

## Platelet Indices be a New Biomarker for Periodontal Disease

### Abstract

**Background:** Platelets play an important role in inflammation and hemostasis. Periodontitis, a chronic inflammatory disease, is linked to an increase in platelet activation leading to increased risk for atherosclerosis and cardiovascular diseases. **Aim:** The aim was to evaluate whether platelet indices (mean platelet volume [MPV], platelet distribution width [PDW], and plateletcrit [PCT]) can be a biomarker for determining the severity of periodontal disease and to assess the relation between platelet indices in patients with periodontitis and healthy controls. **Materials and Methods:** The study included 3 groups – moderate periodontitis, severe periodontitis, and systemically healthy controls without periodontitis. Clinical parameters recorded were clinical attachment level and probing pocket depth and venous blood samples were drawn for the analysis of MPV, PDW, and PCT. **Results:** ANOVA test with *post hoc* Tukey's test was used to compare among 3 groups. Statistical analysis of platelet indices was done using sample *t*-test. The mean values of MPV, PDW, and PCT gradually increased from normal to severe periodontitis. **Conclusion:** Periodontitis, a chronic inflammatory process, causes not only increase in the quantity of platelets but also causes platelet activation which leads to change in platelet size, platelet shape, and platelet aggregation. As periodontitis causing platelet activation which seems to be a contributing factor in the development of cardiovascular diseases.

**Keywords:** Biomarker, cardiovascular diseases, chronic periodontitis, platelet indices

### Introduction

Periodontitis is an oral disease which manifests as local inflammation involving the supporting tissues of the teeth, that is the periodontium, which results in attachment loss and bone loss. Periodontitis aside from causing a local inflammatory reaction can also exert a wide range of systemic effects.<sup>[1]</sup> Activation of the inflammatory response to dental plaque present in periodontitis has been associated with progress to atherothrombosis and may lead to coronary artery disease. A major cause of death worldwide. Transient bacteremia in patients with periodontitis causes increased levels of pro-inflammatory mediators. The systemic inflammation causes increase in platelet number and activation of platelets.<sup>[2]</sup> Platelet activation initiates the release of pro-inflammatory mediators which in turn activates pro-inflammatory receptors which results in binding of platelets to endothelial cells and leukocytes, these cause inflammatory and thrombotic changes in the vasculature. This activation

of platelet causes changes in platelet size, platelet form, platelet accretion, and liberation of platelet components. When the platelets attach to endothelial cells, the shape of the platelet changes from discoid to spherical with pseudopod formation. Usually, the periodontal pathogens like *Porphyromonas gingivalis* activate platelets and cause platelet aggregation through HgP44 (hemagglutinin domain protein). Thus, platelet activation leads to several systemic manifestations, atherosclerosis, and coronary vascular diseases.<sup>[2]</sup>

Platelet Indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Plateletcrit (PCT), are used as potential biomarkers for early diagnosis of thromboembolic diseases. Platelet activation results in changes in the shape of platelet due to increase in platelet swelling and pseudopodia formation which leads to an increase in MPV and PDW.<sup>[3]</sup> MPV is analogous to the mean corpuscular volume (MCV) of red blood cells.<sup>[4]</sup> The primary objective of the present study is to assess the reliability of platelet indices (MPV, PDW, and PCT) as a useful biomarker for determining the severity of periodontitis.

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## Materials and Methods

### Study population

This cross-sectional observational study was carried out on 75 participants within the age group of 35–50 years, who were reported to the outpatient department of periodontology, Mamata Dental College, Khammam. The duration of the study was from June 2019 to January 2020. The study protocol was approved by the Human Ethics Committee of Mamata Dental College and Hospital, Khammam. All the participants were explained about the study and written informed consents were obtained during examination.

### Inclusion criteria

1. Patients of age between 35 and 50 years
2. Patients diagnosed without chronic periodontitis (Group C) and with periodontitis (Group A and B)
3. Patients without any history of previous periodontal therapy.

### Exclusion criteria

1. Pregnancy and lactating females
2. Patients under antibiotic medication in the last 3 months
3. Smokers and alcoholic patients
4. Patients with any other systemic diseases.

