

ORIGINAL RESEARCH

Oral contraceptives (OCP'S) -Dark Shadow effect on IL-6 Levels & Periodontium- An Original Research

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ABSTRACT

Background and aims: Periodontal disease is the commonest dental infectious diseases affecting up-to 90% of adults. The oral cavity, particularly periodontal tissues is affected by the use of external hormones particularly by oral contraceptives. Hormonal contraceptives are agents that are based on the effects of gestational hormones and they prevent ovulation. This study evaluates the effect of contraceptives drugs on health of periodontal tissues and levels of IL-6 in gingival crevicular fluid. **Materials and methods:** Thirty patients who had not used oral contraceptives (control) and thirty patients using oral contraceptives (case) were examined clinically and their medical history, dosage and usage of oral contraceptives were recorded. Periodontal indices such as bleeding on probing, plaque index, probing pocket depth, clinical attachment loss and levels of IL-6 in gingival crevicular fluid were measured. Student's t-test and Mann-Whitney test were used to analyze data. **Results:** Mann-Whitney test showed a statistically significant difference in the mean of clinical attachment levels in the case and control groups ($P < 0.05$) and highly statistically significant difference in the mean of IL-6 levels ($P < 0.001$), probing pocket depth ($P < 0.05$) and radiographic bone loss between the case and control groups ($P < 0.05$). **Conclusion:** It seems that use of oral contraceptives may affect the periodontal health status of patients, leading to more gingival inflammation and periodontal bone loss. Therefore, patients must have a strict oral hygiene care and educated about the potential implications.

Key words: periodontitis, oral contraceptives, interleukin-6, bone loss.

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INTRODUCTION

Over the past 20 years, oral contraceptives have been known to be a popular method of pregnancy control. They work by artificially altering the levels of the sex hormones (estrogen and progesterone). Oral Contraceptives (OCPs) constitute the most widely used class of drugs, used by approximately 50 million women worldwide. (1,2) Hormones used externally have a detrimental effect on the human body. Women in particular experience hormonal variation under both physiological and non-physiological

circumstances, including the use of oral contraceptives or hormone therapy. These pose a huge impact on the general and oral health of women. (3-5) The growth and differentiation of periodontal tissues, as well as cell proliferation, might be impacted by oral contraceptives (6). OCPs inhibit the luteinizing and follicle-stimulating functions of the pituitary gland, inhibiting the release of an ovum by the ovary and promoting contraception. To prevent ovulation, hormonal contraceptives work by using gestational hormones to induce a hormonal condition that mimics

the state of pregnancy and prevents ovulation. It has been shown that human gingiva contains receptors for progesterone and estrogen.⁽⁷⁾ Existence of these receptors might provide evidence that periodontal tissues are a target for the gestational hormones and results in several implications for women's health associated with the use of oral contraceptives.

OCPs cause both oral and systemic adverse effects. Thromboembolic and cardiovascular complications are the principal adverse effects, along with acne, breast tenderness, skin pigmentation, and changes in the menstrual flow^(8,9) Orally, OCPs are known to cause periodontal disease in the initial phase and periodontitis in the advanced stage⁽¹⁰⁾. Periodontal disease is a multifactorial condition in which inappropriate interaction between the host immune response and a specific group of bacterial pathogens leads to the destruction of connective and bone tissues supporting the tooth.

The oral cavity reflects overall health and is a target organ for many unfavorable reactions brought on by drug side effects. Receptors for progesterone and estrogen are present in the human gingiva, and these receptors act as target tissues for both hormones.^(7,11) The female body experiences hormonal fluctuations during pregnancy, puberty, menopause, and postmenopause. Periodontal inflammatory diseases usually occur in response to such fluctuations. Because oral contraceptive hormone reactions resemble those in pregnant individuals, gestational hormones account for periodontal breakdown⁽¹²⁾.

Changes in estrogen and progesterone levels also affect inflammatory mediators like interleukin-6 (IL-6). During periodontal inflammation (particularly gingivitis), a hormonal imbalance raises IL-6 mRNA levels in fibroblasts, leading to increased inflammatory gingival responses⁽¹³⁾.

The conflicting and ambiguous nature of the evidence relating to the periodontium's reaction to OCPs among women on these pills justifies the necessity for additional research and a thorough analysis of how OCPs impact periodontal health in women taking oral contraceptives.

