

Original Article

# Differences in Periodontal Parameters, Serum Vitamin D, Calcium, Phosphorus, Alkaline Phosphatase and C-Reactive Protein Between Perimenopausal and Postmenopausal Women with Periodontitis

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## Abstract

**Objective:** The study aimed to evaluate and compare the differences in periodontal and biochemical parameters between perimenopausal and postmenopausal women with periodontitis.

**Methods:** A cross-sectional study was conducted on 100 women with chronic periodontitis, aged 40-60 years, divided into 50 perimenopausal and 50 postmenopausal groups. Periodontal parameters (plaque index PI, gingival index GI, gingival bleeding index GBI, simplified debris index DI-S, simplified calculus index CI-S, simplified oral hygiene index OHI-S, clinical attachment loss CAL, and pocket depth PD) measurements and blood samples were collected to estimate vitamin D, calcium Ca, phosphorous P, alkaline phosphatase ALP and C-reactive protein CRP.

**Results:** The mean values of clinical periodontal parameters were significantly higher in the postmenopausal group as compared to the perimenopausal group ( $P < 0.05$ ), except for CI-S ( $P > 0.05$ ). For the biochemical parameters, the mean serum level of AIP, Ca, and P were within the normal reference ranges, with non-significant differences reported between both groups regarding ALP and P ( $P > 0.05$ ). While serum Vit.D level was more significantly reduced in the postmenopausal group ( $P < 0.05$ ), and CRP levels were increased in both groups, but with non-significant differences ( $P > 0.05$ ).

**Conclusions:** Postmenopause could more significantly affect the progression & severity of periodontal disease and vitamin D deficiency than peri menopause due to reducing circulating estrogen level.

**Keywords:** Calcium, Perimenopause, Periodontitis, Postmenopause, Vitamin D.

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## Introduction

Female, through certain stages in their reproductive life cycle, undergoes alterations and fluctuates in the level of sex steroid hormones circulating in their bloodstream, with a specific variation in the level of progesterone and estrogen in women, which may have direct and indirect effects on oral health in the form of inflammation, gingivitis, periodontitis and altered microorganism<sup>(1)</sup>.

Sex hormones have been long recognized as having some role in periodontal disease, changes in sex hormones have long been considered to affect periodontal tissues and periodontal disease progression as in menopause, the rapid decline in estrogen levels, can lead to systemic bone loss<sup>(2)</sup>. Estrogen is a steroid sex hormone that is related to periodontal health. Estrogen receptors are expressed in the oral cavity's periodontium and mucosa; thus, this hormone's levels are directly associated with the oral cavity status<sup>(3)</sup>.

The perimenopausal phase is the menopausal transition period that begins a few years before the last menstrual period and concludes a year afterward; it can continue for four to ten years. Perimenopause, also known as climacteric<sup>(4)</sup>, is a period in a woman's life that experiences significant physical, emotional, and psychological changes.

Menopause is a physiological stage in which women experience adaptive changes in their systemic and oral status. It means "without estrogen." It is when cyclic ovarian function, as manifested by menstruation, ceases. The sudden decrease in estrogen levels during the menopause phase is the main cause of primary osteoporosis, which also affects jaw bones, may lead to a reduction in bone mineral density, and could be considered a factor in the progression of periodontal diseases<sup>(5)</sup>.

The postmenopausal phase begins around 12 months following menopause. The transitional time before menopause can be psychologically stressful and confusing; however, there is also a sense of being free from the monthly routine and discovering a new status toward maturity<sup>(6)</sup>. However, postmenopausal estrogen deficiency affects the immune system because it improves the body's immune system. The changes in the immune system make individuals susceptible to the development of periodontitis<sup>(5,7)</sup>.

Vitamin D is a fat-soluble vitamin that plays a role in maintaining the homeostasis of various biological systems. It has tumor-suppressing, anti-inflammatory,

and antibacterial properties and an essential role in bone metabolism and calcium homeostasis; it can modulate innate and adaptive immune function and cardiovascular function<sup>(8)</sup>. Calcium and phosphorus minerals play an important and extensive role in the nucleic acid synthesis, energy metabolism, muscle contraction, enzyme activity, and bone mineralization<sup>(9)</sup>. Bone turn indicators such as serum calcium and alkaline phosphatase aid bone growth and mineralization.

