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PLATELET INDICES AND PERIODONTAL DISEASES: IN PURSUIT OF A NOVEL BIOMARKER

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ABSTRACT

PURPOSE: Platelets plays an important role in inflammation and haemostasis. Periodontitis a chronic inflammatory disease shown to be associated with an increase in platelet activation leading to increased risk for atherosclerosis and cardiovascular diseases.

AIM: To evaluate whether platelet indices (MPV, PDW, and PCT) would be a useful biomarker for determining severity of periodontal disease and to assess the platelet indices in patients with periodontitis and compare to matched healthy controls.

MATERIALS AND METHODS: Study included 3 groups- Moderate Periodontitis, Severe periodontitis, and systemically healthy controls without periodontitis. Clinical parameters were recorded i.e.; CAL and probing pocket depth and venous blood samples were drawn for the analysis of MPV, PDW, PCT.

RESULTS: The periodontitis and the platelet indices are statistically analysed. Comparison among 3 groups was done using Anova test with post-hoc tukey's test. Comparison of mean platelet indices was done using one sample t- test.

CONCLUSION: Chronic inflammatory process in patients with periodontitis results in not only increasing in the number of platelets but also causes platelet activation which leads to change in platelet size, platelet shape, platelet aggregation. As periodontitis causing platelet activation which seems to be a contributing factor in the development of cardiovascular diseases.

INTRODUCTION

Periodontitis is a common disease that manifest as local inflammation affecting the supporting tissues of the teeth resulting in attachment loss and bone loss. The dental plaque present in periodontitis leads to activation of inflammatory response that can progress to atherothrombosis. The most common cause of death is due to Coronary artery disease. Periodontitis aside from causing a local inflammatory reaction can also exert a wide range of systemic effects [1]. Transient bacteraemia in patients with periodontitis causes increased levels of pro inflammatory mediators [2].

The systemic inflammation causes increase in platelet number and activation of platelets[3]. Platelet activation leads to release of pro inflammatory mediators and exposure of pro inflammatory receptors which results in binding of platelets to endothelial cells and leukocytes, these causes inflammatory and thrombotic changes in the vasculature. These activation of platelet causes changes in platelet size, platelet shape, platelet aggregation, and release of platelet constituents. When the platelets attach to endothelial cells the shape of the platelet changes from discoid to spherical with pseudopods formation. Usually the periodontal pathogens like P.Gingivalis activates platelets and causes platelet aggregation through HgP44 [hemagglutinin domain protein][3]. Platelet activation leads to several systemic manifestations atherosclerosis, coronary vascular diseases.

Platelet indices are potentially useful markers for the early diagnosis of thrombo embolic diseases. An increase in both mean platelet volume (MPV) and platelet distribution width (PDW) due to platelet activation, resulting from platelet swelling and pseudopodia formation was hypothesized[4]. Most important parameters among them are platelet crit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW). Platelet activation leads to changes in platelet shape with increase in platelet swelling leading to an increase in MPV and PDW. Mean platelet volume (MPV) is comparable to the mean corpuscular volume (MCV) of red blood cells [5]. The primary objective of the study is to evaluate whether platelet indices (MPV, PDW, and PCT) would be a useful biomarker for determining severity of periodontitis.

MATERIALS AND METHODS

STUDY POPULATION

A cross sectional observational study was conducted on 75 participants with age 35- 50 years, who are reported to the department of periodontology, Mamata Dental College, Khammam. The protocol had been approved by the institutional committee of Research Ethics, Mamata dental college. All the participants were explained about the study and written informed

consents were obtained.
All The participants were divided into 3 group of 25 each which:
Group A- 25 Patients with Moderate Chronic Periodontitis,
Group B- 25 Patients suffering from Severe Chronic Periodontitis,
Group C- 25 Controls of systemically healthy patients.

INCLUSION CRITERIA:

1. Patients of age between 35 – 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 medication in last 3-6 months.
3. Smokers and alcoholic patients.
4. Patients with any other systemic diseases.