Despite the worldwide use of OCPs, there is limited research on the effects of IL-6 on periodontium.

Thus, the present study evaluated the levels of IL-6 in gingival crevicular fluid and its effect on the gingival tissues and the alveolar bone. The study also assessed the impact of OCPs on periodontal health in females taking such pills using clinical measurements like bleeding on probing, probing pocket depth, and clinical attachment loss to diagnose periodontal disorders to reflect the pathogenesis and aetiology of the condition and its association with OCPs.

MATERIALS & METHODOLOGY

This descriptive investigative research was carried out on 60 female patients aged between 17–40 years. The

60 females were divided into two groups. Women who were using oral contraceptives and were referred to Sri Guru Ramdas Institute of Dental Sciences & Research, Amritsar, for dental care were included in the case group. The control group included women without oral contraceptive use and normal periodontal levels. Pregnant patients, patients with any systemic diseases, patients under any medication, patients undergoing any periodontal treatment, patients receiving any wide-spectrum antibiotics, smokers, and patients drinking alcohol were excluded from the study. Ethical approval was obtained from the institutional ethical committee to carry out the research. Written consent was obtained after patients were informed about the study and before the data collection.

A detailed questionnaire was completed by each patient, who recorded a full medical history, smoking habits, and contraceptive pill usage before the clinical examination. Specifically, the type of OC and the duration of the medication were recorded for the case group. For both the case group and control group, their periodontal indices, such as bleeding on probing, probing pocket depth, and clinical attachment loss, were also recorded for each patient. The mandibular bitewing radiographs were recorded using Carestream film no. 2 to measure the radiographic bone loss. The bone loss was calculated from the Cemento-Enamel Junction (CEJ) to the alveolar crest for horizontal bone loss and from the CEJ to the base of the osseous defect for vertical bone loss.

To measure the levels of IL-6, patients were asked to rinse their mouths. After isolation, sampling of gingival cervical fluid was performed at three sites (two anterior regions and one posterior region) employing three #25 paper points. Each paper point was placed in the gingival sulcus and left there for three minutes. It was then removed and placed in a test tube containing normal saline and an intermediate fluid before being transported to the laboratory. The samples were kept at 26 degrees Celsius in a special box filled with dry ice. The samples were placed on a shaker for 15 minutes and then centrifuged for 10 minutes at 3500 rpm. The supernatants, thus obtained, were used for the analysis of IL-6 levels by the ELISA method. A diagnostic kit for IL-6 was used (BD OptEIA, BD Biosciences, San Diego, US).

The Mann-Whitney test was used to compare the means of BOP, to compare the means of IL-6 levels, PD, CAL, and radiographic bone loss in the case and control groups. Analysis was done using SPSS 19.0 version.

RESULTS

The present descriptive study was conducted among 60 females aged 18 to 35 years. The mean age was 29.37 and 27.08 years for the case group and control group, respectively. Both groups' mean ages were non-significant, with a p-value greater than 0.05.

The Mann-Whitney test showed statistically significant differences in the means of clinical attachment levels between the case and control groups ($P < 0.05$) (Table 1).

The Mann-Whitney test showed statistically highly significant differences in the means of pocket depths ($P < 0.001$) and radiographic bone loss ($P < 0.001$) between the case and control groups. (Table 1 & Figure 1).

There was a highly significant difference in the of IL-6 levels ((P value - 0.001) between the two groups (Table 1 & Figure 2)

The Pearson correlation for correlating bone loss with IL-6 levels in case groups revealed a positive & weak relationship between IL-6 levels and radiographic bone loss with r value 0.0952 (Figure 3).

Table 1: Periodontal parameters in the test and control groups

Variable	Controls(n=30)		Cases(n =30)		Z value [#]	P value [#]
	Mean	±SD	Mean	±SD		
Pocket Depth	2.63	0.928	4.33	1.184	5.196	<0.001**
Clinical Attachment	2.17	1.555	2.87	1.196	2.224	0.026*
Radio-Graphic Bone Loss	1.77	1.251	3.23	1.569	3.615	<0.001**
IL-6levels	134.83	18.855	116.20	16.380	3.366	0.001*

Figure 1: Means of Pocket depth. Clinical attachment loss and Radiographic bone loss.