ALP is considered a marker of osteoblastic activity; it plays a role in bone metabolism. In the periodontium, it is part of the normal turnover of the periodontal ligament, root cementum, and bone homeostasis. Therefore, it can be used as a diagnostic marker of periodontitis in postmenopausal women<sup>(10)</sup>. CRP is a non-specific acute-phase inflammatory marker generated in response to various injuries other than periodontitis, such as infections, trauma, and hypoxia, and is controlled by cytokines. Postmenopausal women have been shown to have greater inflammation, which has been linked to a decrease in circulating estrogens<sup>(11)</sup>.

To the best of our knowledge, this is the first study aimed to evaluate clinical periodontal parameters (PI, GI, GBI, DI-S, CI-S, OHI-S, PPD, and CAL), biochemical bone parameters (vitamin D, Ca, P and ALP) and systemic marker of inflammation (CRP) in perimenopausal and postmenopausal women with periodontitis in Kurdistan region, Erbil City, Iraq.

## Patients and methods

### Setting and time of the study

The current study was conducted in Rizgary Hospital, Erbil city, Kurdistan Region of Iraq. The study was carried out between October 2021 to January 2022. The institutional ethical committee approved the study of the College of Dentistry / Hawler Medical University/ Erbil / Iraq (ethical approval number: 69 at 12/9/2021).

### Study design and sample selection

A cross-sectional study was conducted on 100 women with periodontitis who visited Rizgary hospital for an executive general health checkup, aged 40-60.

The patients were randomly divided into two groups, each consisting of 50 individuals.

Group I: Included 50 perimenopausal women with periodontitis.

Group II: Included 50 postmenopausal women with periodontitis.

The inclusion criteria for the selection of participants: were systemically healthy women, ages ranged from 40-60 years, having at least 15 natural teeth, and chronic periodontitis (mild, moderate, or severe) according to the 1999 International Workshop for a Classification of Periodontal Diseases and Conditions, 1999<sup>(12)</sup>. In addition, women were considered menopause when they had the absence of menstruation for more than 12 months. Finally, women were considered perimenopause when they had not yet entered menopause. In addition, they often suffer from amenorrhea, which lasts for at least 60 days, or an extension of the menstrual cycle for >7 days, and have experienced at least three symptoms of menopause.

The exclusion criteria for selection of participants were women: below 40 years of age, with long-term steroid application, with a history of calcium or phosphorus supplements intake, with previous vitamin D application, on hormone replacement therapy and Oophorectomy, on drug-altering serum calcium level, under medication in the preceding six months, suffering from a systemic disease (history of cardiovascular disease, history of diabetes, hypertension, liver disease, endocrine disorder), cancer, pregnant or planning for pregnancy, smokers/or alcoholic, with history of a known infective disease other than periodontitis, using of an antibiotic in the preceding three months, and on the history of receiving periodontal treatment within previous three months.

The study design was explained to all volunteers before the conduction of the study and informed written consent was approved and signed by all participants before the procedure was carried out.

### Data collection

Perimenopause and postmenopausal status were determined by interviewing each participant: If they had suffered from pain during the menstruation cycle before; did the menstrual cycle extend for a long before, and How long the subject had not been menstruating? Physical and psychosocial symptoms were also reported among the studied women, including Feeling tired or worn out, decreased physical strength and stamina, muscle and joint pain, hot flushes, and night sweats<sup>(13)</sup>.

