Int. j. adv. multidisc. res. stud. 2024; 4(3):673-678

Received: 07-04-2024
Accepted: 17-05-2024

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

PCOD and Periodontal Disease: A Narrative Review

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Abstract

Objective: The objective of this narrative review is to summarize the current knowledge on the correlation between Polycystic ovarian disease (PCOD and periodontal disease and to make recommendations for monitoring and improving oral health of females with PCOD by creating awareness.

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age[1].About 1 in 5 Indian females are affected with PCOD.Previous studies also showed that periodontal diseases are associated with different components of the metabolic syndrome[1].

Methods: To conduct this narrative review, PubMed was used to search for peer-reviewed articles on the Correlation between PCOD and periodontal disease. No limits were placed on the year of publication, but only articles translated into English were considered. Search terms used included "PCOD", "periodontitis", "Periodontal disease", "oral health" and "dental".

Results: Studies reveal that PCOD and periodontal disease are strongly connected. A Meta-analysis revealed that PCOS females have 28% more risk towards PD, and PD females have 46% more risk to have PCOS[2]. Recent studies also suspects that PD females possess high risk to trigger PCOD[3]. PCOD females with PD had higher gum bleeding, periodontal pocket depth and clinical attachment loss than non-PCOS females with PD[4].

Conclusion: This narrative review revealed a high risk of periodontal disease in PCOD patients. With the knowledge about the risk factors, it is very assertive to avoid such an easily preventable disease by simple precautions. PCOD becoming a leading disease in India, it is necessary to create awareness about its consequences to reduce the co-morbidities and improve the quality of life.

Keywords: PCOD, Periodontal Disease, India

Introduction

Polycystic ovarian disease (PCOD) has become very common among females of reproductive age group. It is one of the frequently diagnosed disease in medical practices. Prevalence of PCOD in India ranges from 3.7 to 22.5 percent. About one in five females in India are affected by PCOD.

Polycystic ovarian disease has various effects on the patient's body. Classically, PCOS is characterized by the presence of menstrual abnormalities (oligomenorrhea or amenorrhea), chronic anovulation or oligoovulation, clinical/biochemical evidence of hyperandrogenism (hirsutism, acne, or androgenic alopecia), and ultrasound findings [4]. Patients with this gender-specific form of metabolic syndrome are at higher risk for developing insulin resistance (IR), obesity, dyslipidemia, cardiovascular disease (CVD), and hypertension [5, 6]. Moreover, recent studies have shown the higher prevalence of impaired glucose tolerance (IGT), type II diabetes mellitus (DM), and lipid profile disturbances in women with PCOS [7, 8, 9].

'It is proved that individuals with PCOD are more susceptible to periodontal disease (PD) than females without any pathologies2. Meta-analysis revealed that PCOD females have 28% more risk towards periodontal disease3 recent studies also suspects that PD females possess high risk to trigger PCOD3. Periodontal diseases are chronic inflammatory processes that may lead to tooth loss by affecting tooth-supporting tissues, including the gingiva, alveolar bone, and periodontal ligaments. In addition to the role of bacterial infections, earlier studies have demonstrated the association of periodontal diseases and systemic conditions such as dyslipidemia, obesity, IR, DM, and CVD.

PCOD females with PD had higher gum bleeding, periodontal pocket depth and clinical attachment loss than non-PCOS females with PD4. Previous studies showed higher levels of oxidative stress and systemic inflammatory markers such as

interleukin-6 and C-reactive protein in both periodontal diseases and PCOS [14, 15, 16]. This association may be explained by the role of oxidative stress as the potential link between periodontitis and PCOS based on some recent studies [17, 18]. This might suggest a possible common pathophysiologic mechanism in concur manifestations of these conditions

Materials and Methods

Because there were few studies conducted on this topic, a systematic literature review was not possible, so a traditional or "narrative" literature review was used, which is appropriate when studies on the topic are lacking [18, 19]. In their landmark paper, Collins and Fauser encourage scientific writers to choose wisely when selecting whether to do a narra-tive review compared to a systematic review [18]. They acknowledge the scientific strengths of the systematic review study design, but then emphatically point out that systematic review methodology may be inadequate at best and harmful at worst to apply to some topics [18].

