the mandibular arch.

Intra-examiner reproducibility was carried out for PPD and CAL by repeating measurements after 48 h on 10 patients. It was determined by calculating the percentage of sites. The scores were found with 90% accuracy (matching within ±1 mm) with a kappa value of 0.82 for PPD and 0.81 for CAL.

#### *PCOS Phenotype and Hirsutism Score*

PCOS phenotypes were identified by the Rotterdam criteria [14]. The modified Ferriman-Gallwey (mFG) scoring system was used for hirsutism [23].

#### *Sample Size*

A sample size of 92 participants (46 per group) was calculated using G-power software (G-power version 3.1.9.4, Germany) to detect a difference of 0.5 mm in CAL ( $SD \pm 0.7$ ) with effect size of 0.7 [16] and alpha error = 0.05 at power 90%. We enrolled 100 subjects (50 per group), considering the possibility of attrition of patients due to multiple visits to confirm the diagnosis of PCOS, biochemical investigations, and periodontal examinations.

#### *Statistical Analysis*

The normality of data was examined by Shapiro-Wilk test, and the results depicted nonnormal distribution. For intergroup comparisons of variables, the Mann-Whitney U test was applied. Spearman correlation test was applied to assess the relationship among variables. Multiple linear regression (stepwise) analysis was used to explore the association of dependent variable (CAL) and independent variables (GI, PI, PPD, BOP, BMI, WC, WHR, age, hsCRP).

## **Results**

Out of 173 individuals, 21 declined to participate, and 52 patients did not meet the inclusion criteria. Thus, 100 patients were enrolled and completed the present study. Table 1 shows the demographic, anthropometric, clinical, and biochemical data of the subjects. BMI, WC, and WHR were within normal limits in both PCOS groups. Serum levels of hsCRP were comparable between the groups. Significantly higher CAL was observed in the adult group than in adolescents, while GI, PI, BOP%, and PPD did not show significant difference between the groups (Fig. 1). Oral hygiene habits were similar in all the patients. Most patients belonged to middle socioeconomic class. A majority of patients had moderate hirsutism, and PCOS phenotype A was found in 33 individuals in each group. Significant high scores ( $p \leq 0.05$ ) in GT and KTW were found in adolescent PCOS females.

Table 2 depicts the distribution of sites of PPD and CAL and the periodontal disease status. The mean number of sites with PPD 3–4 mm and CAL 1–2 mm was significantly more in adults compared to adolescents ( $p \leq 0.05$ ). Nonsignificant difference in frequency of patients having healthy gingiva and gingivitis was noticed in both PCOS cohorts ( $p > 0.05$ ). However, a statistically significant higher frequency of patients having periodontitis with stage 1 ( $n = 11$ ) and stage 2 ( $n = 02$ ), and grade A ( $n = 12$ ) and grade B ( $n = 01$ ) was observed in the adult group as compared to adolescents (Fig. 1).

Table 3 exhibits the results of Spearman's correlation analysis. Age was negatively correlated with PCOS while positively and significantly correlated with CAL. Serum levels of hsCRP were correlated significantly and positively with PPD, BMI, and WC. Multiple linear regression analysis showed that CAL was significantly associated with GI and age (Table 4).

## Discussion

The present study was conducted to assess the periodontal status in terms of periodontal inflammation and destruction, and systemic inflammation in newly diagnosed adolescents with PCOS compared with adult females with PCOS. Two age groups were taken into consideration, adolescents with PCOS and adults  $\leq 40$  years of age with PCOS, as there is a change in the course of PCOS with age; amelioration of PCOS has been documented converting it from a reproductive disease to a metabolic disorder [17]. BMI, WC, and WHR were found within normal limits and comparable in both groups, ruling out the possibility that obesity may act as a confounding factor for local and systemic inflammation. Smokers were excluded as smoking is risk factor that may influence the results of the study.