### Clinical Examination

Clinical periodontal parameters were assessed for all participants by a single trained examiner using the dental mirror, periodontal probe (Dental probe UNC-15), and dental explorer. The thickness of plaque was measured according to Silness and Loe<sup>(14)</sup>, the extent and severity of gingival inflammation were measured according to GI by Loe and Silness<sup>(15)</sup>, the presence or absence of bleeding on probing was assessed according to gingival bleeding index by Ainamo and Bay<sup>(16)</sup>, measurement of oral hygiene health status according to OHI-S by Green and Vermillion<sup>(17)</sup>, the amount of debris and calculus were measured according to debris index-S and calculus index-S by Green and Vermillion<sup>(17)</sup>, probing pocket depth was measured in mm from the gingival margin to the base of the pocket. Clinical attachment loss was measured in mm from the cemento-enamel junction to the base of the pocket according to Lindha et al<sup>(18)</sup>. For PD&CAL the examination was done at six sites for each tooth, with three reading for labial – buccal site : mesiolabial (buccal), mid labial (buccal), distolabial (buccal) and three reading for lingual- palatal site: mesiolingual (palatal), mid lingual (palatal) and distolingual (palatal).

### Serum Sample collection

5ml of fasting venous blood sample was collected from each woman. The blood sample was stored in a gel tube for 30 minutes, centrifuged at 3000 rpm for 10-20 minutes to obtain clear supernatant, and transferred immediately to the laboratory for estimation of biochemical parameters. Serum vitamin D, calcium Ca, phosphorus P, and alkaline phosphatase levels ALP were estimated to be biochemical markers of bone turnover. C-reactive protein CRP was estimated as a systemic marker of inflammation. The standard methods for the assays were based on the guideline provided by the reagent manufacturer (Human Gm Bh, Germany) of HumaStar 300, a fully automated analyzer. The normal reference ranges for serum calcium were considered as 8.5–10.5 mg/dL, serum phosphorous was 3.4–4.5 mg/dL, normal activity of serum ALP was 30–125 U/L, C-reactive protein was up to 5mg/L and 25(OH) D was >75 nmol/L (serum 25(OH) D less than 50 nmol/L was considered as deficient, from 50-75 was considered as insufficient. More than 75 was considered as optimal).

### Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 25). The Chi-square test of association was used to compare proportions. Fisher's exact test was used when the expected frequency (value) was less than 5 of more than 20% of the table's cells. The normality of data was assessed using the Shapiro-Wilk

test. Student's t-test for two independent samples (unpaired t-test) was used to compare the means of two groups of normally distributed data. The Mann-Whitney test was used for the non-normally distributed data, *p*-value of  $\leq 0.05$  was considered statistically significant.

## Results

### Demographic profile of the study

Table 1 shows a total of 100 women who participated in the study, the average age ranged from 40-60 years, and the mean age was  $50.2 \pm 5.2$  years old. Fifty women were perimenopausal with a mean age of  $45.8 \pm 2.3$  years old, and fifty women were postmenopausal with a mean age of  $54.6 \pm 3.2$  years. From 40-44 years, 13 women were perimenopausal; from 45-49 years, 37 women were perimenopausal. While from 50-54 years, 21 women were postmenopausal, and from 55-59 years, 29 women were postmenopausal.

### Clinical and biochemical Data

Table 2 shows the mean values of clinical parameters in peri and postmenopausal groups. The result showed that the mean value of plaque index (PI), gingival index (GI), gingival bleeding index (GBI), pocket depth (PD), clinical attachment level (CAL), debris index-simplified (DI-s), calculus index-simplified (CI-s) and oral hygiene index-Simplified (OHI-S) in postmenopausal women were  $1.46 \pm 0.29$ ,  $1.66 \pm 0.26$ ,  $56.78\% \pm 15.14$ ,  $4.57 \pm 0.23$ mm,  $3.52 \pm 0.40$ mm,  $2.09 \pm 0.77$ ,  $1.38 \pm 0.73$ ,  $3.46 \pm 1.26$  respectively. For perimenopausal women the mean values were  $1.38 \pm 0.21$ ,  $1.48 \pm 0.25$ ,  $46.25 \pm 18.80\%$ ,  $4.34 \pm 0.16$  mm,  $3.28 \pm 0.46$ mm,  $1.76 \pm 0.61$ ,  $1.12 \pm 0.68$ ,  $2.91 \pm 1.12$  respectively. The same table also shows that more than 30% of the sites involve

attachment loss in both postmenopausal ( $47.52\% \pm 12.74$ ) and perimenopausal women ( $36.56\% \pm 11.43$  groups).