One example they cite constituting a case where choosing a systematic review instead of a narrative review would be a weakness rather than a strength is the case of a historical review, which they describe as an "irreplaceable means of tracing the development of a clinical concept, and the narrative thread could be lost in the strict rules of systematic review" [18]. These strict rules would include specifying inclusion and exclusion criteria for articles included in the review, while a narrative review does not seek to include all the articles on a topic, and allows for selecting articles based on their relevance to the topic.

For this narrative review, PubMed was used to search for peer-reviewed articles on the Correlation between PCOD and periodontal disease. No limits were placed on the year of publication, but only articles translated into English were considered. Search terms used included "PCOD", "periodontitis", "Periodontal disease", "oral health" and "dental"

Result

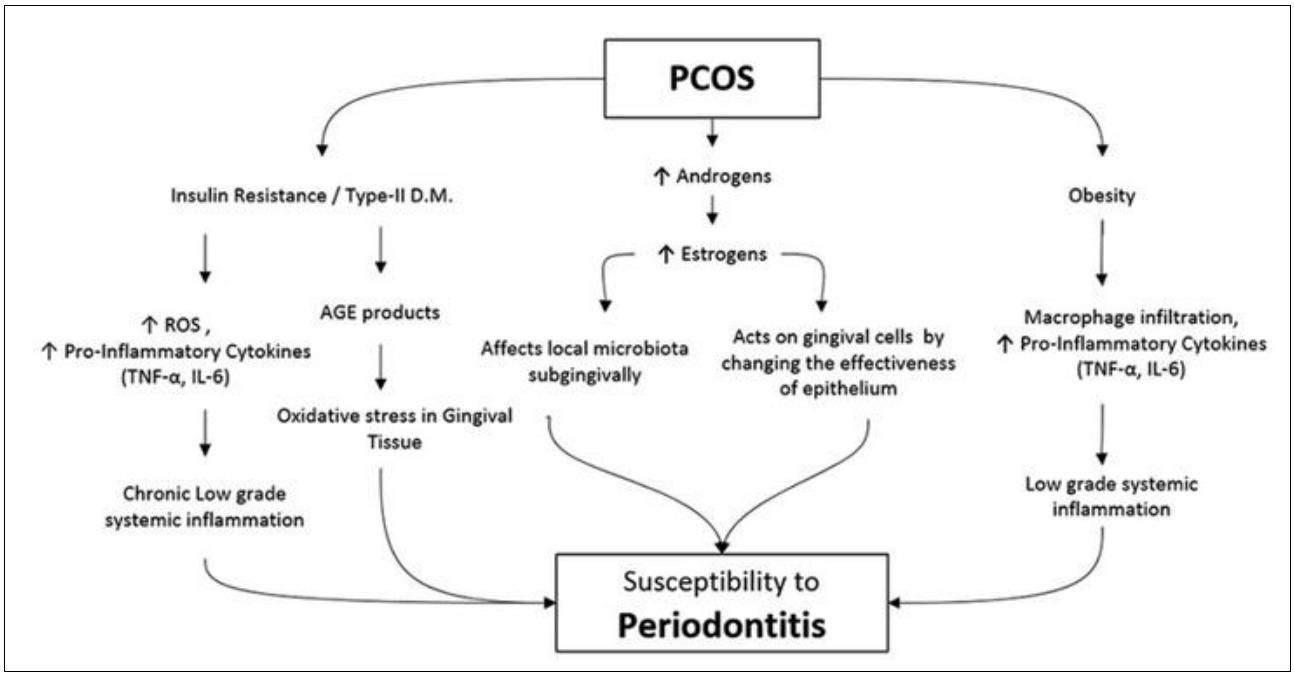
Various studies prove the association with increased risk of periodontal disease and PCOD. PCOD may worsen the periodontal condition by causing gingival inflammation, increased periodontal probe depth (PPD) and CAL (clinical attachment loss)3. PCOD might exacerbate the periodontal condition that is caused by plaque, through various pathophysiological links, namely, low-grade systemic inflammation, oxidative stress, Insulin resistance(IR), AGE products, and systemic hormonal levels.