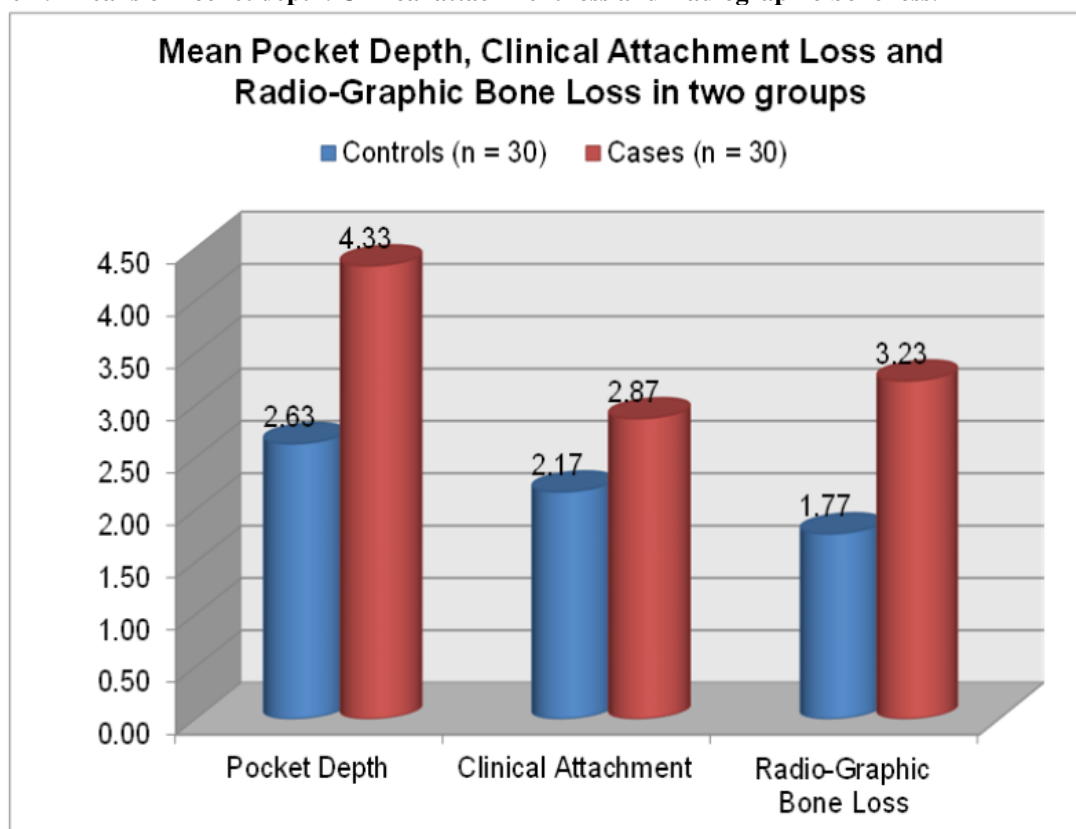


Figure 2: Means of IL- 6 Levels