For comparison between the two groups regarding clinical parameters, significant differences existed except for CI-s ( $P=0.079$ ). The same table shows that the mean values of PI, GI, GBI, PD, CAL, DI-s, and OHI-S were significantly higher in the postmenopausal group compared with the perimenopausal group: PI ( $p = 0.001$ ), GI-s ( $p < 0.001$ ), GBI ( $p = 0.003$ ), PD ( $p < 0.001$ ), CAL ( $p = 0.006$ ), DI-s ( $p = 0.023$ ), and OHI-S ( $p = 0.024$ ).

Table 3 shows biochemical parameters; the mean serum levels of V.D, CRP, ALP, P, and Ca were  $29.12 \pm 14.77$ ,  $5.22 \pm 4.68$ ,  $75.82 \pm 29.09$ ,  $3.71 \pm 0.62$ ,  $9.77 \pm 0.50$  respectively in the postmenopausal group, while for the perimenopausal group, the mean level was  $37.58 \pm 18.19$ ,  $6.07 \pm 4.23$ ,  $72.44 \pm 20.34$ ,  $3.52 \pm 0.73$ ,  $9.46 \pm 0.48$  respectively. For comparison between the two groups, no significant differences existed regarding CRP ( $p = 0.079$ ), ALP ( $p = 0.923$ ), and P ( $p = 0.170$ ). Regarding Vit.D, the mean levels were more significantly reduced in the postmenopausal group than in the perimenopausal group: Vit. D ( $p = 0.028$ ), while the mean level of Ca was more significantly increased in the postmenopausal group compared to the perimenopausal group ( $p = 0.001$ ), as shown in Table 3.

Table 4 shows oral hygiene status in peri and postmenopausal women groups. The result showed significant differences existed between both groups ( $P=0.036$ ). In postmenopausal women, 2% had good oral hygiene status, 34% had fair oral hygiene status, and 64% had poor oral hygiene status. For perimenopausal women, 4 % had good, 56% had fair, and 40 % had poor oral hygiene status.

Table 1: Age distribution of the studied sample.

	Post-menopausal	Peri-menopausal	Total	
Age	No. (%)	No. (%)	No. (%)	P-value
40-44	0 (0.0)	13 (26.0)	13 (13.0)	
45-49	0 (0.0)	37 (74.0)	37 (37.0)	
50-54	21 (42.0)	0 (0.0)	21 (21.0)	< 0.001**
55-59	29 (58.0)	0 (0.0)	29 (29.0)	
60	0(0.0)	0(0.0)	0(0.0)	
Mean $\pm$ S.D	$54.6 \pm 3.2$	$45.8 \pm 2.3$	$50.2 \pm 5.2$	< 0.001*
Total	50 (100.0)	50 (100.0)	100 (100.0)	

\*By Mann Whitney test. \*\*By Chi square test.

Table 2: Means of clinical parameters (PI, GI, GBI, DI-s, CI-s, OHI-s, PD, CAL) in peri and post-menopausal groups, with the extent of chronic periodontitis.

Parameters	Post-menopausal		Peri-menopausal		P-value
	Mean± S.D	Min-Max	Mean± S.D	Min-Max	
PI	1.46±0.29	0.03-2.16	1.38±0.21	1.06-2.06	0.001*
GI	1.66±0.26	1.28-2.30	1.48±0.25	1.19-2.22	< 0.001*
GBI %	56.78±15.14	10.0-80.0	46.25±18.80	3.6-80.0	0.003†
PD (mm)	4.57±0.23	4.17-5.25	4.34±0.16	4.0-4.7	< 0.001*
CAL (mm)	3.52±0.40	2.55-4.44	3.28 ±0.46	2.01-4.20	0.006†
DI-S	2.09±0.77	0.5-4.10	1.76±0.61	0.6-3.60	0.023†
CI-S	1.38±0.73	0-3.10	1.12±0.68	0.1-2.80	0.079*
OHI-S	3.46±1.26	1.0-6.9	2.91±1.12	1.2-5.90	0.024*
Extent of CP CAI (%)	47.52±12.74	29.0-90.0	36.56±11.43	23.0-88.0	< 0.001*

†By t test for two independent samples. \*By Mann Whitney test.