Diagnosis of periodontitis severity was made according to: Case definition proposed for population – based surveillance of periodontitis [6], as follows:

Moderate periodontitis include ≥ 2 interproximal sites with attachment loss ≥ 4mm (not on the same tooth), or ≥ 2 interproximal sites with probing depth ≥ 5mm (not on the same tooth) ,

Severe periodontitis ≥ 2 interproximal sites with clinical attachment loss ≥6mm (Not on same tooth) and ≥ 1 interproximal site with probing depth ≥5mm.

Group C- patients have no evidence of mild, moderate or severe periodontitis.

The clinical periodontal examination was performed by single examiner.

Intra examiner agreement was good, with an 0.82 value.

Probing depth is measured distance from free gingival margin to bottom of periodontal pocket or base of gingival sulcus. Clinical attachment level is measured from cemento-enamel junction to base of sulcus or pocket.

The armamentarium used for the present study include mouth mirror, UNC 15 probe, 2 ml syringe, vials containing ethylene diamine tetra acetic acid [EDTA], tourniquet, sterile cotton, surgical gloves, automated analyser-F-19(Fig:1). Periodontal examination is performed by single examiner for all the participants included in the study.

INVESTIGATIONS:

Peripheral Venous blood samples were collected by venepuncture from antecubital fossa into standardized tube containing EDTA [7], for determination of platelet indices. The samples were processed in auto analyser- F-19 in Central Lab, Mamata General Hospital.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS version 18. P-value of < 0.05 was considered statistically significant. Comparison of mean platelet indices among the 3 groups was done using Anova test with post – hoc Tukey's test (Table-I). Comparison of mean platelet indices with cut-off 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. MPV 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 PCT levels showed significant changes from normal to diseased. 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 suggest 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).

DISCUSSION

Periodontal disease is an inflammatory process that occurs in the tissues surrounding the teeth in the response to bacterial plaque. This inflammation leads to alveolar bone destruction and loss of tissue attachment to the teeth [8].The bacteria present in the plaque biofilm causes an inflammatory response from the body. An either local or systemic inflammatory stimulus induces activation of platelets or endothelial cells. Further the interaction between pathogens and platelets leads to development of cardiovascular diseases[3]. Periodontitis is associated with an increased risk of cardiovascular disease.

Platelets are smallest of the formed elements in blood, a disk – shaped, non-nucleated blood element, that are derived from bone marrow megakaryocyte [5]. Large platelets possess higher metabolic and enzymatic activity, and show higher thrombogenic potential [9]. Platelets and neutrophils are known to adhere to each other and form platelet-neutrophil complexes (PNCs).Mainly Platelet P-selectin and the Mac-1 complex of neutrophils are the main regulators that forms PNCs, PNCs have been proposed to play a role in the development of multi-organ failure [10].Activated platelets regulate chemokine release by the monocytes in inflammatory lesions[1]. Platelets are essential for primary hemostasis and endothelial repair, but also play a key role in atherogenesis and thrombus formation [11].

This is the first study which uses all the platelet indices in patients with chronic periodontitis. Peripheral blood film is used for evaluation of platelet number, size, distribution, and their structure are identified in autoanalyser-F-19.Results from present study indicate that individuals with severe periodontitis have higher levels of platelet count compared to moderate and healthy controls[1]. According to present study MPV, PCT and PDW showed significant changes in severe periodontitis compared to moderate and healthy individuals.

In comparison to smaller ones, larger platelets have more granules, aggregate more rapidly with collagen, have higher thromboxane A2 level and express more glycoprotein Ib and IIb/IIIa receptors[2]. These suggest that MPV can be affected by many inflammatory and cardiovascular risk factors [12]. Fay et al[13] stated that during pregnancy an increase in platelet aggregation and decrease in number of circulating platelets occur with gestation. Khakendar et al [14] reported a study on platelet volume indices in patients with coronary artery disease and acute myocardial infarction and results found that MPV and PDW levels are raised in patients with MI and Angina. Platelet volume indices are helpful in identifying larger platelets that causes coronary thrombosis leading to MI.