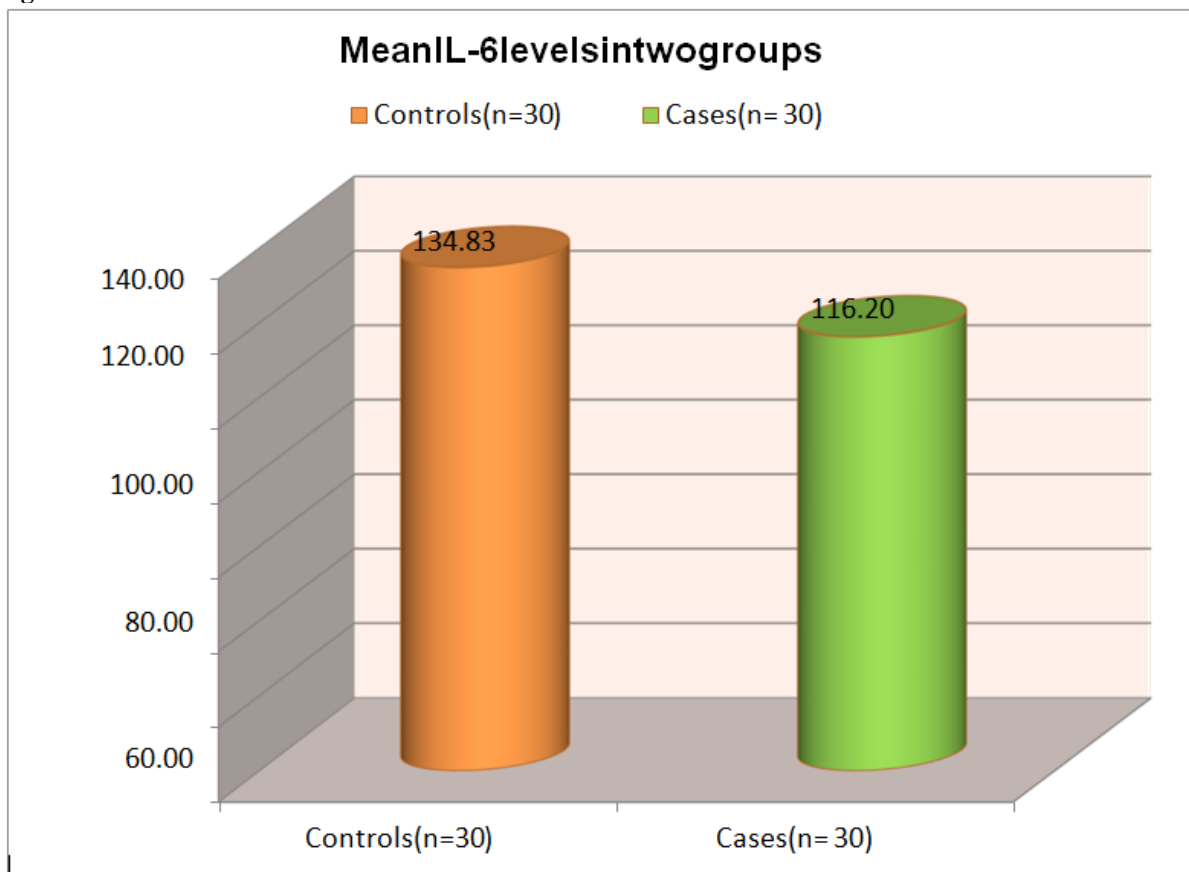
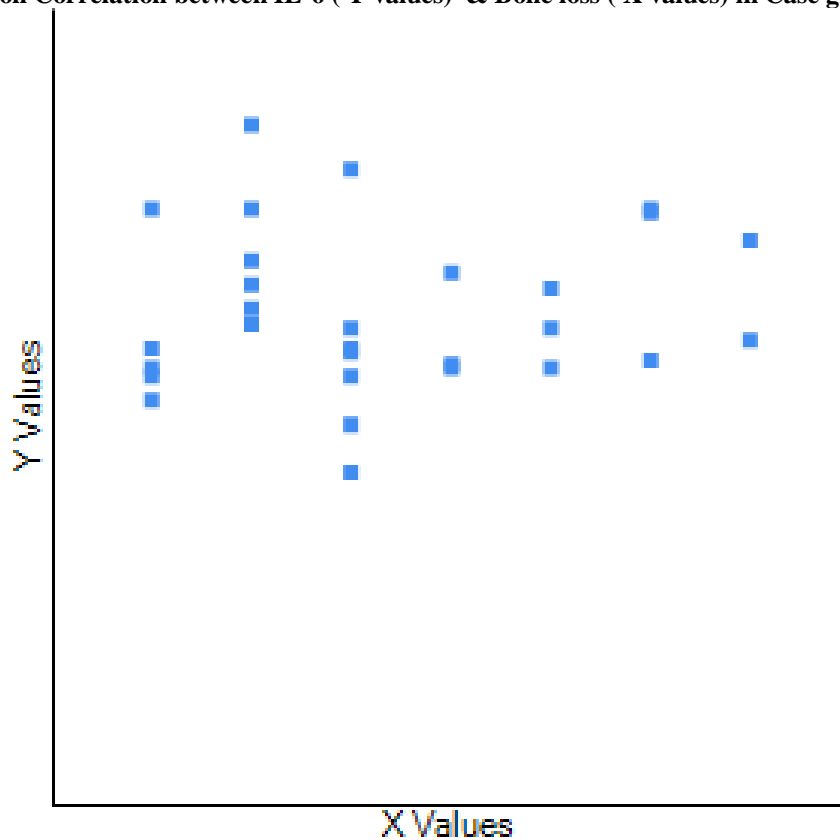