Table 3: Means of biochemical parameters (V.D, CRP, Ca, P, ALP) in peri and post-menopausal groups.

Parameters	Post-menopausal		Peri-menopausal		P-value
	Mean± S.D	Min-Max	Mean± S.D	Min-Max	
V.D (nmol/L)	29.12±14.77	5.22-60.17	37.58±18.19	10.64-66.6	0.028*
CRP (mg/L)	5.22±4.68	1.1-15.50	6.07±4.23	1.1-16.50	0.078*
ALP(U/L)	75.82±29.09	35.0-186	72.44±20.34	27-118	0.923*
P(mg/dl)	3.71±0.62	2.16-5.24	3.52±0.73	1.99-5.10	0.170†
Ca(mg/dl)	9.77±0.50	8.13-10.67	9.46±0.48	8.1-10.38	0.001*

†By t test for two independent samples. \*By Mann Whitney test.

Table 4: Oral hygiene status OHS (assessed by oral hygiene index OHI-S scores) in peri and postmenopausal groups.

Oral hygiene		Post-menopausal	Peri-menopausal	Total	p*-value
OHI-S scores	Status	No. (%)	No. (%)	No. (%)	
0.0-1.2	Good	1 (2.0)	2 (4.0)	3 (3.0)	0.036
1.3-3.0	Fair	17 (34.0)	28 (56.0)	45 (45.0)	
≥ 3.1	Poor	32 (64.0)	20 (40.0)	52 (52.0)	
Total		50 (100.0)	50 (100.0)	100 (100.0)	

\*By Fisher's exact test.

## Discussion

In the present study, the results show that the mean age of the perimenopausal group was (45.8 ± 2.3) years, which is consistent with similar findings conducted by other studies<sup>(6,19)</sup>. In contrast, the mean age of the postmenopausal group was (54.6 ± 3.2) years.

### Clinical periodontal parameters

The results of the present study show that chronic periodontitis was more significant in the postmenopausal women group, and the mean values of clinical parameters (PI, GI, GBI, PPD, CAI, DI-S, CI-S & OHI-S) were more significantly increased in the

postmenopausal group as compared to perimenopausal group (P< 0.05).

The increase in the mean value of clinical parameters in peri and postmenopausal groups may be due to the hormonal imbalance, which significantly affects the periodontium<sup>(5)</sup>. Also, the decrease in the estrogen level, typically in menopausal ages, may negatively affect periodontium's health. In addition, the quantitative changes in sex steroid hormones can lead to changes in inflammatory mediators, vascular permeability, and the growth and differentiation of fibroblasts<sup>(20)</sup>.

Since CAL provides a better overall estimation of the amount of damage on the periodontium as it shows cumulative disease over time at a site rather than

persistent active disease. Therefore, CAL was considered a better parameter for determining the amount of periodontal tissue damage. The present study showed that clinical attachment loss was present in both groups but more significantly in the postmenopausal group. The biological mechanism for periodontal attachment loss in postmenopausal women might be explained by reduced healing qualities of bones with low bone mass density<sup>(21)</sup> and decreased collagen synthesis<sup>(22)</sup>.

Since periodontitis classification was based on the condition's extent and severity, the extent can be characterized as localized =  $\leq 30\%$  of sites involved and generalized =  $> 30\%$  of sites involved. In the present study, the results showed that the extent of periodontal tissue damage in both groups occurred in more than 30 % (generalized CP) but with a more significant extent of periodontal tissue damage in the postmenopausal group ( $P < 0.001$ ). Indicating that postmenopause could significantly affect the extent of periodontal tissue damage.

