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Original Article

Effect of Non-surgical Periodontal Therapy on Platelet-to-Lymphocyte Ratio and Neutrophil-to-Lymphocyte Ratio in Chronic Periodontitis

Nida Malik[1,*], Veena Kalburgi[2], Saba Malik[3], Sumedha Srivastava[4], Harshita Verma[5], Kalpana Sharma Rai[6]
[1] Department of Periodontics, People's College of Dental Sciences and Research Centre, Bhopal, Madhya Pradesh, INDIA.
[2]Department of Periodontology, People's College of Dental Sciences and Research Centre, Bhopal, Madhya Pradesh, INDIA.
[3]Consultant Prosthodontist, Bhopal, Madhya Pradesh, INDIA.
[4]Department of Periodontology, People's College of Dental Sciences and Research Centre, Bhopal, Madhya Pradesh, INDIA.
[5]Department of Periodontics, Bharati Vidhyapeeth Dental College, Pune, Maharashtra, INDIA.
[6]Department of Endodontics, Peoples College of Dental Science and Research Center, Bhopal, Madhya Pradesh, INDIA.

ABSTRACT

Introduction: Haematological investigations have for long being considered as potential diagnostic and prognostic markers in the pathogenesis of Chronic Periodontitis. An exaggerated understanding of these markers with the consideration of relatively new markers Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) obtained from the peripheral blood count may serve as a potential marker in the understanding of the correlation of Chronic Periodontitis and Systemic Inflammatory Response. These markers haven't been extensively studied in context to Periodontitis. **Materials and Methods:** 60 Patients were enrolled and 90 samples were collected. Group A-Experimental (30 Patients) who were assessed at baseline and Post-treatment after 4 weeks and Group B-Controls (30 Patients). GI, PI, PPD, CAL, Neutrophil Count, Lymphocyte Count and Platelet counts were obtained. NLR was calculated as the ratio to Neutrophil to Lymphocyte and PLR was calculated as the ratio of Platelet to Lymphocyte. Statistical analysis of the data was performed. **Results:** The results varied significantly in both the groups and in the diseased group at baseline and post-treatment. The ROC cut off values for NLR and PLR was found to be 1.5 and 92.5 respectively which may be used as prognostic values for Chronic Periodontitis. **Conclusion:** Both the novel markers, NLR and PLR can successfully be used in the assessment of Chronic Periodontitis with the ease of applicability and can also be used further to rule out any ongoing systemic inflammatory challenge.

Keywords: Chronic Periodontitis, Neutrophil, Lymphocyte, Platelet, Systemic Inflammatory response, Inflammatory markers.

Correspondence

Dr. Nida Malik,

(Post Graduate Student, III Year), People's College of Dental Sciences and Research Centre, Bhopal-462001, Madhya Pradesh, INDIA.

Email id: dr.nidamalik05@gmail.com

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INTRODUCTION

Periodontitis is a multifactorial infectious disease that manifests itself as the inflammation and destruction of the supporting structures of the teeth.[1] Inflammation and inflammatory cells are the mainstay in the aggravation or regression of periodontal destruction. Recent studies suggest a strong correlation between Periodontitis and systemic well-being of the patient, that is, it not only affects the local integrity and function of the Periodontal apparatus but also results in a notable increase systemic inflammatory burden.[2] Peripheral blood parameters undergo a lot of changes in response to periodontal destruction and are frequently associated with an increase in systemic Inflammatory response.[2] In light of Extensive microbial plaque associated with Periodontal Destruction, the chronic nature of the disease and the exuberant local and systemic response to microbial assault, it is reasonable to hypothesize that this infection may influence the overall health and the course of some systemic diseases. Recently several research groups have demonstrated that periodontitis is associated with elevated numbers of White blood cells. These observations indicate that periodontitis patients may have a subclinical inflammatory reactions.