Diagnosis of periodontitis severity was made according to the case definition given for population-based surveillance of periodontitis,<sup>[5]</sup> as follows:

Moderate periodontitis includes  $\geq 2$  interproximal sites with attachment loss  $\geq 4$  mm (not on the same tooth), or  $\geq 2$  interproximal sites with probing depth  $\geq 5$  mm (not on the same tooth), Severe periodontitis  $\geq 2$  interproximal sites with clinical attachment loss  $\geq 6$  mm (not on the same tooth) and  $\geq 1$  interproximal site with probing depth  $\geq 5$  mm.<sup>[5]</sup>

All the study subjects were divided into 3 groups of 25 each into:

- Group A – 25 systemically healthy patients suffering from moderate chronic periodontitis
- Group B – 25 systemically healthy patients suffering from severe chronic periodontitis
- Group C – 25 systemically healthy patients who have no evidence of mild, moderate, or severe periodontitis.

The clinical periodontal examination was carried out by a single examiner for all the study subjects. Intraexaminer accountability was good, with a value of 0.82. Probing pocket depth (PPD) and clinical attachment level (CAL) were measured for all the study subjects using the UNC-15 probe after meeting the inclusion criteria and grouped accordingly. PD was measured as the distance from the free gingival margin to the bottom of the periodontal pocket or base of the gingival sulcus. CAL was measured from cemento-enamel junction to base of sulcus or pocket.

Investigations: peripheral venous blood samples were collected in the vial containing EDTA by venepuncture from the antecubital fossa using a syringe, for determination of platelet indices. The platelet indices (MPV, PDW, and PCT) were determined using an automated cell counter [Unitron BioMedicals F-19 - Figure 1] within 24 h after collection of the sample, in the Hematology Laboratory of Mamata General Hospital, Khammam.

### Statistical analysis

All data obtained were statistically analyzed using SPSS version 18 (International Business Machines Corporation [IBM], Armonk, New York, United States).  $P < 0.05$  was considered statistically significant. A comparison of mean platelet indices among the 3 groups was done using ANOVA test with *posthoc* Tukey's test [Table 1]. A comparison of mean platelet indices with cutoff values was done using one sample *t*-test [Table 2].

## Results

A total of 75 participants belonging to 3 groups were evaluated for platelet indices. The mean MPV levels in healthy individuals 9.13, moderate periodontitis it is 11.44, and in severe periodontitis levels increased to 12.17. The MPV and mean PCT levels showed significant changes from normal to diseased individuals. The mean PCT levels in normal individuals 0.19 in moderate periodontitis is 0.3 and in severe periodontitis it is 0.42. The mean PDW levels in healthy individuals are 10.5 in moderate periodontitis it is 10.6 and in severe periodontitis it is 10.8.

Graph 1 shows the mean values of MPV, which gradually increased from normal (9.13) to severe periodontitis (12.17). Graph 2 suggests the mean values of PCT, which increased from normal (0.19) to severe periodontitis (0.42). Graph 3 shows the mean values of PDW, a slight change from normal (10.5) to severe periodontitis (10.8).



Figure 1: Hematological autoanalyzer (Unitron Biomedicals)

**Table 1: ANOVA with *post hoc* Games-Howell test**

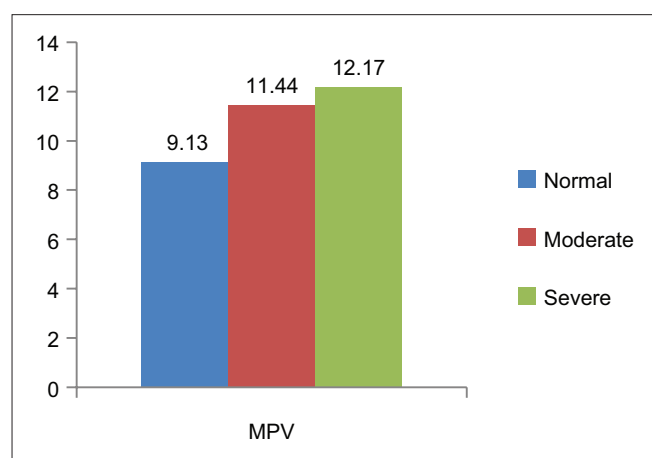
	Group (mean±SD)			P	Post hoc test
	Normal	Moderate	Severe		
MPV	9.13±0.93	11.44±1.40	12.17±0.53	<0.001 (significant)	Severe > moderate > normal
PCT	0.19±0.04	0.30±0.06	0.42±0.09	<0.001 (significant)	Severe > moderate > normal
PDW	10.51±2.71	10.61±1.58	10.87±1.40	0.805	-