The severity of periodontitis was based on the amount of clinical attachment loss. It was divided into three levels: slight (1–2 mm CAL), moderate (3–4 mm CAL), and severe ( $\geq 5$  mm CAL)<sup>(12)</sup>. In the present study, both groups had moderate severity but with a more significant increase in attachment loss in the postmenopausal group ( $3.52 \pm 0.40$ ) as compared to the perimenopausal group ( $3.28 \pm 0.46$ ) ( $P = 0.006$ ). Indicating that menopause could significantly affect the severity of periodontitis.

Similar to the present results for greater periodontal severity in the postmenopausal group. A study was conducted on 46 postmenopausal and 15 premenopausal women with chronic periodontics to evaluate oral and periodontal parameters such as PD, CAL, and missing teeth MT. The study revealed a significant association between menopausal status and clinical attachment loss and reported that menopause could significantly affect the extent or severity of periodontitis<sup>(23)</sup>.

In contrast to our results, a study conducted by Alves et al. (2015)<sup>(24)</sup> on 102 women with chronic periodontitis (68 menopausal and 34 premenopausal) reported that menopause could not significantly affect the severity of periodontal disease or tooth loss. They found that other factors such as age, smoking, and plaque accumulation might exert a greater influence on the progression of periodontal disease rather than menopause itself<sup>(24)</sup>. Also, in contrast to the results, a cross-sectional study was conducted on 27 perimenopausal women and 36

postmenopausal women with chronic periodontitis. This study reported no significant differences in PI, PD, CAL, DI, CI, OHI, and papillary bleeding index PBI between perimenopausal and postmenopausal women groups, with no significant difference in periodontitis severity between both groups<sup>(6)</sup>.

Since oral hygiene status of each subject was divided into three categories: good (0–1.2), moderate (1.3–3.0), and bad (3.1–6.0)<sup>(17,25)</sup>. Therefore, in the present study the result showed that 64% of postmenopausal women had poor oral hygiene, while the 56% of perimenopausal women had fair oral hygiene showed that the postmenopausal women group had bad oral hygiene while the perimenopausal women group had moderate oral hygiene, with significant differences between both groups. This is consistent with previous findings, which reported a relationship between periodontal health status and oral hygiene. Furthermore, it also revealed that participants with poorer oral hygiene and harsher tooth wear significantly exhibited poorer periodontal status<sup>(25)</sup>.

#### **Biochemical parameters in perimenopausal and postmenopausal women.**

Regarding biochemical parameters, the result showed significant differences in the mean serum level of V. D and Ca between both groups, with non-significant differences in the mean level of CRP, ALP, and P between both groups.

Regarding vitamin D, the present study showed a significant reduction in the mean level of V.D in both groups, but with more significant reduction (deficiency) in the postmenopausal group as compared to the perimenopausal group ( $p = 0.028$ ). This is because estrogen normally increases the activity of 1- $\alpha$ -hydroxylase, which is responsible for the activation of vitamin D and upregulates the vitamin D receptor. Although during menopausal stages, there is a gradual reduction in the amount of estrogen produced by the ovaries<sup>(26)</sup>, this decline in estrogen production is thought to promote V.D deficiency, and the ensuing V.D challenge is related to a decrease in the number of V.D receptors.

Vitamin D deficiency may also result from several factors, such as inadequate sun exposure and poor Nutrition<sup>(27)</sup>. In addition, penetration of ultraviolet rays into the skin is also impaired by various factors such as lassitude, season, skin pigmentation, and protection of sun-exposed areas by sunscreen or clothing; the agency has also been shown to affect vitamin D synthesis

primarily through a lesser capability of skin biosynthesis<sup>(28)</sup>.

A study reported that vitamin D deficiency was reported in 37.80% of perimenopause and 51.21% of postmenopausal women, vitamin D insufficiency was reported in 2.43% of perimenopause and 6.09% of postmenopausal women, and only 2.43% of perimenopausal women were sufficient for serum vitamin D level<sup>(27)</sup>. A study by Shukar-Udin et al. (2013) reported that 63% of perimenopausal women and 37% of menopausal women had compromised vitamin D<sup>(28)</sup>.

