Does periodontitis affect mean platelet volume (MPV) and plateletcrit (PCT) levels in healthy adults?

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INTRODUCTION

Periodontitis is an inflammatory disease of chronic nature in the supporting tissues of the teeth. More than one factor is involved in its etiology; however, biofilms of dysbiotic plaques are the main cause of the disease. During the course of periodontitis, the supporting tissues of the teeth are progressively destructed¹. The harmful effects of periodontitis are not only restricted to the oral cavity but also have an impact on the general health status of the individual. Microorganisms and/or their products and the inflammatory mediators can access the systemic circulation through the ulcerated pocket epithelium and initiate
a systemic acute-phase response by activating the immune system. Periodontitis may cause bacteremia, endotoxemia, and low-grade systemic inflammation, and it is potentially associated with the impairment of well-being by causing, among others, cardiovascular diseases (CVDs), adverse pregnancy outcomes, respiratory system diseases, and diabetes mellitus.

Periodontal inflammation can exacerbate systemic conditions through the pathological changes caused by leukocytes. Leukocytes, especially neutrophils, produce a number of specific molecules directly responsible for the inflammatory response, which can be a risk factor for atherosclerosis and cardiovascular complications. The other major component of the blood is the platelets, which are closely associated with inflammation. When they are activated, pro-inflammatory mediators are released, and pro-inflammatory receptors are exposed. This, in turn, causes platelets to bind to WBC and endothelial cells. Pathogens existing in the periodontal tissues may readily stimulate platelets and WBC, and this activation might be involved in aggravating atherothrombosis.

Several studies in the literature have reported that high levels of systemic inflammation markers were detected in periodontitis compared to healthy controls. Among these, total white blood cells (WBC), neutrophils, lymphocytes, serum globulin, C-reactive protein, and platelets were listed. Furthermore, it has been suggested that elevated levels of these markers, particularly high leukocyte counts and high levels of C-reactive protein, as well as increased platelet activation, can help establish the relationship between periodontitis and cardiovascular diseases (CVD).

Complete blood count (CBC) tests are commonly used in clinical practice. Plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) are indices specific to platelet morphology and proliferation kinetics, and these parameters can be derived from CBC tests. In the literature, white blood cell (WBC) and platelet counts, PDW, and MPV have been used in several studies to investigate the association between periodontal disease and CVD; however, the results were contradictory. As far as we have observed, the association of PCT with periodontal diseases has not been investigated yet. PCT is an index providing information on the total platelet mass. The following formula is used to calculate PCT: PCT = Platelet count X MPV/10000. The levels of PCT normally vary in range from 0.22% to 0.24%. Therefore, assessing the PCT value can give us more accurate information about inflammation and increased thrombogenic events.

In this study, we aimed to investigate PCT levels in the CBC of patients suffering from stage 3 periodontitis as compared to those of healthy individuals without periodontal disease.

**METHODS**

Approval by the Clinical Research Ethics Committee of Bolu Abant Izzet Baysal University was obtained prior to the conduct of the study. The study was conducted in compliance with ethical standards according to the current version of the Declaration of Helsinki. After informing the eligible volunteers of the objective and procedures of the study, written consent was obtained from the subjects to enroll them in the study. The sample size was calculated considering Type I errors (0.05), targeted power (0.80), and effect size (0.50) due to the PCT value (p<0.05). The minimum sample size required was calculated as 51.

The study participants comprised 57 patients (28 females and 29 males) with Stage 3 Periodontitis and 57 periodontally healthy subjects (31 females and 26 males). The age range of the participants was between 18 and 50 years. Since individuals older than 50 years might have already developed atherosclerotic processes or might have comorbid diseases, they were excluded from the study as these potential conditions could interfere with the results of the complete blood count tests. Patients were diagnosed with Stage 3 Periodontitis or were determined to be periodontally healthy based on the criteria proposed by the International Workshop for Classification of Periodontal Diseases and Conditions in 2017. The study was conducted at the Department of Periodontology between July 2018 and December 2018.

**Inclusion and exclusion criteria**

Patients were included in the study if they were systemically healthy and found to have a probing depth (PD) of ≥6 mm and interdental clinical attachment level (CAL) of ≥ 5 mm, if they had tooth loss of ≤4 teeth due to periodontitis, and if they had radiographically detected bone loss reaching the mid-third of the root and beyond. Periodontally healthy subjects were included in the study if they had no radiographically detected bone loss and if they had no sites with clinical attachment loss and no sites with probing depth (PD) of >3 mm in their oral cavity.
Individuals were excluded if they had a history of cardiovascular disease, diabetes mellitus, hypertension, upper respiratory tract infections, smoking, hypov/hyperthyroidism, chronic renal failure, malignancy, any hematological abnormalities, or any medication use such as antiplatelet agents, anticoagulants, antihyperlipidemic, angiotensin-converting enzyme inhibitors, and steroids. Individuals who had been treated for periodontitis in the past 6 months were also excluded.

