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Estimation and comparison of serum procalcitonin levels in patients with chronic periodontitis and chronic migraine after non-surgical periodontal therapy: a clinico biochemical study

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Abstract

Aim: To evaluate and compare the effect of non-surgical periodontal therapy on the levels of serum procalcitonin (PCT) in patients with chronic periodontitis and chronic migraine.

Material and methods: Study population comprised 120 patients divided into 4 groups. Group I systemically and Periodontally healthy persons (n=30), Group II Periodontally healthy individuals along with chronic migraine (n=30), Group III systemically healthy along with chronic periodontitis individuals (n=30) and Group

IV patients with CM and CP (n=30). PCT levels and periodontal parameters were evaluated and compared in all 4 groups at baseline. Group III and IV participants underwent non-surgical periodontal therapy were reassessed for periodontal parameters after 1 and 3 months post-treatment and PCT was reassessed 3 months after SRP.

Results: Mean values, standard deviation and percentage change in the values of periodontal parameters and PCT were analysed using one way ANOVA test. Paired t-test applied between test group III and IV to analyse the change in parameters from 1 and 3 months post-treatment. Level of significance s set as $P<0.05$.

Conclusion: A significant decrease in levels of serum PCT in Group III and IV 3 months post scaling and root planing showed the effectiveness of periodontal therapy on systemic inflammation.

Keywords: Procalcitonin (PCT), Scaling and Root Planing (SRP), Chronic periodontitis (CP), Chronic Migraine (CM).

Introduction

Periodontitis is defined as "an inflammatory disease of the supporting tissues of teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of periodontal ligament and alveolar bone with increased probing depth formation, recession, or both."[1]

In periodontal disease, a series of inflammatory mediators like proteins, enzymes, imunoglobulin, host cells, hormones, bacteria and their products, volatile compounds and ions are released in saliva, gingival crevicular fluid and blood following periodontal tissues destruction which acts as a biomarker in detection of infection.[2]

One form of these biomarkers is procalcitonin (PCT) which is found to be very low in blood of healthy people. PCT is pro inflammatory and cytokine like mediator.[6] Its expression has been regulated by proinflammatory cytokines such as TNF-α, IL-6.[7] PCT is a useful indicator to determine the degree of infection, predicting the prognosis and monitoring response to the treatment.[3]

Procalcitonin (PCT) is the 116 amino acid polypeptide precursor of calcitonin, a calcium regulatory hormone. Serum PCT levels are elevated in patients with sepsis and in those with systemic inflammation correlates with measurement of serum PCT level has been considered as a diagnostic method.[4]

In microbial infections, rate of PCT level increases rapidly. During migraine attacks, PCT in serum is increased, which suggests that this acute phase reactant could be involved in migraine pathogenesis owing to the fact that migraine pain is considered to be a type of sterile inflammation.[5] On the other hand, periodontal infection has been linked to elevated levels of serum PCT, and it is further influenced by the severity of the disease. Accordingly, periodontal inflammation that occurs within the gingiva releases a great number of pro-inflammatory mediators that could play a pivotal role in the development of migraine attacks, which may result in chronic migraine (CM). It seems, therefore, reasonable to speculate that chronic periodontitis (CP) may contribute to increased PCT serum concentrations in CM. Therefore, the aim of the present study was to measure and compare the serum PCT levels in patients with chronic periodontitis and chronic migraine.

Material and methods

The present research study was conducted on 120 subjects visiting the Outpatient Department of Periodontology and Oral Implantology, Sri Guru Ram Das Institute of Dental Sciences and Research, Sri Amritsar. The research protocol was initially submitted to institutional ethical committee. After ethical approval, all subjects were

verbally informed and written consent was taken from the participants before inclusion in the study.

Criteria for selection of patients:

Inclusion criteria

- Subjects aged between 20-50 years.
- Patients with chronic generalized moderate to severe periodontitis.
- Subjects with chronic migraine with and without aura.
- Cooperative patients willing to sign the consent form.

Exclusion criteria

- Subjects < 15 teeth (excluding third molars).
- Smokers, alcoholics, tobacco chewers, and drug addicts.
- Patients who had received periodontal treatment in the previous 3 months.
- Systemic antibiotics, corticosteroids, and/or immunosuppressant therapy within 3 months prior to periodontal assessment.
- Systemic diseases except for chronic migraine.
- Pregnant or lactating mother.