Regarding Ca, the present study showed a significant difference between post  $9.77 \pm 0.50$  and perimenopausal  $9.46 \pm 0.48$  women groups. However, both groups had serum Ca levels within the normal reference range of 8.5 to 10.5 mg/dL. In addition, the normal serum level of Ca in the perimenopausal group agreed with other studies<sup>(29,30)</sup>. While for post menopause, the normal serum Ca level may be due to a good lifestyle, physical activity<sup>(31)</sup>, and good dietary intake of calcium<sup>(32)</sup>. Similar to our results, a study conducted on 173 peri and postmenopausal women to determine serum Ca levels reported that similar serum Ca levels were found in both groups<sup>(33)</sup>. In contrast, a cross-sectional study reported a marked significant decrease in serum Ca level in postmenopausal women compared to premenopausal women<sup>(34)</sup>.

Regarding ALP, the present study showed no significant difference in the mean value of ALP between both groups. Both groups had serum ALP levels within the normal reference range of (30-125U/L). In postmenopausal and perimenopausal groups, ALP activity levels were ( $75.82 \pm 29.09$  U/L) and ( $72.44 \pm 20.34$ U/L) respectively, with non-significant differences existing between both groups. Similar results were reported by Bhattarai et al. (2014), who reported that ALPs activity level was within the normal reference ranges in both post and premenopausal groups<sup>(35)</sup>. In addition, Onyeukwu and Nsonwu(2007) reported no significant changes in calcium, phosphorus, and ALP levels between early and late postmenopausal periods<sup>(36)</sup>.

In contrast to our results, a study reported a significant increase in serum alkaline phosphatase levels among postmenopausal ( $p < 0.001$ )<sup>(10)</sup>. This contrast may be due to the differences in the study population and geographical variations.

Regarding phosphorus, the result showed no significant difference in the mean levels of serum phosphorus between both women groups and both groups within the normal reference range of 3.4–4.5 mg/dL. Similar

results were also reported by Kumari et al. (2020)<sup>(30)</sup>. At the same time, another study showed that serum P levels differed significantly between the different age groups. The study reported that the age group 1–17 years had the highest serum phosphate levels, whereas the age group 18–44 had the lowest serum phosphate levels<sup>(37)</sup>. Another study reported that the cause of decreasing serum phosphorus levels was due to the reduction in the daily mineral intake<sup>(38)</sup>.

Regarding the systemic marker of inflammation, CRP levels were slightly increased than the normal reference range of (up to 5 mg/L) in both postmenopausal and postmenopausal women groups, but non-significant differences existed between both groups.

However, epidemiological studies that investigated the association between serum estradiol levels and inflammatory markers in women (particularly when categorized by menopausal status) have shown inconsistent and conflicting results. Some observational studies found a positive association between serum estradiol levels and inflammatory markers in postmenopausal women<sup>(39)</sup> and an inverse association in premenopausal women<sup>(40)</sup>. However, Maggio et al. (2011) reported that age-related changes in sex hormones contribute to the development of a proinflammatory state<sup>(39)</sup>.

Regarding this cross-sectional study, the Data was analyzed, and the differences in periodontal parameters, periodontal health status, bone parameters, and systemic markers of inflammation between perimenopause and postmenopause women groups were estimated without evaluating the effect of non-surgical periodontal therapy on those parameters which could also be one of the limitations in this study.

## Conclusions

Since the primary cause of periodontitis is bacterial plaque. Estrogen deficiency in women after menopause can be considered as one of the factors that contribute to more periodontal disease progression (throughout more significant increase in PI, GI, GBI, PD, CAL, DI-S & OHI-S) and more significant reduction of vitamin D (vitamin D deficiency) than perimenopausal women. The present study also showed that other bone marker levels, such as Ca, P & AIP were within the normal reference range points. The systemic marker of inflammation (CRP) was increased in both groups with non-significant differences.

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