Clinical examination

All clinical parameters were evaluated by a single experienced periodontist (G.U), and a calibration exercise was performed to obtain acceptable interexaminer reproducibility. Periodontal examinations were performed with a Williams probe (Hu-Friedy, Chicago, IL, USA). The clinical parameters of PD, plaque index (PI), and clinical attachment level (CAL) were measured for every tooth present in the oral cavity. The measurements were performed at six sites (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, distolingual), and the results were recorded in approximation to the nearest whole millimeter. The distance from the bottom of the pocket to the cementoenamel junction was defined as CAL, which was measured and recorded. The mean PD and the mean CAL values were calculated by dividing the total score of all teeth by the total number of teeth examined during the study. The periodontal probe was carefully and gently introduced into the gingival sulcus to calculate the percentage of BOP, even one site with BOP was recorded as (+) for each individual tooth.

Blood examinations

CBC and platelet volumes were tested simultaneously with optical and impedance measurements (Cell Dyn 3700; Abbott Diagnostics, Lake Forest, Illinois, USA). Platelet count, the levels of hemoglobin (Hb), hematocrit (HCT), red blood cells (RBC), red cell distribution width (RDW), mean corpuscular volume (MCV), neutrophil and lymphocyte counts, total number of WBC, MPV, and PCT were recorded for each patient.

STATISTICAL ANALYSIS

Statistical analyses were conducted with the SPSS software (SPSS 20.0 for Windows, IBM Co, Chicago, IL, USA). The distribution of the variables in study groups was analyzed by the Kolmogorov-Smirnov test. Normally distributed variables were compared by the t-test, and the results were expressed as mean ± standard deviation. Variables that did not conform to a normal distribution were compared with the Mann-Whitney U test. The chi-square test was used for comparing nonparametric variables between the study groups. A p-value, lower than 0.05, was accepted to indicate a statistical significance.

RESULTS

There were no significant differences in age and gender between the study groups (p>0.05). PD and CAL were found to be statistically different between the groups (p<0.001) (Table 1).

| TABLE 1. GENERAL CHARACTERISTICS OF THE STUDY GROUPS |
|-----------------------------------------------------|
| Baseline characteristics                | Stage III Periodontitis Mean± SD (n=57) | Control Mean± SD (n=57) | p       |
| Age (years)                               | 37.4±7.0                                  | 35.6±7.0                       | NS      |
| Male/female                               | 29/28                                     | 26/31                                    | NS      |
| PD (mm)                                   | 6.10±0.72                                 | 1.89±0.42                              | <0.001  |
| CAL (mm)                                  | 6.21±0.81                                 | 1.85±0.40                              | <0.001  |
| BOP (%)                                   | 63±15                                     | 14±4                                    | <0.001  |

SD: Standard deviation, PD: Probing Depth, CAL: Clinical attachment level, BOP: Bleeding on probing, PI: Plaque index

| TABLE 2. LABORATORY DATA OF STUDY GROUPS |
|------------------------------------------|
|                                       | Periodontitis Mean± SD (n=57) | Control Mean± SD (n=57) | p       |
| WBC, (u/mm³)                            | 8.02±2.68                    | 6.87±1.30                    | 0.004   |
| RBC, (u/mm³)                            | 4.87±0.56                    | 4.96±0.58                    | 0.283   |
| Haemoglobin (gr/dl)                     | 13.92±1.76                   | 14.29±1.69                   | 0.258   |
| Haematocrit (%)                         | 41.78±4.94                   | 42.67±4.83                   | 0.337   |
| MCV (FL)                                | 85.82±6.50                   | 86.17±5.19                   | 0.748   |
| RDW (%)                                 | 18.80±1.18                   | 15.20±1.51                   | 0.212   |
| Platelet counts (k/mm³)                 | 258.52±51.11                 | 240.48±54.58                 | 0.073   |
| MPV (FL)                                | 8.75±1.32                    | 8.22±1.08                   | 0.021   |
| PCT (%)                                 | 0.223±0.04                   | 0.196±0.04                   | 0.001   |
| Neutrophil, (u/mm³)                     | 4.79±2.36                    | 3.99±1.08                    | 0.021   |
| Lymphocyte, (u/mm³)                     | 2.46±1.14                    | 2.14±0.56                    | 0.060   |