Several pathophysiological links between PCOD and periodontal disease have been suggested in literature including low-grade systemic inflammation, Insulin Resistance (IR), oxidative stress, advanced glycation end products as well as systemic hormonal levels1. Hence, we can contemplate that there exists a two-way relationship between PCOD and periodontal disease.

Androgen production is a major trait of PCOD and essential for follicles. Although the overproduction of luteinizing hormone is evident, the absence of the optimum level of the hormone results in higher levels of progesterone and estrogen production.

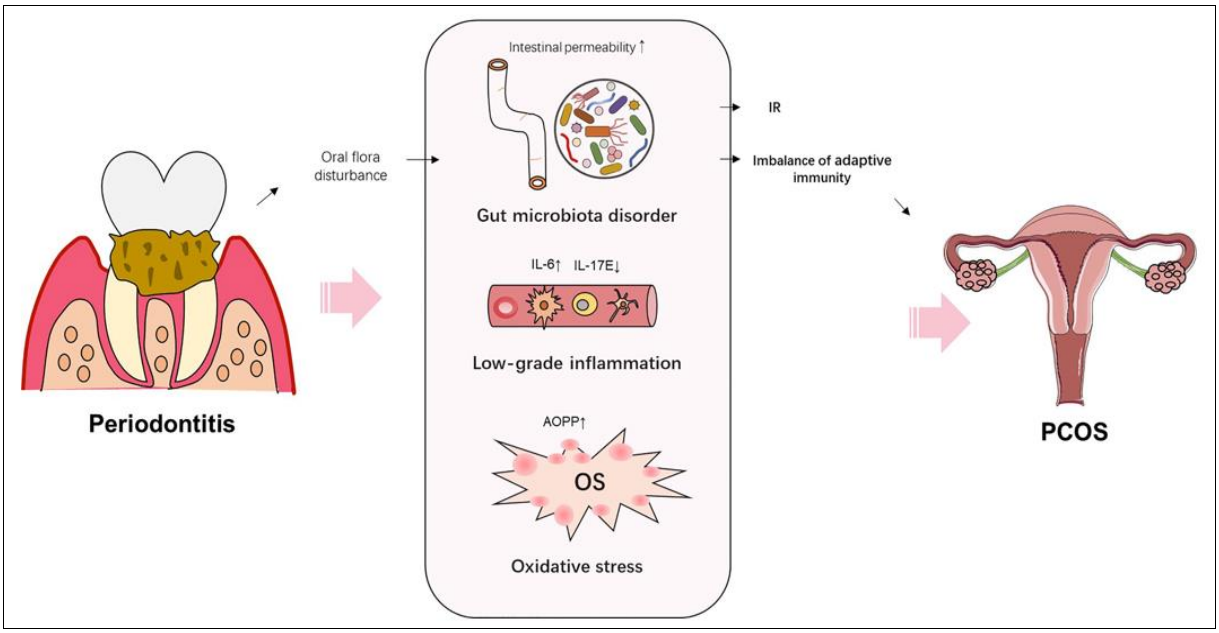
Such hormonal changes in PCOD are likely to influence the salivary levels of putative periodontal pathogens, or their systemic antibody responses, particularly when associated with gingival inflammation.