Subjects who fulfilled the inclusion and exclusion criteria were divided into 4 groups viz. group I, group II, group III and group IV each with no discrimination of sex, caste, religion or socio- economic status.

Group I: Systemically and periodontally healthy subjects.

Group II: Periodontally healthy subjects with chronic migraine (CM).

Group III: Systemically healthy subjects with chronic periodontitis (CP).

Group IV: Subjects with chronic periodontitis (CP) and chronic migraine (CM)

After their selection subjects of all four groups were assessed for periodontal parameters (Plaque index, Gingival index, Sulcus bleeding index, Probing pocket depth, and Clinical attachment level) and biochemical parameters (Procalcitonin level).

Following the initial examination, full mouth scaling and root planing was done in patients with chronic periodontitis (group III and IV) and periodontal parameters were reassessed in group III and group IV after 1 month and 3 months.

Periodontal Parameter

Following parameters will be assessed in all 120 subjects:

- Plaque index (Silness and Loe , 1964)
- Gingival index (Loe and Silness ,1963)
- Bleeding index: Sulcus bleeding index (Muhlemann H.R. and Son S,1971)
- Pocket probing depth (PPD)
- Clinical attachment level (CAL)

Neurological Parameters

CM was defined according to International Classification of Headache Disorders 3rd edition criteria.[6] Patients diagnosed with CM, if they presented headache occurring on 15 or more days per month for more than 3 months. In addition, time of CM evolution (in months), intensity of headache using the visual analog scale (VAS), number of days with headaches per month, and type of migraine was registered.

Biochemical Analysis

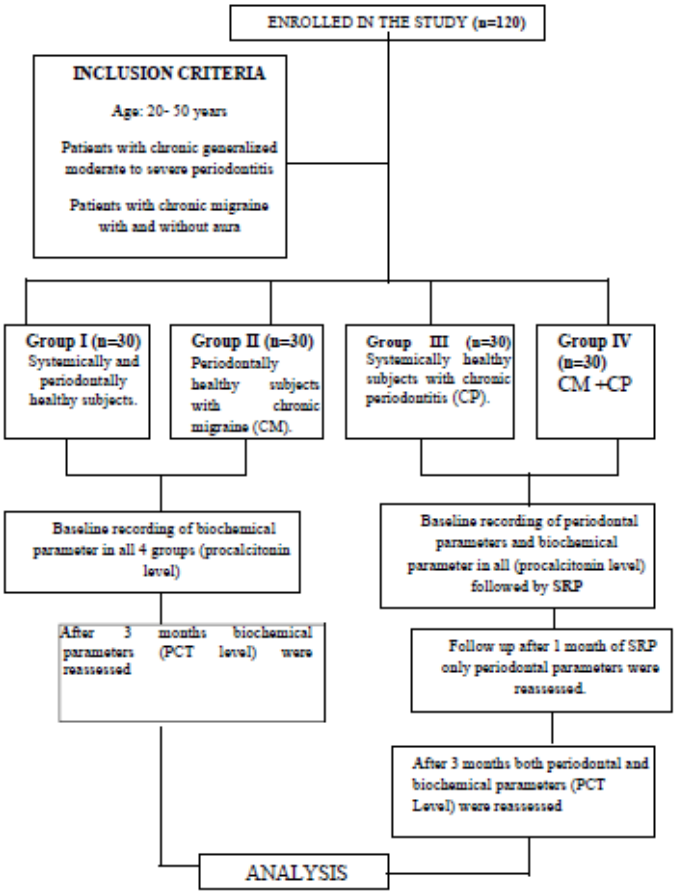
Blood samples were analysed for the serum procalcitonin (PCT) levels using Biovendor ELISA Kit and ELISA Reader.

Collection of blood samples:

Fasted samples were obtained in the morning in a pain free period (at least 12 hours from the last migraine attack). Briefly, two millilitres (mL) of venous blood was collected from the antecubital fossa by venepuncture using a 20- gauge needle with a 2 mL syringe. Blood samples were allowed to clot at room temperature and after 1 hour, serum was separated from blood by centrifugation and 0.5 mL of extracted serum was immediately transferred to 1.5

mL aliquots.

Study Design



Statistical Analysis

The analysis was performed with a statistical software package for social sciences version 17.0 (SPSS, Version 17.0, Inc, Chicago). The mean values, standard deviation and percentage change in the values of periodontal.

parameters and serum procalcitonin were analysed using one way ANOVA test. Paired t-test was applied to evaluate the comparison of periodontal and biochemical parameters between the test group-III and group-IV to analyse the change in parameters from 1 month and 3 months post-treatment. Level of significance was P<0.05, P> 0.05 Non significant, P<0.001 Highly Significant.