Mean levels of hsCRP were high in both adolescents with PCOS ( $2.56 \pm 3.49$  mg/L) and adults with PCOS ( $2.77 \pm 3.84$  mg/L). Though we have not compared hsCRP levels with systemically healthy controls, we have previously reported significantly higher levels of hsCRP in newly identified adult PCOS females compared to healthy females [16]. The results of the present study showed elevated levels of hsCRP in adolescents with PCOS comparable to adult women with PCOS, suggesting that the influence of PCOS on low-grade systemic inflammation is initiated at an early age. Taşkömür et al. [24] demonstrated higher levels of hsCRP in normal weight and overweight adolescents with PCOS as compared to weight-matched healthy controls. Mažibrada et al. [25] also reported significantly higher levels

of hsCRP in PCOS adolescent girls compared with healthy controls and found an association of the pro-inflammatory indices hsCRP and fibrinogen with anthropometric and lipid parameters of adolescent girls with PCOS.

Plaque levels were similar in both the groups, ruling out possible confounding effects of plaque on the other parameters. Gingival inflammation and sites with BOP were high and comparable between adult and adolescent females with PCOS. Healthy females were not evaluated in the present study, but Wendland et al. [8] reported comparable gingival score and BOP % between healthy adolescents and PCOS adolescent girls. However, higher levels of the pro-inflammatory cytokines IL-1 $\beta$ , IL-6, and TNF- $\alpha$  were reported in adolescents with PCOS [8]. Our previous study showed significantly more gingival inflammation and BOP% in PCOS adults as compared to matched healthy controls with similar plaque scores [16]. The significantly high gingival inflammation in their study may be due to enhanced systemic inflammation caused by PCOS, and this chronic inflammatory status can account for increased periodontal inflammation.

We observed a higher number of sites with PPD 3–4 mm in adults than in adolescents with PCOS. Previous studies compared PCOS groups with healthy controls and reported a lack of significant difference in mean PPD in adolescents with PCOS versus healthy controls [7], and in adults with PCOS [14] with their matched healthy controls. In our study, mean PPD was comparable in both PCOS groups. However, significantly more sites with PPD 3–4 were observed in adults compared to adolescents. Early intervention to control gingival inflammation is required in these patients as the presence of generalized periodontal inflammation may initiate periodontal destruction in adolescents with PCOS. CAL is a more reliable periodontal parameter in detecting the extent of lost periodontal support around a tooth compared to pocket depth alone. Mean CAL and mean number of sites with CAL (1–2 mm) were significantly higher in adults than in adolescents. Porwal et al. [16] and Rahiminejad et al. [15] reported more CAL in the adults with PCOS compared to healthy controls. Significantly high measures of CAL in adult PCOS females suggest the possible influence of long-standing PCOS on the breakdown of periodontal tissue. However, the levels of systemic inflammatory markers in adults were not higher compared to adolescents; this could be attributed to the chronic state of periodontal inflammation in adults which along with long-standing PCOS may act synergistically in increasing the systemic inflammation, and marginally increase in CAL. Though statistically significant this might not be adequate to demonstrate the impact of periodontal destruction on hsCRP levels.

**Table 1.** Demographic data, anthropometric parameters, hsCRP levels, PCOS phenotype, hirsutism score, periodontal parameters, and phenotype