Streptococcus oralis was significantly higher in women with PCOD and gingivitis, than systemically or periodontally healthy women. It is also hypothesised that the sexual hormonal changes (hyperandrogenism, hyperestrogenism and hyperprogesteronism) in PCOD induce chronic low-grade inflammation affecting the capillary system and the angiogenesis process1Subsequently, it disrupts the defence system of periodontal tissues to the microbial plaque by altering the proliferation of oral flora and inducing pro-Inflammatory cytokines1.



Potential mechanisms by which PDD might increase the risk of PCOS- PDD leads to low-grade inflammation and oxidative damage

PDD is characterized by chronic inflammation induced by the subgingival biofilm. Various studies have demonstrated that multiple proinflammatory cytokines and reactive oxygen species (ROS) are involved in the systemic effects of PDD on systemic diseases, such as DM, MS, and obesity (88). PDD increases the risk of PCOS by mediating the anti-inflammatory and proinflammatory pathways. Higher concentrations of IL-6 in GCF, saliva, and serum were found in PCOS women with gingivitis, compared with PCOS women with healthy periodontium (16). Another study found that the expression of anti-inflammatory cytokine IL-17E was decreased in PCOS women with gingivitis, compared with PCOS women with healthy periodontium (24). In addition, PDD increases the oxidative damage and induces OS. Dharuman *et al*. found higher levels of advanced oxidation protein products (AOPP, a marker of oxidative damage) in the serum and saliva of PCOS women accompanied with PDD, when compared with that of PCOS women with good periodontal heath (28). Hence, PDD might function as a risk factor for PCOS through promoting inflammation and oxidative damage.



Discussion

From the above studies it is proved that PCOD patients have high susceptibilty to develop periodontal disease.Inflammation is a key factor in the pathophysiology of both PCOS and periodontal disorders. Low-grade chronic inflammation, a characteristic hallmark of PCOS, is expected to play a substantial role in the development of periodontal disorders. Numerous pieces of research have shown that inflammatory cytokines like tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), and interleukin-6 play a role in the connection between PCOS and periodontal disorders. CRP which is considered one of the essential markers of inflammation is seen raised in many diseases including PCOS [20]. Periodontitis patients exhibit increased blood CRP levels

First reported study about this risk was by Dursun *et al*.Then a study by Ozcaka *et al* revealed that PCOS and gingival inflammation act synergistically.Akcali *et al*. proved that levels of MMPs were high in serum of both PCOD and patients with periodontal disease.

There are many studies on the relationship between PCOD and periodontal disease, but the studies on analysing the levels of awareness, knowledge about this are not much available.

Studies linking PCOS and periodontal diseases

S. No	Author	Study
1.	Dursun *et al*. [49]	Reported an association between PCOS and periodontal diseases for the first time.
2.	Ozcaka *et al*. [50]	Examined the levels of proinflammatory cytokines in gingival crevicular fluid (GCF), saliva, and serum in patients with and without polycystic ovary syndrome (PCOS).
3.	Akcali *et al*. [51]	Analyzed the levels of matrix metalloproteinase-8 (MMP-8) and tissue inhibitors of MMP-1 (TIMP-1) in saliva and serum samples from women with polycystic ovarian syndrome who have varied degrees of gingival inflammation.
4.	Kellesarian *et al*. [52]	association between periodontal disease and polycystic ovary syndrome
5.	Rahiminejad *et al*. [53]	prevalence of periodontal disease in women with polycystic ovary syndrome and healthy controls

Conclusion

In India, due to rapidly increasing incidence of PCOD among females, there is an urgent need to assess the present levels of knowledge and execute necessary extents of awareness programs to educate the citizens better and improve their quality of life.

Oral hygiene practices being the easiest preventive measure will be mindfully followed by these patients only after the awareness. Health-care professionals, gynecologists, and endocrinologists in particular would need to proactively create awareness among patients diagnosed with PCOD to maintain good oral hygiene at all times and refer to dentist

to avoid periodontal implications as this hormonal disorder can worsen the vulnerability to plaque-induced periodontal disease".