Discussion

Procalcitonin (PCT), a protein of 116 amino-acids with molecular weight of 13 kDa, was discovered 25 years ago as a prohormone of calcitonin produced by C-cells of the thyroid gland and intracellularly cleaved by proteolytic enzymes into the active hormone.34 It was observed that at the baseline, the mean PCT levels in group I, group II, group III and group IV were 3.49 ± 2.14 pg/ml,31.12 ± 12.64 pg/ml, 32.48 ± 4.11 pg/ml and 134.28 ± 69.54 pg/ml respectively (table 3).

Group I patients were systemically and periodontally healthy, a low serum PCT values was obtained. A statistically significant difference in the levels of PCT were obtained when compared with other groups this fact was also supported in the studies conducted by Gendrel D et al. (1997) [7] , Ziebolz D et al. (2007) [8] , Vikse J et al. (2015) [9] , Samsudin I et al. (2017)[10] , Leira Y et al (2018).[4]

Samsudin I et al. (2017)[10] stated that serum PCT concentration in healthy individuals is typically <0.1 µg/L. In the presence of bacterial infection, PCT increases, and the degree of rise correlates with the severity of the infection. Patients with localised infection have smaller increases of PCT in comparison to those with generalised sepsis, severe sepsis.

Group II (CM) patients showed statistically higher significant PCT levels as compared to group I (Healthy) but less than group III (CP) and group IV (CM+CP) at baseline. This was due to the fact that chronic migraine is a sterile infection in response to which serum PCT levels get increased in the serum results are in accordance with the studies conducted by Turan H et al. (2011) [5] , Gonzalez et al. (2016) [11] , Yılmaz N et al. (2017) [12] , Leira Y et al. (2018) [4] , Mahajan R et al. (2020) [13]

Yılmaz N et al. (2017)[12] in a study concluded that serum levels of procalcitonin were shown to be significantly higher in migraine patients during the attack

period compared with migraine patients in the interictal period

In group III (CP) at baseline PCT levels recorded were higher as compared to control group (Group I) stating the fact that CP is a polymicobial disease and in response to it inflammatory biomarkers increased. At an interval of 1 month and 3 months post SRP improvement in the periodontal parameters along with statistically significant reduction of (21.53 ± 3.37 pg/ml) decline in the serum PCT was observed, owing to the effectiveness of SRP over bacterial load that subsided systemic inflammation in response to which serum PCT levels get declined. The results of present study stated that this is due to the fact that in chronic periodontitis bacterial components such as lipopolysaccharides may also be disseminated into the blood circulation. These endotoxins along bacterial components are a potent stimulator for the production of ProCT and can promote the systemic release of calcitonin precursors from nearly all tissues of the body therefore a high serum level of PCT was detected in chronic periodontitis patients. This fact was supported by Balog et al. (2002) ,[14] Bassim CW et al. (2008),[15] Hendek et al. (2015),[16] Redman et al. (2016) ,[17] Leira Y et al. (2019)[18]

Giannopoulou et al. (2016)[19] reported that PCT levels were elevated in periodontitis and their levels fell following non-surgical periodontal therapy and steadily increased in the consecutive months. This supports the notion of an active role of PCT in periodontal inflammation and further confirms the relationship between local and serum PCT levels with periodontal inflammation. Out of all four groups, group IV (CM+CP) showed highest PCT concentration as compared to group I, II and III. As the inflammation was due to both periodontitis and chronic migraine, so at baseline highest PCT was figured out as compared to group I, II and III. Three months after SRP when PCT levels were reevaluated, a statistically significant reduction of (9.22±48.86 pg/ml) in the levels of PCT was recorded, due to the effectiveness of SRP over bacterial burden after resolution of inflammation. As pockets formation leads to ulcerations in the pocket lining which offer an easy access for periodontal bacteria which leads to secretion of inflammatory mediators like PCT to the systemic circulation in chronic periodontitis. Meningeal sterile inflammation seems to occur in migraine it is feasible to believe that proCT is released during interictal state of chronic migraineurs. In periodontal inflammation acute-phase reactants are produced locally and disseminated systemically due to endotoxemia. This chronic low grade inflammatory state could be responsible for the overexpression of neurogenic biomarkers like PCT during the interictal state of chronic migraineurs which may lead to chronification of migraine. These results are in accordance to the studies conducted by Bassim CW et al. (2008) [16] , Turan H et al. (2011) [11], Hendek MK et al. (2015) [17] , Leira Y et al. (2018) [4], Leira Y et al. (2019) [19] , Mahajan R et al. (2020) [14] From above findings, it can be concluded that, within the limits of this study CM and CP have significantly higher serum proCT levels than patients with CM only, CP only, or systemically and periodontally healthy individuals. CP independently contributes to elevated serum proCT levels in CM patients.