Variables	Group-1 ( <i>n</i> = 50) adolescents			Group-2 ( <i>n</i> = 50) adults			<i>p</i> value	
		95% CI	median		95% CI	median		
Age, years, mean ± SD <sup>a</sup>	17.9±1.52	LB-17.44 UB-18.28	18.00	24.14±3.58	LB-23.16 UB-25.17	23.00	<b>0.000<sup>c</sup></b>	
BMI, kg/m <sup>2</sup> , mean ± SD <sup>a</sup>	21.55±2.76	LB-22.02 UB-23.52	21.10	22.73±2.76	LB-22.01 UB-23.51	22.85	<b>0.01<sup>c</sup></b>	
WC, cm, mean ± SD <sup>a</sup>	75.74±6.55	LB-76.09 UB-80.67	76.2	78.33±8.48	LB-75.89 UB-80.74	76.2	0.11	
WHR, mean ± SD <sup>a</sup>	0.79±0.04	LB-0.77 UB-0.79	0.78	0.78±0.04	LB-0.77 UB-0.79	0.78	0.42	
hsCRP, mg/L, mean ± SD <sup>a</sup>	2.56±3.49	LB-1.80 UB-3.97	1.39	2.77±3.84	LB-1.79 UB-3.91	1.31	0.94	
Patients with PCOS phenotype, <i>n</i> (%) <sup>b</sup>	A B C D	33 (66) 13 (26) 0 4 (8)		33 (66) 11 (22) 1 (2) 5 (10)			0.73	
Patients with hirsutism score, <i>n</i> (%) <sup>b</sup>	Mild Moderate Severe	17 (34) 23 (46) 10 (20)		11 (22) 29 (58) 10 (20)			0.37	
GI, mean ± SD <sup>a</sup>		1.13±0.38	1.02–1.24	1.25	1.21±0.35	1.11–1.31	1.21	0.59
PI, mean ± SD <sup>a</sup>		0.94±0.41	0.83 to 1.06	1.04	1.11±0.31	1.03–1.20	1.09	0.07
PPD, mm, mean ± SD <sup>a</sup>		1.62±0.43	1.50–1.74	1.43	1.59±0.41	1.48–1.72	1.41	0.78
BOP, %, mean ± SD <sup>a</sup>		40.11±23.83	33.36–46.56	39.00	38.08±22.67	32.02–44.46	35.50	0.63
CAL, mm, mean ± SD <sup>a</sup>		0.02±0.07	0.007–0.04	0.000	0.13±0.29	0.06–0.21	0.000	<b>0.03<sup>c</sup></b>
Overall selected teeth, GT, mm <sup>a</sup>		0.92±0.28			0.82±0.30			<b>0.03<sup>c</sup></b>
Periodontal phenotype <sup>a</sup> , KTW, mm, mean ± SD <sup>a</sup>		3.41±0.74			3.08±0.53			<b>0.01<sup>c</sup></b>
Patients with brushing frequency per day <sup>b</sup> , <i>n</i>	Once Twice	34 16		42 8			0.06	
Patients with brushing technique <sup>b</sup> , <i>n</i>	Horizontal vertical Horizontal+ vertical	15 17 18		32 7 11			<b>0.002<sup>c</sup></b>	