The above data demonstrates a positive relationship between PCOS and periodontal disorders. Women with PCOS are at a higher risk of suffering from periodontal problems which can compromise their lifestyle. Evidence showed a bidirectional link between the two. Periodontal disease can also produce persistent subclinical inflammation that results in IR and the onset of type 2 diabetes, which is a common symptom of PCOS. Moreover, both diseases also share common risk factors which support the association. Early diagnosis for any periodontal disease is very crucial. It can help to prevent further complications leading to healthy periodontal health. Therefore, healthcare professionals would need to encourage women diagnosed with PCOS to maintain proper oral hygiene and encourage them to see a dentist on a frequent basis in order to avoid future periodontal risk.

The result of the study is expected to provide us an idea about the present extent of knowledge available about the link between PCOD and periodontal disease which inturn will help us formulate effective awareness programs to improve the quality of life of these patients. Reiterating the fact that about 20% of Indian women are affected with PCOD, as health care professionals especially dentists,it is the need of the hour to create awareness and this study will help us in effectively executing the same.

References

1. 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. Doi: 10.4103/1735-3327.170547. PMID: 26759585; PMCID: PMC4696351
2. Wadia R. Polycystic ovarian syndrome & periodontitis. Br Dent J. 2020; 229(2):125. Doi: 10.1038/s41415-020-1953-4. PMID: 32710063
3. Vanessa Machado, Cláudia Escalda, Luis Proença, José João Mendes, João Botelho. Is There a Bidirectional Association between Polycystic Ovarian Syndrome and Periodontitis? J Clin Med, 2020, 9-44.
4. Reena Wadia. Polycystic ovarian syndrome & periodontitis. British Dental Journal, 2020, 125.
5. Fathima F Farook, Ka Ting Ng, Nuzaim MNM, Wen J Koh, Wan Y Teoh. Association of Periodontal Disease and Polycystic Ovarian Syndrome: A Systematic Review and Meta-analysis with Trial Sequential Analysis. Open Dentistry Journal, 2019, 1-7.
6. Cecilia Fabiana Márquez-Arrico, Javier Silvestre-Rangil, Milagros Rocha. Association between Periodontal Diseases and Polycystic Ovary Syndrome: A Systematic Review. Journal of Clinical Medicine, 2020, 1-12.
7. Sri Chandana Tanguturi, Sreenivas Nagarakanti. Polycystic Ovary Syndrome and Periodontal disease: Underlying Links a Review. Indian Journal of Endocrinology and Metabolism, 2018, 267-273.
8. Aliye Akcalı, Nagihan Bostanci, Georgios N. Belibasakis. Association between Polycystic Ovary Syndrome, Oral Microbiota and Systemic Antibody Responses. Plos one 9 (9). Journal pone, 2014, l-10.
9. Rathi N, Reche A. Risk of Periodontal Diseases in Women with Polycystic Ovary Syndrome: An Overview. Cureus. 2023; 15(10):e47169. Doi: 10.7759/cureus.47169. PMID: 38021744; PMCID: PMC10652058.
10. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab. 2004; 89:2745-2749. [PubMed] [Google Scholar]
11. Aubuchon M, Legro RS. Polycystic ovary syndrome: Current infertility management. Clin Obstet Gynecol. 2011; 54:675-684. [PubMed] [Google Scholar]
12. Tanguturi SC, Nagarakanti S. Polycystic ovary syndrome and periodontal disease: Underlying links - a review. Indian J Endocrinol Metab. 2018; 22:267-273. [PMC free article] [PubMed] [Google Scholar]
13. Fuertes-Martín R, Moncayo S, Insenser M, *et al*. Glycoprotein A and B height-to-width ratios as obesity-independent novel biomarkers of low-grade chronic inflammation in women with polycystic ovary syndrome (PCOS). J Proteome Res. 2019; 18:4038-4045. [PubMed] [Google Scholar]
14. Silva N, Abusleme L, Bravo D, *et al*. Host response mechanisms in periodontal diseases. J Appl Oral Sci. 2015; 23:329-355. [PMC free article] [PubMed] [Google Scholar]
15. Jaedicke KM, Preshaw PM, Taylor JJ. Salivary cytokines as biomarkers of periodontal diseases. Periodontol 2000; 70:164-183. [PubMed] [Google Scholar]
16. Boström EA, Kindstedt E, Sulniute R, *et al*. Increased eotaxin and MCP-1 levels in serum from individuals with periodontitis and in human gingival fibroblasts exposed to pro-inflammatory cytokines. PLoS One. 2015; 10:0. [PMC free article] [PubMed] [Google Scholar]
17. Gurav AN. The implication of periodontitis in vascular endothelial dysfunction. Eur J Clin Invest. 2014; 44:1000-1009. [PubMed] [Google Scholar]
18. Craddock HL. Consequences of tooth loss: 2. dentist considerations-restorative problems and implications. Dent Update. 2010; 37:28-32. [PubMed] [Google Scholar]
19. Azziz R, Adashi EY. Stein and Leventhal: 80 years on. Am J Obstet Gynecol. 2016; 214:247. [PubMed] [Google Scholar]
20. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: Pathophysiology, presentation, and treatment with emphasis on adolescent girls. J Endocr Soc. 2019; 3:1545-1573. [PMC free article] [PubMed] [Google Scholar]
21. Freire M, Nelson KE, Edlund A. The oral host-microbial interactome: An ecological chronometer of health? Trends Microbiol. 2021; 29:551-561. [PubMed] [Google Scholar]
22. Akcalı A, Bostanci N, Özçaka Ö, Öztürk-Ceyhan B, Gümüş P, Buduneli N, *et al*. Experimental gingivitis during pregnancy and post-partum: Clinical, endocrinological, and Association between polycystic ovary syndrome, oral microbiota and systemic antibody responses. PLoS One. 2014; 9:0. [PMC free article] [PubMed] [Google Scholar]
23. Chigasaki O, Aoyama N, Sasaki Y, *et al*.