Neutrophils and Lymphocytes along with their role in Innate and adaptive immunity respectively, also hold a key position in the pathogenesis of periodontitis.[3] Platelets, too, have an important role in inflammation as they are involved in the formation to platelet-leukocyte aggregate and T-cell mediated immune responses leading to the expression of a variety of pro-inflammatory cytokines. WBC, for long has been considered as a primitive marker of systemic inflammation and also correlates to host response to a variety of stimuli.[4] The host reaction to gingival microorganisms is characterized in part by increase in the polymorphonuclear leukocyte counts, which is one of the most important steps in host defence. An exaggeration of leukocytes and neutrophils of has been noted in the pathogenesis of Periodontitis.[5-7]

Neutrophil-to-Lymphocyte ratio (NLR) and Platelet-to-Lymphocyte ratio (PLR), in addition to the above mentioned parameters may be considered as potential markers to assess inflammatory response in chronic periodontitis patients.[1-2]

Both, NLR and PLR are reported and published markers of systemic inflammatory response including a wide range of systemic diseases like Rheumatoid Arthritis,[8] Hematological malignancies, respiratory,[9] gastrointestinal, cardiovascular dysfunctions like acute coronary syndrome and the most recent being, the SARS Covid 19.[10] NLR and PLR can be easily calculated as a simple ratio of neutrophil and lymphocyte counts and platelet and lymphocyte counts in a peripheral blood.[2,10]

NLR may serve as a promising marker for predicting the severity of tissue destruction in Periodontitis. It is directly or indirectly related to systemic inflammation due to its biochemical and cellular activities and

also for its strong correlation to inflammatory markers like CRP. This ratio reflects two complimentary immune pathways as the biologic effect of Neutrophil includes curbing of apoptosis and phagocytosis, while that of Lymphocyte includes adaptive immune responses.[11]

Platelets regulate the release of pro-inflammatory mediators such as chemokines and cytokines which play a vital role in the progression of Periodontitis through the activation of acquired immune system. As the immune response worsens its leads to a permanent damage of the bone as well as an irrepairable attachment loss. Cytokines are the peptide mediators with the key function of cell signalling and communication. Their function varies from cell proliferation, cell differentiation, immune responses to inflammatory responses. Chemokines, on the other hand, are a large sub group of cytokines with the ability to regulate leukocytes and their activation.[12] Since NLR and PLR are ratios, they are relatively more stable when compared to individual parameters which may otherwise be altered under specific conditions like dehydration, over hydration.[13]

MATERIALS AND METHODS

60 participants were recruited in the study after obtaining the Institutional Ethical Clearance (EC201915). Group A- Experimental comprised of 30 Chronic Periodontitis patients whose NLR and PLR was assessed at baseline and 4 weeks post treatment. Group B- Control comprised of 30 systemically and periodontally healthy patients whose NLR and PLR was assessed at baseline.

Inclusion Criteria

Patients aged between 25-60 years with severe periodontitis having more than 20 teeth with no systemic involvement and a probing pocket depth of ≥ 5 mm in more than 30% of thesites involved.

Exclusion Criteria

Smokers, Medically compromised patients, Pregnant or lactating females or patients who have undergone periodontal therapy or antibiotic prophylaxis in last 6 months were excluded from the study.

Clinical Parameters to be measured

Gingival Index, Plaque Index, Probing Pocket Depth (PPD), Clinical Attachment level (CAL), Complete blood count to calculate NLR and PLR of the patients.

Data Collection

5ml of Blood was drawn from the antecubital fossa of the arm using a 21 Gauge syringe at the baseline before non-surgical periodontal therapy and patients were given oral hygiene instructions. Four Weeks later, samples were collected again for chronic periodontitis patients after non-surgical periodontal therapy. After withdrawal, blood was transported to an anticoagulant vial to prevent clotting and sent to the laboratory. The vial consisted 2ml of K3-EDTA (Ethylene Diamine Tetra-acetic Acid). After proper mixing, the vial was placed in the automated cell counter. Horiba Yumizen H500 automated cell counter was used.

Statistical Analysis

Statistical analysis of data is done by SPSS 23.0 Software. Unpaired -T test, Correlation, Paired *t*-test, Chi Square test and ROC Curve was used in data analysis. *P* value <0.05 was considered as significant.