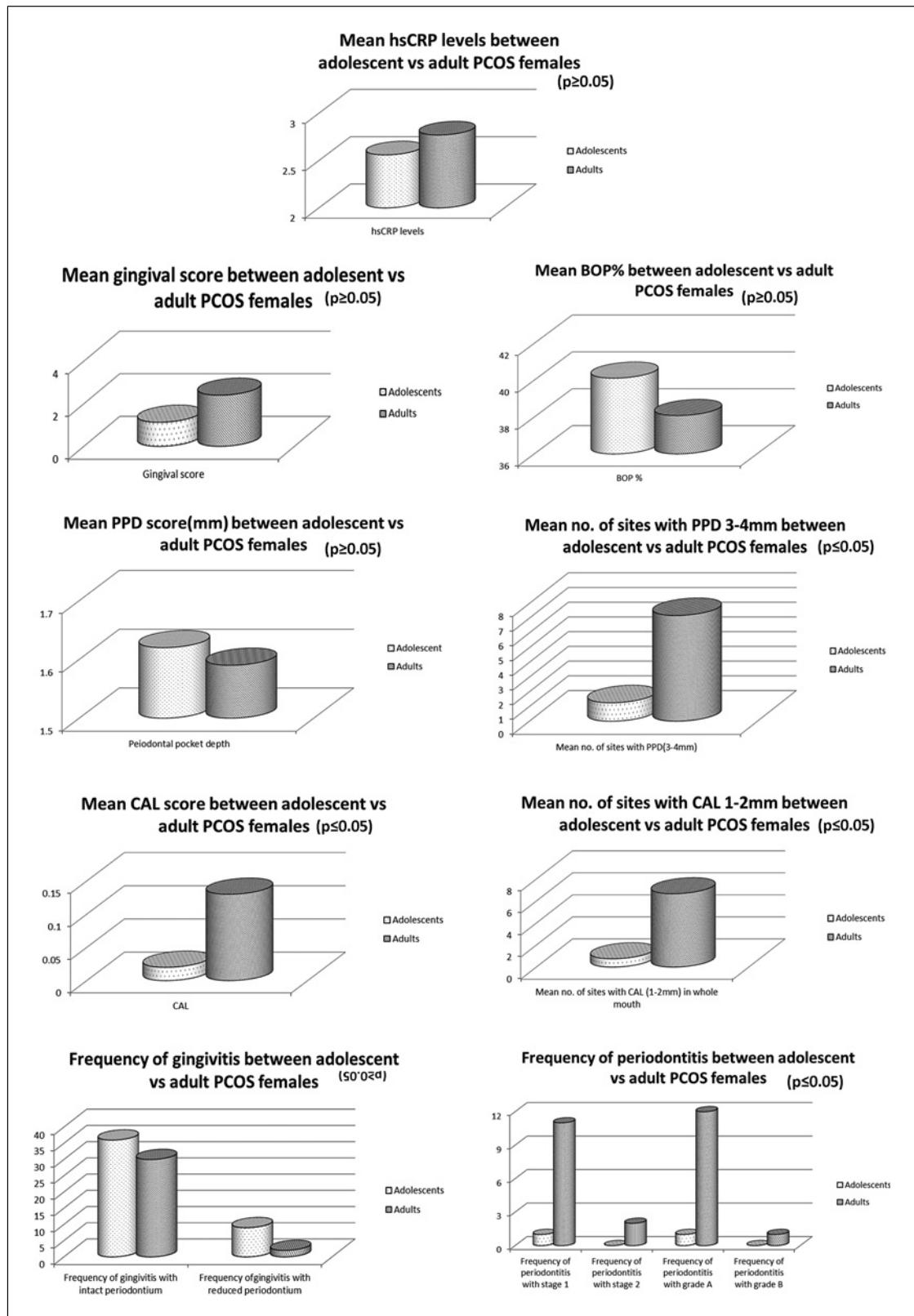
SD, standard deviation; LB, lower bound; UB, upper bound; CI, confidence interval; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; hsCRP, high-sensitivity C-reactive protein; GI, gingival index; PI, plaque index; PPD, probing pocket depth; BOP, bleeding on probing; CAL, clinical attachment level; GT, gingival tissue thickness; KTW, keratinized tissue width. <sup>a</sup>Mann-Whitney U test. <sup>b</sup> $\chi^2$  test. <sup>c</sup>Statistically significant (*p* ≤ 0.05).

Multiple regression analysis was used to determine the strength of association of variables with CAL in PCOS population. The results of the analysis showed a statistically significant association of age and gingival inflammation with CAL demonstrating an increase in 0.12 of CAL could be expected per 1 year increase in age and increase in 0.232 CAL expected in presence of gingival inflammation.

A significant difference was observed in GT and KTW with more scores in adolescents than in adults. Comparison of these results was not possible, as these had not

been assessed in women with PCOS in the previous study. It may be speculated that long-term hyperandrogenic state and excess levels of estrogen in women with PCOS may influence the cells and matrix of gingival tissue [26], and this may influence GT and KTW.

Among the PCOS phenotypes, phenotype A was common with similar prevalence (66%) in adults and adolescents. Fruzzetti et al. [27] also reported similar prevalence of phenotype A (73.4%) and concluded that the prevalence and characteristics of the primary PCOS



**Fig. 1.** Comparison of biochemical and periodontal parameters and distribution of periodontal diseases between adolescents and adults with PCOS.