Porphyromonas gingivalis, the most influential pathogen in red-complex bacteria: A cross-sectional study on the relationship between bacterial count and clinical periodontal status in Japan. J Periodontol. 2021; 92:1719-1729. [PubMed] [Google Scholar]
24. Li N, Li Y, Qian C, *et al*. Dysbiosis of the saliva microbiome in patients with polycystic ovary syndrome. Front Cell Infect Microbiol. 2020; 10:624504. [PMC free article] [PubMed] [Google Scholar]
25. Henne K, Schilling H, Stoneking M, Conrads G, Horz HP. Sex-specific differences in the occurrence of Fusobacterium nucleatum subspecies and Fusobacterium periodonticum in the oral cavity. Oncotarget. 2018; 9:20631-20639. [PMC free article] [PubMed] [Google Scholar]
26. Qi X, Yun C, Sun L, *et al*. Gut microbiota-bile acid-interleukin-22 axis orchestrates polycystic ovary syndrome. Nat Med. 2019; 25:1225-1233. [PMC free article] [PubMed] [Google Scholar]
27. Bao J, Li L, Zhang Y, *et al*. Periodontitis may induce gut microbiota dysbiosis via salivary microbiota. Int J Oral Sci. 2022; 14:32. [PMC free article] [PubMed] [Google Scholar]
28. Kelly CC, Lyall H, Petrie JR, Gould GW, Connell JM, Sattar N. Low grade chronic inflammation in women with polycystic ovarian syndrome. J Clin Endocrinol Metab. 2001; 86:2453-2455. [PubMed] [Google Scholar]
29. Loos BG, Craandijk J, Hoek FJ, Wertheim-van Dillen PM, van der Velden U. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. J Periodontol. 2000; 71:1528-1534. [PubMed] [Google Scholar]
30. Nicklas BJ, You T, Pahor M. Behavioural treatments for chronic systemic inflammation: Effects of dietary weight loss and exercise training. CMAJ. 2005; 172:1199-1209. [PMC free article] [PubMed] [Google Scholar]
31. Barber TM, Hanson P, Weickert MO, Franks S. Obesity and polycystic ovary syndrome: Implications for pathogenesis and novel management strategies. Clin Med Insights Reprod Health. 2019; 13:1179558119874042. [PMC free article] [PubMed] [Google Scholar]
32. Orio F Jr, Palomba S, Cascella T, *et al*. The increase of leukocytes as a new putative marker of low-grade chronic inflammation and early cardiovascular risk in polycystic ovary syndrome. J Clin Endocrinol Metab. 2005; 90:2-5. [PubMed] [Google Scholar]
33. Kumar BP, Khaitan T, Ramaswamy P, Sreenivasulu P, Uday G, Velugubantla RG. Association of chronic periodontitis with white blood cell and platelet count - a case control study. J Clin Exp Dent. 2014; 6:0-7. [PMC free article] [PubMed] [Google Scholar]
34. Vrbikova J, Hainer V. Obesity and polycystic ovary syndrome. Obes Facts. 2009; 2:26-35. [PMC free article] [PubMed] [Google Scholar]
35. Carmina E, Bucchieri S, Esposito A, *et al*. Abdominal fat quantity and distribution in women with polycystic ovary syndrome and extent of its relation to insulin resistance. J Clin Endocrinol Metab. 2007; 92:2500-2505. [PubMed] [Google Scholar]
36. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction. 2015; 149:0-27. [PubMed] [Google Scholar]
37. Murri M, Luque-Ramírez M, Insenser M, Ojeda-Ojeda M, Escobar-Morreale HF. Circulating markers of oxidative stress and polycystic ovary syndrome (PCOS): A systematic review and meta-analysis. Hum Reprod Update. 2013; 19:268-288. [PubMed] [Google Scholar]
38. Liu Z, Liu Y, Song Y, Zhang X, Wang S, Wang Z. Systemic oxidative stress biomarkers in chronic periodontitis: A meta-analysis. Dis Markers. 2014; 2014:931083. [PMC free article] [PubMed] [Google Scholar]
39. Akcalı A, Bostanci N, Özçaka Ö, *et al*. Gingival inflammation and salivary or serum granulocyte-secreted enzymes in patients with polycystic ovary syndrome. J Periodontol. 2017; 88:1145-1152. [PubMed] [Google Scholar]
40. Krishnan A, Muthusami S. Hormonal alterations in PCOS and its influence on bone metabolism. J Endocrinol. 2017; 232:0. [PubMed] [Google Scholar]
41. LaMonte MJ, Hovey KM, Genco RJ, Millen AE, Trevisan M, Wactawski-Wende J. Five-year changes in periodontal disease measures among postmenopausal females: The Buffalo OsteoPerio study. J Periodontol. 2013; 84:572-584. [PubMed] [Google Scholar]
42. Kalyan S, Patel MS, Kingwell E, Côté HC, Liu D, Prior JC. Competing factors link to bone health in polycystic ovary syndrome: Chronic low-grade inflammation takes a toll. Sci Rep. 2017; 7:3432. [PMC free article] [PubMed] [Google Scholar]
43. De Leo V, Musacchio MC, Cappelli V, Massaro MG, Morgante G, Petraglia F. Genetic, hormonal and metabolic aspects of PCOS: An update. Reprod Biol Endocrinol. 2016; 14:38. [PMC free article] [PubMed] [Google Scholar]
44. Güncü GN, Tözüm TF, Cağlayan F. Effects of endogenous sex hormones on the periodontium--review of literature. Aust Dent J. 2005; 50:138-145. [PubMed] [Google Scholar]
45. Mascarenhas P, Gapski R, Al-Shammari K, Wang HL. Influence of sex hormones on the periodontium. J Clin Periodontol. 2003; 30:671-681. [PubMed] [Google Scholar]
46. Noyan V, Yucel A, Sagsoz N. The association of bone mineral density with insulin resistance in patients with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2004; 115:200-205. [PubMed] [Google Scholar]
47. Kemer Doğan ES, Kırzıoğlu FY, Doğan B, Fentoğlu Ö, Kale B, Çarsancaklı SA, Orhan H. The role of menopause on the relationship between metabolic risk factors and periodontal disease via salivary oxidative parameters. J Periodontol. 2018; 89:331-340. [PubMed] [Google Scholar]
48. Lim SS, Norman RJ, Davies MJ, Moran LJ. The effect of obesity on polycystic ovary syndrome: A systematic review and meta-analysis. Obes Rev. 2013; 14:95-109. [PubMed] [Google Scholar]
49. Witchel SF, Burghard AC, Tao RH, Oberfield SE. The diagnosis and treatment of PCOS in adolescents: An update. Curr Opin Pediatr. 2019; 31:562-569. [PubMed]