SD: Standard deviation, WBC: White blood cells, RBC: Red blood cells, MCV: Mean Cell Volume, RDW: Red cell distribution width, MPV: Mean platelet volume, PCT: Plateletcrit.
PCT was found to be higher in the periodontitis group, and this difference was statistically significantly higher ($p=0.001$) (Table 2). The periodontitis group was found to have statistically significant higher levels of WBC count and MPV compared to the control group ($p=0.004$, $p=0.021$; respectively). PCT, MPV, and WBC distribution of the control and periodontitis group are shown in Figure-1. There were no statistically significant differences between the two groups regarding the other parameters investigated in the study, including the RBC count, HB and HCT levels, MCV, and RDW ($p>0.05$) (Table 2). The correlations between the parameters were also tested in the two groups (N=114). In Table 3, the statistically significant correlations between the parameters investigated are shown.

**DISCUSSION**

Recent studies demonstrated that periodontitis and systemic diseases such as cardiovascular diseases and diabetes were strongly related. Aggravated systemic inflammatory responses and reactions to maintain homeostasis may be the key factors to provide insight into the relationship between periodontal disease and systemic conditions.

It is known that infections increase WBC and neutrophil counts, and it has been proposed that these increases might be linking infections with systemic diseases, including CVDs. In our study, an increase in the WBC and neutrophil counts were detected in the periodontitis group compared to the healthy controls. The presence of a high number of leukocytes in the systemic circulation makes the blood more viscous, facilitating the adherence of the circulating cells to the endothelial lining of the blood vessels. This latter change also increases the viscosity of the blood. Decreased blood flow might be involved in the development of CVD. Similar to our results, Kumar et al. reported that patients suffering from periodontitis had high WBC counts compared to controls, and the differences were statistically significant. Conversely, the study by Rao et al. showed no statistically significant differences in WBC count between both groups.

Platelets play a crucial role in managing vascular integrity and regulating hemostasis, and they are involved in the fundamental biological process of chronic inflammation associated with disease pathology, thrombosis, and atherogenesis. Platelet activity can be evaluated with platelet indices such as MPV, platelet counts, PDW, and PCT. Previous studies have

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**TABLE 3. THE STATISTICALLY SIGNIFICANT CORRELATIONS BETWEEN BLOOD COUNT PARAMETERS AND CLINICAL PERIODONTAL PARAMETERS**

|         | WBC  | MPV  | PCT  | Neutrophil |
|---------|------|------|------|------------|
| **r**   |      |      |      |            |
| Mean PD | 0.221* | 0.019 | 0.253** | 0.007 | 0.344** | p<0.001 | 0.202* | 0.032 |
| Mean CAL| 0.237* | 0.012 | 0.251** | 0.007 | 0.344** | p<0.001 | 0.221* | 0.019 |
| BOP     | 0.210* | 0.026 | 0.271** | 0.004 | 0.359** | p<0.001 | 0.195* | 0.040 |

Correlation analysis was performed using Pearson’s correlation analyses. **Correlation is significant at the 0.01 level. * Correlation is significant at the 0.05 level. MPV: Mean platelet volume, PCT: Plateletcrit, WBC: White blood cells. PD: Probing Depth, CAL: Clinical attachment level, BOP: Bleeding on probing.
shown that platelet counts increase in cardiovascular diseases and vascular complications\textsuperscript{14,15}. In our study, we detected a higher platelet count in the periodontitis group, but the difference was not statistically significant. This higher platelet count may be explained due to dental plaque bacteria, including the periodontal pathogen \textit{Porphyromonas gingivalis}, which induces platelet activation and aggregation\textsuperscript{6}. Similarly, several studies in the literature observed higher platelet counts in periodontitis patients\textsuperscript{16}. Differently, Kumar et al.\textsuperscript{11} reported statistically lower platelet counts in the periodontitis group.

In recent years, it has been reported that MPV can also be used as a marker of inflammation in different inflammatory diseases\textsuperscript{17}. Different studies in the literature have reported that MPV has a positive or negative correlation with inflammatory activity\textsuperscript{17,18}. Thus, Ekici et al.\textsuperscript{19} reported a strong association between MPV and angiographic severity of coronary artery disease. In our study, MPV value was found to be higher in the group of patients with periodontitis. Czerniuk et al.\textsuperscript{18} reported similar findings. On the other hand, some studies in the literature have demonstrated decreased MPV in periodontitis\textsuperscript{20,21}, and others concluded that MPV values were not statistically different between the periodontitis groups and periodontally healthy groups\textsuperscript{22,23}. In the studies we have mentioned, there are different and contradictory results regarding MPV and platelet counts. These might be due to the different severity of periodontitis in the studies and differences in the technological methods and modes of measurements used. Also, genetic and environmental factors may affect platelet indices of different populations. Also, in our study, there were no statistically significant differences between the two groups in RBC count, HB, and HCT levels. Conversely, Rao et al.\textsuperscript{12} found that the mean Hb level in the periodontitis group was statistically lower compared to the control group.