**Table 2.** Distribution of periodontal parameters (mean ± SD) in the study population

Variables	Adolescents with PCOS		Adults with PCOS	p value
Mean no. of sites with PPD (3–4 mm) in whole mouth, mean ± SD <sup>a</sup>	1.25±5.25		7.18±13.73	<b>0.004<sup>c</sup></b>
Mean no. of sites with PPD (>4 mm) in whole mouth, mean ± SD <sup>a</sup>	0		0.38±1.84	0.08
Mean no. of sites with CAL (1–2 mm) in whole mouth, mean ± SD <sup>a</sup>	0.75±2.98		6.66±12.95	<b>0.007<sup>c</sup></b>
Mean no. of sites with CAL (3–4 mm) in whole mouth, Mean ± SD <sup>a</sup>	0.20±0.93		0.81±2.96	0.433
Mean no. of sites with CAL (≥5 mm) in whole mouth, mean ± SD <sup>a</sup>	0		0.21±1.14	0.08
Frequency of periodontally healthy patient <sup>b</sup>	GH + IP GH + RP	4 0	4 1	0.71
Frequency of gingivitis <sup>b</sup>	G + IP G + RP	36 9	30 2	1.00
Frequency of periodontitis <sup>b</sup>	Stage 1 Stage 2 Grade A Grade B	1 0 1 0	11 2 12 1	<b>0.001<sup>c</sup></b> <b>0.001<sup>c</sup></b>

SD, standard deviation; PPD, probing pocket depth; CAL, clinical attachment level; GH + IP, gingival health with intact periodontium; GH + RP, gingival health with reduced periodontium; G + IP, gingivitis with intact periodontium; G + RP, gingivitis with reduced periodontium. <sup>a</sup>Mann-Whitney U test. <sup>b</sup> $\chi^2$  test. <sup>c</sup>Statistically significant ( $p \leq 0.05$ ).

**Table 3.** Correlation among the variables using Spearman correlation analysis

Variables	Age	CAL	hsCRP	PPD	BMI	WC
Group correlation	-0.839 <sup>a</sup>	-0.227 <sup>b</sup>	-0.028	0.014	-0.215 <sup>b</sup>	-0.130
Significance (two-tailed)	<b>0.000<sup>c</sup></b>	<b>0.023<sup>d</sup></b>	0.779	0.892	<b>0.032<sup>d</sup></b>	0.196
Age		0.253 <sup>b</sup> <b>0.011<sup>d</sup></b>	0.007 0.947	0.092 0.364	0.208 <sup>b</sup> <b>0.038<sup>d</sup></b>	0.166 0.100
CAL			-0.077 0.446	0.399 <sup>a</sup> <b>0.000<sup>c</sup></b>	0.043 0.671	-0.003 0.977
hsCRP				0.215 <sup>b</sup> <b>0.032<sup>d</sup></b>	0.260 <sup>a</sup> <b>0.009<sup>c</sup></b>	0.254 <sup>b</sup> <b>0.011<sup>d</sup></b>
PPD					-0.034 0.736	-0.046 0.649
BMI						0.675 <sup>a</sup> <b>0.000<sup>c</sup></b>

CAL, clinical attachment level; hsCRP, high-sensitivity C-reactive protein; PPD, probing pocket depth; BMI, body mass index; WC, waist circumference. <sup>a</sup>Correlation is significant at the <sup>c</sup> $p \leq 0.01$ . <sup>b</sup>Correlation is significant at the <sup>d</sup> $p \leq 0.05$ .

**Table 4.** Association of independent variables with dependent outcomes using multiple linear regression analysis

Dependent Variable	Model predictors	β unstandardized	Standard error	β Standardized	p value	R <sup>2</sup>	95% CI
CAL	Constant	-0.453	0.106		<b>0.000<sup>a</sup></b>	0.252	-0.665 to -0.242
	GI	0.232	0.052	0.399	<b>0.000<sup>a</sup></b>		0.128–0.335
	Age	0.012	0.005	0.235	<b>0.010<sup>a</sup></b>		0.003–0.022

CAL, clinical attachment level; GI, gingival index; BMI, body mass index; PPD, probing pocket depth; CI, confidence interval. <sup>a</sup> $p \leq 0.05$  (statistically significant).

phenotypes are unaffected by aging. In the current study, the percentage of moderate hirsutism (58%) was similar in adults and adolescents (46%). Jain et al. [28] also reported similar prevalence of hirsutism (adolescents 42%, adults 40%) in Indian females with PCOS. Hirsutism is the main manifestation of hyperandrogenism in PCOS.