[Google Scholar]
50. Carmina E, Lobo RA. Use of fasting blood to assess the prevalence of insulin resistance in women with polycystic ovary syndrome. Fertil Steril. 2004; 82:661-665. [PubMed] [Google Scholar]
51. Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: A prospective, controlled study in 254 affected women. J Clin Endocrinol Metab. 1999; 84:165-169. [PubMed] [Google Scholar]
52. Wild RA, Rizzo M, Clifton S, Carmina E. Lipid levels in polycystic ovary syndrome: Systematic review and meta-analysis. Fertil Steril. 2011; 95:1073-1079. [PubMed] [Google Scholar]
53. Wild RA, Carmina E, Diamanti-Kandarakis E, *et al*. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: A consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. J Clin Endocrinol Metab. 2010; 95:2038-2049. [PubMed] [Google Scholar]
54. Cho LW, Jayagopal V, Kilpatrick ES, Atkin SL. The biological variation of C-reactive protein in polycystic ovarian syndrome. Clin Chem. 2005; 51:1905-1907. [PubMed] [Google Scholar]
55. Barry JA, Azizia MM, Hardiman PJ. Risk of endometrial, ovarian and breast cancer in women with polycystic ovary syndrome: A systematic review and meta-analysis. Hum Reprod Update. 2014; 20:748-758. [PMC free article] [PubMed] [Google Scholar]
56. Piovezan JM, Premaor MO, Comim FV. Negative impact of polycystic ovary syndrome on bone health: A systematic review and meta-analysis. Hum Reprod Update. 2019; 25:633-645. [PubMed] [Google Scholar]
57. Dursun E, Akalın FA, Güncü GN, *et al*. Periodontal disease in polycystic ovary syndrome. Fertil Steril. 2011; 95:320-323. [PubMed] [Google Scholar]
58. Özçaka Ö, Ceyhan BÖ, Akcali A, Biçakci N, Lappin DF, Buduneli N. Is there an interaction between polycystic ovary syndrome and gingival inflammation? J Periodontol. 2012; 83:1529-1537. [PubMed] [Google Scholar]
59. Akcalı A, Bostanci N, Özçaka Ö, *et al*. Elevated matrix metalloproteinase-8 in saliva and serum in polycystic ovary syndrome and association with gingival inflammation. Innate Immun. 2015; 21:619-625. [PubMed] [Google Scholar]
60. Kellesarian SV, Malignaggi VR, Kellesarian TV, *et al*. Association between periodontal disease and polycystic ovary syndrome: A systematic review. Int J Impot Res. 2017; 29:89-95. [PubMed] [Google Scholar]
61. 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; 12:507-512. [PMC free article] [PubMed] [Google Scholar]