In the literature, some studies concluded that PCT is a reliable indicator for the diagnosis and treatment of several diseases\textsuperscript{24,25}. According to our findings, PCT was significantly higher in the periodontitis group and positively correlated to periodontal clinical parameters that described the severity of periodontal disease. This data might provide more accurate insight into the platelet mass and function in periodontal diseases. There was increasing evidence that platelet indices, including MPV and PCT, were found to be significantly associated with vascular risk factors\textsuperscript{26}. In the study by Aslan et al.\textsuperscript{27}, 230 patients with carotid artery disease were included, and high PCT levels were demonstrated to be statistically higher in patients with major adverse cardiac and cerebrovascular events. Furthermore, a study showed that there was a strong relationship between PCT and saphenous vein disease and slow coronary flow\textsuperscript{28}. Therefore, high PCT levels in systemically healthy individuals with periodontitis may pose a risk for systemic diseases such as atherosclerotic events.

**Study limitations**

The limitation of our study is the small patient population (57 patients) and the cross-sectional study design. Since the participants did not undergo coronary angiography, we were unable to demonstrate the relationship between PCT and coronary artery disease directly. Further prospective and randomized studies with larger stratified populations are needed to reveal possible effects of periodontitis on CVDs.

**CONCLUSION**

As far as we know, this is the first clinical study to investigate PCT values derived from CBC in patients with periodontitis. We conclude that periodontitis may elevate WBC, MPV, and PCT levels compared to healthy control patients. Furthermore, the prevention and treatment of periodontitis may decrease serum mediators and markers of acute-phase response and may be beneficial in the control of atherosclerosis and other systemic inflammatory diseases.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

**Authors’ contributions**

Concept, study design, and project management were done by Dr. Erdal and Dr. Ustaoglu; statistics and writing were done by Dr. Inanir and Dr. Ustaoglu.

**Conflict of interest**

The authors declare that there is no conflict of interest and funding support. The Clinical Research Ethics Committee of the Bolu Abant Izzet Baysal University approved this study.
RESUMO

OBJETIVO: A periodontite pode estimular a resposta infecciosa e imunitária e causar o desenvolvimento da aterogênese, doença coronária e infarto do miocárdio. O objetivo deste estudo foi comparar os níveis de plaquetócrito (PCT) e de volume médio de plaquetas (VMP) derivados dos testes de hemograma completo (CBC) em doentes que sofrem de periodontite de fase 3 com os de indivíduos saudáveis, sem doença periodontal.

MÉTODOS: O estudo incluiu 57 doentes (28 mulheres e 29 homens) com periodontite de fase 3 e 57 voluntários (31 mulheres e 26 homens) que eram periodontalmente saudáveis. A idade dos participantes do estudo variou de 18 a 50 anos. A condição periodontal dos participantes do estudo foi investigada com profundidade de sondagem, nível de ligação clínica, hemorragia na sonda e índice de placas. Contagem de leucócitos (WBC) e neutrófilos (NWC), níveis de hemoglobina (Hb) e hematócrito (HCT), volume corpuscular médio (VCM) e largura de distribuição das células vermelhas (RDW), contagem de trombócitos, volume plaquetário médio (MPV), plaquetócrito (PCT) e contagem de neutrofilos e linfócitos foram avaliados com base nos resultados do teste CBC dos participantes do estudo.

RESULTADO: Verificou-se que os valores de PCT, WBC, neutrófilos e MPV eram significativamente mais elevados no grupo da periodontite (p<0,05). Não houve diferenças significativas nas contagens de glóbulos vermelhos, Hb, HCT, MCV, RDW; nem nas contagens de plaquetas e linfócitos entre os dois grupos estudados (p>0,05).

CONCLUSÃO: Os níveis de PCT e MPV podem ser um marcador mais útil para determinar um estado trombótico aumentado e a resposta inflamatória em doenças periodontais.

PALAVRAS-CHAVE: Contagem de células sanguíneas. Doenças cardiovasculares. Inflamação. Contagem de leucócitos. Periodontite. Plaquetas. Fatores de risco.

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