Some of the limitations of the study include the lack of evaluation of quantitative and qualitative levels of subgingival microflora, levels of pro-inflammatory cytokines, and assessment of hormonal levels. Systemically healthy adolescents and adults were also not taken into account as matched controls for comparative evaluation. Adult PCOS females were considered as a positive control. A prospective cohort study design would have been better to observe the sequelae of inflammation early in the life of patients with PCOS. A longitudinal prospective study was not possible as these patients required treatment to regulate menstrual cycle and/or to conceive.

## Conclusions

Within the limitations of our study, we conclude that levels of systemic inflammatory markers and periodontal inflammation were raised in newly diagnosed adolescents with PCOS, which were comparable with adults with PCOS who had not started medication for the syndrome. Periodontal tissue breakdown was significantly higher in adults with PCOS as compared to adolescents. Further, periodontal tissue destruction was observed to have a significant association with age and gingival inflammation. Persistent exposure to increased levels of periodontal and low-grade systemic inflammation initiated in adolescents with PCOS may contribute to an exaggerated or altered inflammatory response or periodontal breakdown in young adults with PCOS. These findings suggest that oral healthcare should be implemented, especially in adolescents with PCOS, to prevent the long-term sequelae of local and systemic chronic inflammatory burden.

Healthcare professionals should motivate these patients to maintain good oral hygiene and consult a dentist to avoid periodontal complications.

## Acknowledgments

We thank Post Graduate Institute of Dental Sciences, Rohtak for providing all the facilities during the study.

## Statement of Ethics

Ethical approval was obtained from the Biomedical and Health Research Ethics Committee, Post Graduate Institute of Dental Sciences (Reference Number PGIDS/BHRC/20/23). The study followed the Helsinki Declaration of 1975, amended in 2013. The study was registered on clinicalTrials.gov (NCT05113030). Written informed consent was obtained from all subjects before the initiation of the study. Parents/guardians had given written and verbal consent for adolescent females.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

## Funding Sources

None.

## Author Contributions

All authors contributed to the conception, design, and methodology of the study. All authors contributed equally to data analysis, manuscript writing and approved the final manuscript.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

## References

- March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Hum Reprod.* 2010;25(2):544–51.
- Diamanti-Kandarakis E, Kouli CR, Bergiele AT, Filandra FA, Tsianateli TC, Spina GG, et al. A survey of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile. *J Clin Endocrinol Metab.* 1999;84(11):4006–11.
- Nair MK, Pappachan P, Balakrishnan S, Leena ML, George B, Russell PS. Menstrual irregularity and polycystic ovarian syndrome among adolescent girls-A 2 year follow-up study. *Indian J Pediatr.* 2012;79(Suppl 1):S69–73.
- Taylor AE, McCourt B, Martin KA, Anderson EJ, Adams JM, Schoenfeld D, et al. Determinants of abnormal gonadotropin secretion in clinically defined women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 1997;82(7):2248–56.
- Apter D, Bützow T, Laughlin GA, Yen SS. Metabolic features of polycystic ovary syndrome are found in adolescent girls with hyperandrogenism. *J Clin Endocrinol Metab.* 1995;80(10):2966–73.