Renvert et al [15] reported an increased presence of Streptococci spp., P. gingivalis, T. forsythia and T. denticolain subgingival biofilm in patients with CAD, suggesting a close correlation between periodontitis and acute coronary syndromes. Papanagiotouet al [16] stated that increase in platelet levels and activation in periodontitis patients and that periodontal treatment resulting in lowering of platelet levels.

Şahinet al.[17] reported that PCT is increased in patients with pulmonary tuberculosis, than in pneumonia so they considered PCT as indicator of circulating platelets in a unit volume of blood. Nicu et

al [18] 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 [19] demonstrated that MPV is increased in patients with stable CAD, and that it can be a risk factor for death in patients after myocardial infarction. It has been suggested that MPV could be regarded as a prognostic marker in cardiovascular diseases. Khode[20] reported a study on mean platelet volume and other platelet indices in patients with stable coronary artery disease and acute myocardial infarction there was significantly higher values in patients with AMI (9.65 ± 0.96) as compared to SCAD (9.37 ± 0.88) and controls (9.21 ± 0.58).Z.A. Ozturk et al [21] studied platelet indices in patients with crohn's disease and ulcerative colitis there showed a significant changes in MPV levels so they considered it as biomarker for inflammatory bowel disease. Limitation of the present study is less sample size. The patients with platelet disorders, race/gender are not considered in the present study.

CONCLUSION

From the present study we conclude that platelet indices MPV, PCT, PDWare used as biomarker for periodontitis. As the procedure is simple, practical, cost effective biomarker for periodontal disease. Chronic inflammatory process in patients with periodontitis results in not only increasing in the number of platelets but also causes platelet activation which leads to change in platelet size, platelet shape, platelet aggregation. As periodontitis causing platelet activation which seems to be a contributing factor in the development of cardiovascular diseases. However further studies are needed with larger population to confirm platelets as biomarker for periodontitis.

Table: 1 ANOVA with post-hoc Games Howell test

	Group						p-value	Post-hoc test
	Normal		Moderate		Severe			
	Mean	SD	Mean	SD	Mean	SD		
MPV	9.13	.93	11.44	1.40	12.17	.53	<0.001; Sig	Severe >Moderate > Normal
PCT	.19	.04	.30	.06	.42	.09	<0.001; Sig	Severe >Moderate > Normal
PDW	10.51	2.71	10.61	1.58	10.87	1.40	0.805	-

Values are presented as mean±standard deviation.
MPV: Mean platelet volume, PCT: Platelet crit, PDW: Platelet distribution width

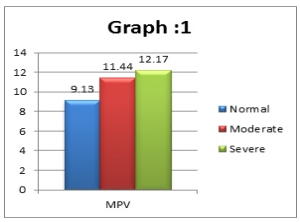
Sig: significant, NS: Non significant

Table: 2 One sample t test

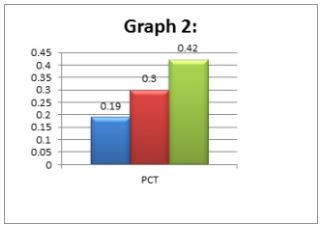
	Normal		p-value	Moderate		p-value	Severe		p-value
	Mean	SD		Mean	SD		Mean	SD	
MPV (10.4)	9.13	.93	<0.001; Sig	11.44	1.40	0.001; Sig	12.17	.53	<0.001; Sig
PCT (0.28)	.19	.04	<0.001; Sig	.30	.06	0.132; NS	.42	.09	<0.001; Sig
PDW (14)	10.51	2.71	<0.001; Sig	10.61	1.58	<0.001; Sig	10.87	1.40	<0.001; Sig

Values are presented as mean±standard deviation.
MPV: Mean platelet volume, PCT: Platelet crit, PDW: Platelet distribution width

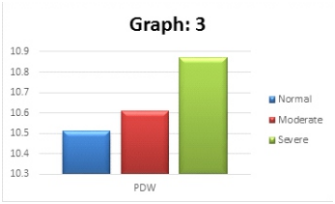
Sig: significant, NS: Non significant



Graph-1 shows the mean values of MPV, which gradually increased from normal (9.13) to severe periodontitis (12.17).



Graph-2 suggest 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).

Fig : 1

FIG 1: Automated analyser-F-19

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