Periodontal Parameters

PI: When mean values of group III and IV was compared from baseline to 3 months a mean reduction of 0.28±0.25 and 0.49±0.24 respectively was seen in both groups and a highly significant (p=0.000) results were obtained.

GI: When overall mean values of group III and IV was compared from baseline to 3 months a mean reduction of

1.29±0.24 and 1.43±0.24 was obtained and a statistically higher significant (p=0.000) results were seen.

SBI: Statistically highly significant reduction (p=0.000) was seen in both group III and IV from baseline to 3 month. An overall mean reduction of 1.62±0.30 and 1.35±0.32 sulcus bleeding index scores were recorded from baseline to 3 months in group III and IV respectively

PPD: An overall reduction of mean probing pocket depth from baseline to 3 months in Group III and IV was recorded as 1.81±0.39 mm and 1.92±0.44 mm respectively and the results were highly significant (p=0.000) from baseline to post-treatment at an interval of 3 months in both groups

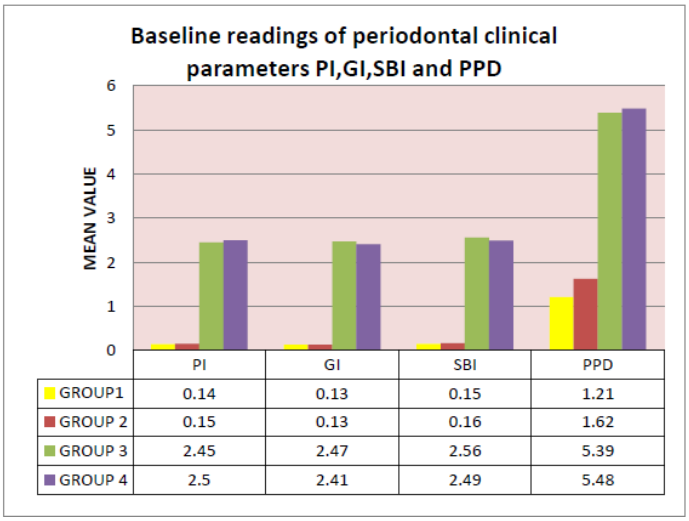
CAL: An overall gain in CAL from baseline to 3 months in Group III and IV recorded as 1.93±0.50 mm and 1.59±1.00 mm respectively and the results were highly significant (p=0.000) from baseline to post-treatment at an interval of 3 months in both groups. It is noteworthy that CM combined with CP have significantly higher serum PCT levels than patients with solitary CM, CP and healthy individuals. Hence, it can be concluded that CP independently contributes to elevated serum PCT levels in CM patients

Table 1: Intergroup comparison of periodontal clinical parameters at baseline in group i, group ii, group iii and group iv

Inter group		PI		GI		SBI		PPD	
		Mean	P - value	Mean	P - value	Mean	P - value	Mean	P - value
Group I	II	-0.00±0.03	1.000	0.00±0.04	1.000	-0.01±0.03	1.00	-0.41±0.10	0.001
	III	-2.30±0.03	0.000	-2.33±0.04	0.000	-2.41±0.03	0.000	-4.17±0.10	0.000
	IV	-2.35±0.03	0.000	-2.28±0.04	0.000	-2.34±0.03	0.000	-4.26±0.10	0.000
Group II	I	0.00±0.03	1.000	-0.00±0.04	1.000	0.01±0.03	1.00	0.411±0.10	0.001
	III	-2.29±0.03	0.000	-2.33±0.04	0.000	-2.39±0.03	0.000	-3.76±0.10	0.000
	IV	-2.35±0.03	0.000	-2.28±0.04	0.000	-2.32±0.03	0.000	-3.85±0.10	0.000
GROUP IIII	I	2.30±0.03	0.000	2.33±0.04	0.000	2.41±0.03	0.000	4.17±0.10	0.000
	II	2.29±0.03	0.000	2.33±0.04	0.000	2.39±0.03	0.000	3.76±0.10	0.000
	IV	-0.05±0.03	0.95	0.05±0.04	1.000	0.07±0.03	0.13	-0.09±0.10	1.000
Group IV	I	2.35±0.03	0.000	2.28±0.04	0.000	2.34±0.03	0.000	4.26±0.10	0.000
	II	2.35±0.03	0.000	2.28±0.04	0.000	2.32±0.03	0.000	3.85±0.10	0.000
	III	0.05±0.03	0.95	-0.05±0.04	1.000	-0.07±0.03	0.13	-0.09±0.10	1.000