Figure 3: Pearson Correlation between IL-6 (Y values) & Bone loss (X values) in Case group



DISCUSSION

Oral contraceptives promote periodontal collapse by lowering dental plaque resistance and can aggravate gingival enlargement in healthy females. Using OCP for an extended period may result in clinical attachment loss (CAL), bleeding on probing, deeper probing depths, and radiographic bone loss, including variations in the IL-6 level (7,14). Nassrawin NA et al also stated that prolonged use of such hormonal pills causes increased gingival inflammation and gingival enlargement. Estrogen and progesterone increase the production of pro-inflammatory cytokines in the body and cause periodontal diseases and gingival microvascular breakdown.

The present study found a significant value for bleeding on probing and increased pocket depth with a p-value less than 0.05. Our results were in concordance with studies done by Mullally et al. (17) and Brusca MI et al (3) who suggested that because patients on OCPs tend to have poorer periodontal health than non-users and show a statistically significant increase in the prevalence of severe periodontitis and major periodontopathogens.

The present study was also in agreement with the studies done by Prachi et al concerning significant differences in bleeding on probing, deeper periodontal pocket depth, and clinical attachment loss (2). The duration of dependency on OCPs is directly proportional to the status of periodontal health, whereas a longer duration of consumption of OCPs indicates poor periodontal status due to increased production of pro-inflammatory cytokines and prostaglandins as a result of elevated levels of the hormones (8,18,19).

Furthermore, significant values for difference in clinical attachment loss (CAL) in OCP's group and without OCP group was present. The OCP group presented with more CAL which was in concordance with the studies conducted by Tilakaratne A et al and GM knight et al (18,19). A vulnerable population is prone to developing gingival abnormalities, which further progress to the periodontium and causes periodontium-related disorders. Women consuming oral contraceptives demonstrate a positive culture for *Candida* species, including *P. gingivalis* and *P. intermedia*. The number of *Bacteroides* species in OCP populations is also significantly higher, making them more susceptible to periodontal disease (3).

In contrast, several recent studies have found that combined oral contraceptives have insignificant effects on periodontal health (15-17). It may be because more recently introduced formulations contain less progesterone and estradiol than conventional hormonal pills (<50 µg estrogen and <1 mg progestin).

A study done by Farhad SZ et al (20) found a significant decrease in the levels of IL-6 which was similar finding in our study showing decreased levels of IL-6. The decrease could be caused by modifications in the microvasculature, elevated

gingival permeability, and elevated prostaglandin generation. Lapp A et al also pointed that progesterone in OCPs significantly decreases the IL-6 output by the fibroblasts present in the human gingiva to the extent of 50% (21).

Oral contraception has a significant impact on bone turnover (22). The results of the present study were in agreement with studies done by various authors (23-25), while various authors contradict the results of the present study (26-27). These differences are due to decreased bone biochemical markers. The biochemical markers for bone formation and bone resorption decreased by 15-24% and 17-28%, respectively, in the OCPs users in contrast to the control group, leading to a decrease in the bone mineral density in the former. This explains the radiographic bone loss in the vulnerable population of the present study. Further, the variation in the results is because of the vast age range studied in the previous and present studies, the length of the study, and the dosing frequency of the OCPs.

The weak correlation between IL-6 and radiographic bone loss in the present study can be attributed to the antagonistic properties of IL-6 and estrogen present in OCPs (28). IL-6 encourages bone resorption, while estrogen impedes IL-6 osteoblast formulation.

The small-scale sample size of the present study is the major limitation of the present study. A larger sample size and a long-term assessment in the form of a longitudinal study are needed to determine the effect of OCPs use on periodontal health in women and to further corroborate the findings of the present study.

CONCLUSION

The current study concluded that long-term use of OCPs can result in bleeding on probing, deeper pocket formation, clinical attachment loss, changes in IL-6 levels, and a decrease in bone mineral density. Hence, OCPs are proven to have detrimental impacts on the gingiva and periodontium. This necessitates establishing an oral hygiene program for raising awareness among the population using hormonal pills so that they make well-informed decisions and are aware of the effects of such pills on their oral health. In addition, to maintain oral hygiene and prevent the adverse effects of OCPs, females should adhere stringently to oral hygiene care. The present study also focuses the attention of the females to adapting alternate birth control methods because of the deleterious impact of OCPs.

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