SD: Standard deviation, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width

**Table 2: One sample t-test**

	Normal (mean±SD)	P	Moderate (mean±SD)	P	Severe (mean±SD)	P
MPV (10.4)	9.13±0.93	<0.001 (significant)	11.44±1.40	0.001 (significant)	12.17±0.53	<0.001 (significant)
PCT (0.28)	0.19±0.04	<0.001 (significant)	0.30±0.06	0.132 (nonsignificant)	0.42±0.09	<0.001 (significant)
PDW (14)	10.51±2.71	<0.001 (significant)	10.61±1.58	<0.001 (significant)	10.87±1.40	<0.001 (significant)

SD: Standard deviation, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width



**Graph 1: Mean platelet volume**

## Discussion

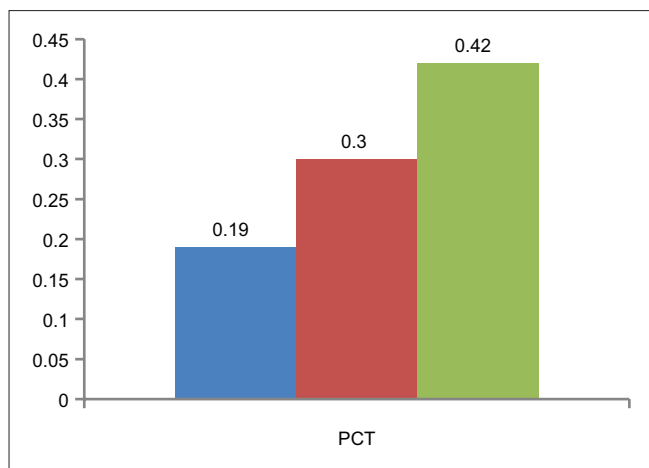
The association between periodontitis and systemic diseases is based on the thought that periodontal pathogens gain access to the bloodstream. This transient bacteremia in case of periodontitis patients triggers a cascade of inflammatory response from the body and causes increased production of pro-inflammatory mediators. Either local or systemic inflammatory stimuli induce increased levels of white blood cells, C-reactive proteins, and activation of platelets or endothelial cells. Thus, the study of these inflammatory biomarkers can be used to assess both periodontal and systemic inflammatory conditions and also support the plausibility of periodontitis as a potential link for an increased risk of cardiovascular disease.<sup>[3]</sup>

Platelets are heterogenous blood elements of varying sizes and densities derived from bone marrow megakaryocyte and are the smallest of the formed elements in blood. They are disk-shaped, nonnucleated blood element.<sup>[4,5]</sup> Large platelets possess the higher metabolic and enzymatic activity and show higher thrombogenic potential.<sup>[6]</sup> The primary function of platelets is for primary hemostasis and endothelial repair. It also plays a key role in atherogenesis

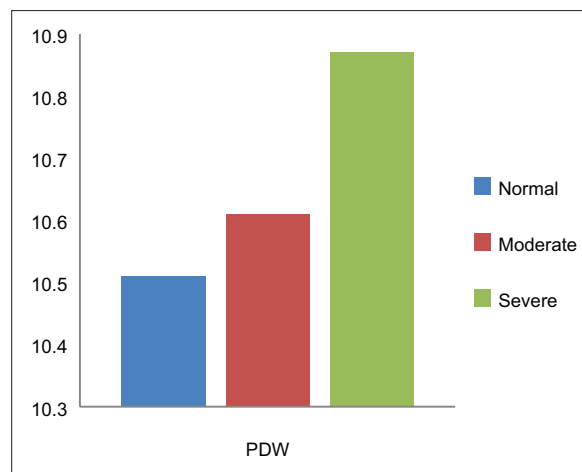
and thrombus formation.<sup>[7]</sup> Platelet activation is the hallmark of acute coronary syndromes. Platelets adhere to neutrophils and form platelet-neutrophil complexes (PNCs) through the integration platelets P-selectin and the Mac-1 complex of neutrophils, which are the main regulators of PNCs. The systemic effects of PNCs and the chemokine release induced by them have been proposed in the development of multiorgan failure<sup>[8]</sup> and the hypothesis linking periodontitis to cardiovascular diseases. In addition to aggregation, platelet size measured as MPV is a marker of platelet function and indicator of increased activity.