** P<0.001: Highly Significant, * P<0.05 Significant, NS: P> 0.05; Non significant

Graph 1



Graph 2

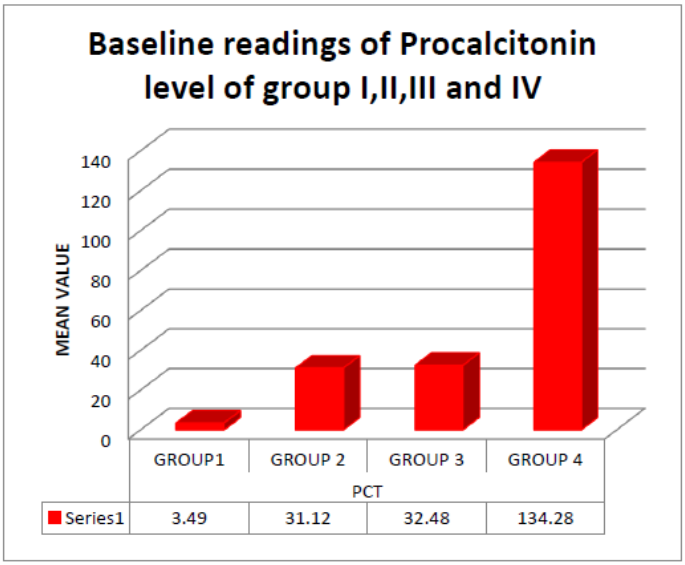


Table 2: Intergroup comparison of procalcitonin at baseline in group - i, group ii, group - iii and group – iv

Inter group comparison		PCT	
		Mean	P – Value
Group I	Group II	-27.62±9.14	0.01*
	Group III	-28.99±9.14	0.01*
	Group IV	-130.78±9.14	0.000**
Group II	Group I	27.62±9.14	0.01*
	Group III	-1.36±9.14	1.000:NS
	Group IV	-103.16±9.14	0.000**
Group IIII	Group I	28.99±9.14	0.01*
	Group II	1.36±9.14	1.000:NS
	Group IV	-101.79±9.14	0.000**
Group IV	Group I	130.78±9.14	0.000**
	Group II	103.16±9.14	0.000**
	Group III	101.79±9.14	0.000**

** P<0.001: Highly Significant, * P<0.05 Significant, NS: P> 0.05; Non significant

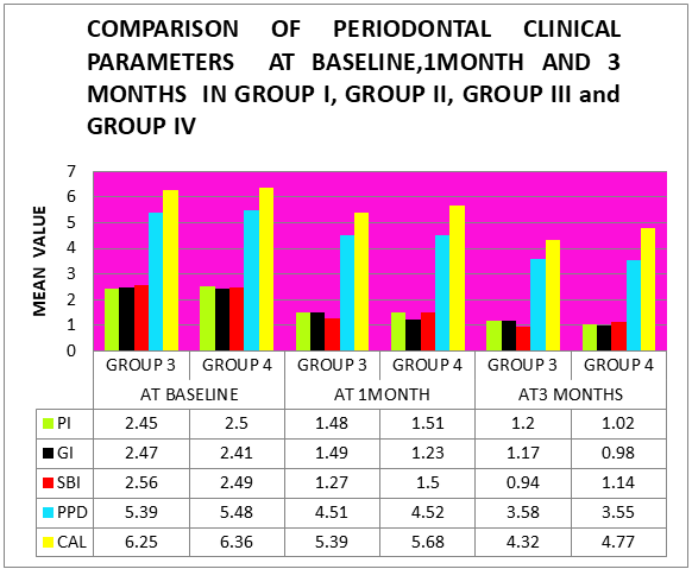
Table 3: Intergroup comparison of periodontal clinical parameters at baseline in GROUP I, GROUP II, GROUP III AND GROUP IV