RESULTS

The mean age in years of Group A was 40.66±6.19 and that of Group B was found to be 38.5±4.85 and each group comprised of 15 Males and 15 females (Table 1). Both NLR and PLR in experimental and control group differed significantly, the latter group having a relatively lower NLR and PLR as compared to former. In the Experimental group both NLR and PLR are significantly reduced after treatment when assessed after 4 weeks (Table 2, 3). The 4 week's time after phase 1 therapy may be a justifiable time frame for achieving reduction in gingival inflammation and thereby reducing systemic inflammation (reduction in TLC and platelet counts).[14]

The ROC cut off value in the Experimental Group for NLR (Sensitivity-0.933 and Specificity-0.9) was 1.51 and that for PLR (Sensitivity-0.9 and Specificity-0.867) was 92.5. Hence these values can be used as prognostic values for Chronic Periodontitis (Table 4).

DISCUSSION

On evaluation of the study, it was revealed that Age and gender had no constraints on the study, where the mean age of the Experimental group was found to be 40.66 and that of the Control group was found to be 38.5. In the light of epidemiological studies there is a strong relation between age and gender predilection towards oral disease. Interestingly, periodontitis has a documented higher prevalence in men as compared to women signifying a possible sex/gender entanglement in the disease pathogenesis however in the present study this correlation is not in accordance with previous work and that there is no statistically

Table 1: Distribution of NLR and PLR according to Baseline and Post Treatment in Group A (Column Width).

	Mean	N	Std. Deviation	*t* value	*p*-value
Baseline NLR	2.56	30	1.168		
Post Treatment NLR	1.46	30	.186	5.307	<0.0001*
Baseline PLR	117.65	30	17.023		
Post Treatment PLR	88.25	30	8.44	8.817	<0.0001*

Table 2: Analysis of NLR & its correlation with clinical parameters before & after Non-Surgical Periodontal Therapy (Column Width).

Variable	Total NLR		NLR in Healthy		NLR (Baseline)		NLR (Post Treatment)	
	r value	*p* value	*r* value	*p* value	*r* value	*p* value	*r* value	*p* value
GI	0.561	<0.0001*	0.007	0.972	0.074	0.698	-0.028	0.882
PI	0.566	<0.0001*	-0.029	0.881	0.105	0.581	-0.222	0.238
Cal	0.608	<0.0001*	--		0.208	0.269	0.062	0.747
PPD	0.600	<0.0001*	---		0.080	0.675	0.216	0.251
Neutrophil	0.658	<0.0001*	0.604	<0.0001*	0.327	0.078	0.252	0.179
Lymphocyte	-0.274	0.034*	-0.387	0.035*	-0.613	<0.0001*	-0.389	0.034*
Platelet	0.060	0.648	-0.422	0.020*	-0.557	0.0001*	-0.299	0.109

Table 3: Analysis of PLR and its correlation with clinical parameters before and after Non- Surgical Periodontal Therapy.

Variable	Total PLR		PLR in Healthy		PLR (Baseline)		PLR (Post Treatment)	
	r value	*p* value	*r* value	*p* value	*r* value	*p* value	*r* value	*p* value
GI	0.723	<0.0001*	-0.192	0.309	0.099	0.604	0.148	0.437
PI	0.752	<0.0001*	-0.193	0.306	0.287	0.124	-0.099	0.604
CAL	0.790	<0.0001*	----		-0.007	0.970	-0.063	0.740
PPD	0.780	<0.0001*	----		-0.259	0.167	-0.069	0.716
Neutrophil	0.591	<0.0001*	-0.142	0.456	-0.196	0.298	-0.154	0.418
Lymphocyte	-0.034	0.799	0.070	0.714	-0.549	0.002*	-0.295	0.113
Platelet	0.531	<0.0001*	0.347	0.060	-0.026	0.890	0.218	0.247

Table 4: Roc Curve.

Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Baseline NLR	.979	.014	.000	.952	1.000
Baseline PLR	.964	.024	.000	.918	1.000

significant difference between experimental and control group (Age- p is 0.137 and for Sex- p is 1).[15]

Traditionally, the total number of white blood cells (leukocytes) and erythrocytes sedimentation rates in peripheral blood have been used as a diagnostic measure to investigate whether a given individual suffers from an infection or inflammatory disease. Leukocytes are an integral part of the innate immune system, these cells are recruited at higher levels during episodes of bacteraemia in periodontitis or leakage into the systemic circulation. In the current study only Neutrophils, Lymphocytes and platelets were taken into account.[16] The mean neutrophil count for the experimental group was 7686.26 whereas in the control group it was 3572.90 which strongly exhibits a statistically significant difference with a *p* value of <0.0001. This finding is in accordance with the study conducted by Anna Pejcic *et al.* wherein they found that the neutrophils were significantly higher ($p<0.001$) in the periodontitis group (7.89×10^9/L) when compared with the healthy controls (4.05×10^9/L).[5] This study also correlated positively with the study conducted by Reetika Gaddale *et al.* where they observed Neutrophilia (5877.3) in Generalized aggressive periodontitis patients when compared with systemically and healthy controls (4812.26), which was highly significant.[6]

The mean Lymphocyte count at baseline in the Experimental group was found to be 3238.3000±915.71793 and that of Control was found to be 2781.133±892.639, that is there is no significant difference in Baseline Lymphocyte count between Experimental and Control groups ($p>0.05$). This finding by far opposes the previous studies by Anna Pejcic *et al.* and Reetika Gaddale *et al.* where potential lymphocytosis with significant difference was noted in Periodontitis patients when compared with the healthy controls.[5-6]

The mean platelet count at baseline of Experimental group was found to be 372740±93306.85 and that of Control was found to be 238400±81209.64. These significant difference in Baseline Platelet count between Experimental and Control group ($p<0.05$). According to Mean Baseline Platelet count is higher in Experimental group in respect to Control group. This finding is consistent with the study conducted by Mario Romandini *et al.* where the platelet count in Periodontitis patients was elevated by more than 13,049/μL suggesting a strong correlation between periodontitis and a considerable increase in platelet count which is explained, at least in part, by an increase in the systemic inflammation.

The mean baseline NLR of Group A (Experimental) participants was found to be 2.56±1.16 and that of Group B (Control) was found to be 1.29±.39. On the other hand the mean baseline PLR of Group A (Experimental) participants was found to be 117.65±17.02 and that of Group B (Control) was found to be 82.84±8.96. Hence both the parameters, NLR and PLR, have a marked difference at baseline in both the groups with $p<0.0001$. Although it would somewhat be difficult to rule out a concrete comparison of these two new markers due to non-availability of sufficient data in the literature.

The mean NLR at baseline was found to be 2.56 ± 1.16 whereas the mean value posttreatment was found to be 1.46 ± .186, on the other hand PLR at baseline was found to be 117.65±17.02 whereas the mean value posttreatment was found to be 88.25±8.44. This finding is in accordance with the study conducted by AB Acharya *et al.* wherein they found a significant difference at baseline and posttreatment in NLR (Baseline 1.9±0.5; Posttreatment 1.48±0.4) and PLR (Baseline 121.08±43.58; Post-treatment 80±26.50).[2]

Intending towards the limitations of the study, an individual to individual study results can infer with contrasting results.

1. Also, the deficient sample size may prove out to be insufficient to conclude.
2. Graduating the follow-up session may also bring changes to the results.

CONCLUSION

It can be concluded that both of these novel markers may be included as potential parameter in studies pertaining to oral-systemic axis to provide a clarity to the impact that chronic periodontitis may have on the systemic health as well as act as a mirror to any underlying subclinical inflammation. Easy availability and uncomplicated calculation make them even more easy to conduct. However further studies need to be conducted with a larger sample size to evaluate these results.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

NLR: Neutrophil to Lymphocyte Ratio; **PLR:** Platelet to Lymphocyte Ratio.

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