- 6 Kumar PS. Sex and the subgingival microbiome: do female sex steroids affect periodontal bacteria? *Periodontol*. 2013;61(1):103–24.
- 7 Wendland N, Opydo-Szymaczek J, Formanowicz D, Blacha A, Jarząbek-Bielecka G, Mizgier M. Association between metabolic and hormonal profile, proinflammatory cytokines in saliva and gingival health in adolescent females with polycystic ovary syndrome. *BMC Oral Health*. 2021;21(1):193.
- 8 Wendland N, Opydo-Szymaczek J, Mizgier M, Jarząbek-Bielecka G. Subgingival microflora in adolescent females with polycystic ovary syndrome and its association with oral hygiene, gingivitis, and selected metabolic and hormonal parameters. *Clin Oral Investig*. 2021;25(3):1485–96.
- 9 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*. 2023;14:1008675.
- 10 Marquez –Arrico CF, Silvestre-Rangil J, Gutierrez-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.
- 11 Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: framework and proposal of a new classification and case definition. *J Periodontol*. 2018;89(Suppl 1):S159–72. Erratum in: *J Periodontol*. 2018; 89(12):1475.
- 12 Huang Q, Dong X. Prevalence of periodontal disease in middle-aged and elderly patients and its influencing factors. *Am J Transl Res*. 2022;14(8):5677–84.
- 13 Akcalı A, Bostancı N, Özçaka Ö, Öztürk-Ceyhan B, Gümüş P, Tervahartiala T, et al. Elevated matrix metalloproteinase-8 in saliva and serum in polycystic ovary syndrome and association with gingival inflammation. *Innate Immun*. 2015;21(6):619–25.
- 14 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):320–3.
- 15 Rahiminejad ME, Moaddab A, Zaryoun H, Rabiee S, Moaddab A, Khodadoust A. Comparison of prevalence of periodontal disease in women with polycystic ovary syndrome and healthy controls. *Dent Res J*. 2015;12(6):507–12.
- 16 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):1380–9.
- 17 Falsetta P, Benelli E, Molinaro A, Di Cosmo C, Bagattini B, Del Ghianda S, et al. Effect of aging on clinical features and metabolic complications of women with polycystic ovary syndrome. *J Endocrinol Invest*. 2021; 44(12):2725–33.
- 18 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):41–7.
- 19 World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation. World Health Organization; 2008. [Accessed 2011 May 16] Available from: <https://apps.who.int/iris/handle/10665/44583>.
- 20 Loe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odontol Scand*. 1963;21:533–51.
- 21 Silness J, Loe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand*. 1964;22:121–35.
- 22 Chapple ILC, Mealey BL, Van Dyke TE, Bartold PM, Dommisch H, Eickholz P, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: consensus report of workgroup 1 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions. *J Clin Periodontol*. 2018;45(Suppl 20):S68–77.
- 23 Ferriman D, Purdie AW. The aetiology of oligomenorrhoea and/or hirsuties: a study of 467 patients. *Postgrad Med J*. 1983;59(687):17–20.
- 24 Taşkömür AT, Erten Ö. Relationship of inflammatory and metabolic parameters in adolescents with PCOS: BMI matched case-control study. *Arch Endocrinol Metab*. 2022; 66(3):372–81.
- 25 Mažibrada I, Djukić T, Perović S, Plješa-Ercegovac M, Plavšić L, Bojanin D, et al. The association of hs-CRP and fibrinogen with anthropometric and lipid parameters in non-obese adolescent girls with polycystic ovary syndrome. *J Pediatr Endocrinol Metab*. 2018; 31(11):1213–20.
- 26 Güncü GN, Tözüm TF, Çağlayan F. Effects of endogenous sex hormones on the periodontium--review of literature. *Aust Dent J*. 2005;50(3):138–45.
- 27 Frizzetti F, Baldari F, Palla G, Fideccia T, Carmina E. Comparison of PCOS phenotypes in adolescent and young adult mediterranean women with possible PCOS. *J Endocrinol Invest*. 2021;44(5):995–1000.
- 28 Jain S, Jain M, Shukla RC. Correlation of clinical, hormonal, biochemical and ultrasound parameters between adult and adolescent polycystic ovarian syndrome: adult and adolescent PCOS. *J Obstet Gynaecol India*. 2022;72(Suppl 1):274–80.