Inter Group		PI		GI		SBI		PPD	
		Mean	P - Value	Mean	P-value	Mean	P-value	Mean	P-value
Group I	II	-0.00±0.03	1.000	0.00±0.04	1.000	-0.01±0.03	1.00	-0.41±0.10	0.001
	III	-2.30±0.03	0.000	-2.33±0.04	0.000	-2.41±0.03	0.000	-4.17±0.10	0.000
	IV	-2.35±0.03	0.000	-2.28±0.04	0.000	-2.34±0.03	0.000	-4.26±0.10	0.000
Group II	I	0.00±0.03	1.000	-0.00±0.04	1.000	0.01±0.03	1.00	0.411±0.10	0.001
	III	-2.29±0.03	0.000	-2.33±0.04	0.000	-2.39±0.03	0.000	-3.76±0.10	0.000
	IV	-2.35±0.03	0.000	-2.28±0.04	0.000	-2.32±0.03	0.000	-3.85±0.10	0.000
Group IIII	I	2.30±0.03	0.000	2.33±0.04	0.000	2.41±0.03	0.000	4.17±0.10	0.000
	II	2.29±0.03	0.000	2.33±0.04	0.000	2.39±0.03	0.000	3.76±0.10	0.000
	IV	-0.05±0.03	0.95	0.05±0.04	1.000	0.07±0.03	0.13	-0.09±0.10	1.000
Group IV	I	2.35±0.03	0.000	2.28±0.04	0.000	2.34±0.03	0.000	4.26±0.10	0.000
	II	2.35±0.03	0.000	2.28±0.04	0.000	2.32±0.03	0.000	3.85±0.10	0.000
	III	0.05±0.03	0.95	-0.05±0.04	1.000	-0.07±0.03	0.13	-0.09±0.10	1.000

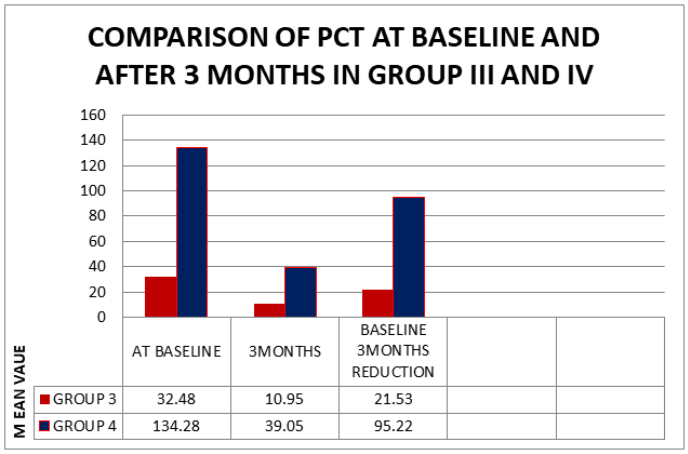
Table 4: Mean Values of Periodontal Clinical Parameters at 1month And 3 months In GROUP- III AND GROUP-IV

Group	AT 1 MONTH		AT 3 MONTHS	
	Group III (MEAN± S.D)	Group IV (MEAN±S.D)	Group III (MEAN± S.D)	Group IV (MEAN± S.D)
Plaque Index (PI)	1.48±0.11	1.51±0.20	1.20±0.21	1.02±0.27
Gingival Index (GI)	1.49±0.27	1.23±0.17	1.17±0.21	0.98±0.17
Sulcus Bleeding Index (SBI)	1.27±0.22	1.50±0.19	0.94±0.30	1.14±0.22
Probing Pocket Depth (PD)	4.51±0.36	4.52±0.59	3.58±0.53	3.55±0.67
Clinical Attachment Level (CAL)	5.39±0.4	5.68±0.84	4.32±0.48	4.77±0.91

Graph 3



Graph 4



Conclusion

PCT is one of the biomarkers that are associated with periodontitis. Measuring the levels of PCT can act as an additional aid in diagnosing the CP, as PCT levels are increased in response to periodontal infection. From above findings, it can be concluded that, within the limits of this study CM and CP have significantly higher serum proCT levels than patients with CM only, CP only, or systemically and periodontally healthy individuals. CP independently contributes to elevated serum proCT levels in CM patients.

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