This study is the first of its kind which uses the entire platelet indices list in patients with chronic periodontitis. Peripheral Blood Film is used for Evaluation of Platelet volume, number, size, distribution and their structure (granularity, diameter and inner complexity) are identified in autoanalyzer (Unitron BioMedicals) [Figure 1]. Results from the present study correlate with other studies to indicate that individuals with severe periodontitis have higher levels of platelet count compared to moderate and healthy controls.<sup>[1]</sup> According to the present study, MPV, PCT, and PDW showed significant changes in severe periodontitis compared to moderate and healthy individuals.

Platelets which are larger in size have more granules, aggregate rapidly with collagen, have higher thromboxane A2 level and express more glycoprotein Ib and IIb/IIIa receptors compared to smaller ones.<sup>[2,8]</sup> This suggests that MPV and PDW can be affected by many inflammatory and cardiovascular risk factors.<sup>[4]</sup> A study by Zhan *et al.*<sup>[7]</sup> showed decrease in platelet size in patients with generalized aggressive periodontitis due to the consumption of large platelets at the site of periodontal inflammation. Fay *et al.*<sup>[9]</sup> stated that during gestation in pregnant females, it is observed that there is an increase in platelet aggregation and decrease in the total number of circulating platelets. Khandekar *et al.*<sup>[10]</sup> in their study on platelet volume indices in patients with coronary artery disease and acute myocardial infraction concluded that MPV and PDW levels



Graph 2: Plateletcrit



Graph 3: Platelet distribution width

are found to be increased in patients with MI and angina. Platelet volume indices are helpful in identifying larger platelets that cause coronary thrombosis leading to MI.<sup>[11,12]</sup>

Renvert *et al.*<sup>[13]</sup> in their study on subgingival microflora in patients with CAD reported an increased presence of *Streptococci* spp., *P. gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, suggesting a close correlation between periodontitis and acute coronary syndromes. Papapanagiotou *et al.*<sup>[14]</sup> stated increase in platelet levels and activation in periodontitis patients and that periodontal treatment resulting in lowering of platelet levels.

Şahin *et al.*<sup>[15]</sup> concluded that PCT is an indicator of circulating platelets in a unit volume of blood from the findings that PCT was increased in patients with pulmonary tuberculosis, than in pneumonia. Nicu *et al.*<sup>[16]</sup> also observed an increased platelet response and more intense formation of platelet-leukocyte complexes as a response to dental biofilm bacteria, which could result in vascular atherosclerosis in patients with periodontitis. Chu *et al.*<sup>[17]</sup> stated that MPV was found to be increased in patients with stable CAD, and that it can be a risk factor for death in patients after myocardial infarction. Hence, from the above reports, it can be concluded that MPV could be regarded as a prognostic biomarker in cardiovascular diseases. Khode *et al.*<sup>[8]</sup> assessed MPV and other platelet indices in patients with stable coronary artery disease and acute myocardial infarction and found that there were significantly higher values in patients with AMI ( $9.65 \pm 0.96$ ) as compared to SCAD ( $9.37 \pm 0.88$ ) and controls ( $9.21 \pm 0.58$ ). Temelli *et al.*<sup>[18]</sup> in their recent study found a relationship between coronary artery disease with or without periodontitis to platelet indices. Ozturk *et al.*<sup>[19]</sup> correlated platelet indices in patients with Crohn's disease and ulcerative colitis and found a significant change in MPV levels thus, considered it as a biomarker for inflammatory bowel disease. The present study has a less sample size which is a major limitation. The other contributing factors like patients with platelet disorders and race/gender of the patients were not considered in the present study.

## Conclusion

We conclude from our study that platelet indices MPV, PCT, and PDW can be used as simple, practical, and cost-effective biomarker for periodontitis. The chronic inflammatory response triggered by periodontitis results in platelet aggregation and platelet activation which leads to a change in platelet number, size, and shape. This leads to a change in the platelet indices, thus proving as a reliable biomarker for the assessment of both periodontal and cardiovascular disease. However, further studies with a larger population are required to confirm platelets as a biomarker for periodontitis and its link to cardiovascular diseases.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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