RESEARCH PAPER

Change in Neutrophil to Lymphocyte Ratio following Non-Surgical Periodontal Therapy in Patients with Type 2 Diabetes Mellitus and Periodontitis

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ABSTRACT

Background: Periodontitis is a chronic inflammatory disease with well-established bidirectional association with type 2 diabetes mellitus (T2DM). Systemic inflammatory burden in such patients can be assessed using simple haematological markers such as the neutrophil-to-lymphocyte ratio (NLR), which reflects the balance between innate and adaptive immune responses.

Aim: To evaluate the change in neutrophil-to-lymphocyte ratio following non-surgical periodontal therapy (NSPT) in well-controlled T2DM patients with periodontitis.

Materials and Methods: A longitudinal clinical study was conducted among 45 controlled T2DM patients (HbA1c $\leq$ 7%) diagnosed with periodontitis. Clinical periodontal parameters including probing pocket depth (PPD), clinical attachment level (CAL), full-mouth plaque score (FMPS), and full-mouth bleeding score (FMBS) were recorded at baseline and 8 weeks after NSPT. Peripheral blood samples were collected for complete blood count analysis, and NLR was calculated. Statistical analysis was performed using paired t-test and ANOVA, with significance set at $p < 0.05$.

Results: All periodontal parameters showed significant improvement following NSPT ($p < 0.001$). Neutrophil counts did not show a significant change ($p = 0.807$), whereas lymphocyte counts increased significantly post-therapy ($p < 0.001$). NLR demonstrated a statistically significant reduction from baseline (1.98 ± 0.30) to post-treatment (1.81 ± 0.25) ($p = 0.002$). Baseline NLR values increased significantly with advancing stages of periodontitis.

Conclusion: Non-surgical periodontal therapy significantly reduces systemic inflammatory burden, as reflected by decreased NLR, in well-controlled T2DM patients with periodontitis. NLR may serve as a simple and reliable adjunctive biomarker for monitoring systemic inflammation following periodontal therapy.

Keywords: periodontitis, diabetes mellitus type 2, neutrophil-lymphocyte ratio, periodontal therapy, inflammation

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INTRODUCTION

Periodontitis is a chronic inflammatory disease primarily initiated by pathogenic microorganisms within the dental biofilm.[1] Severe periodontal disease was identified as the 11th most prevalent condition worldwide according to the Global Burden of Disease Study in 2016.[2] The prevalence of periodontal disease increases with advancing age.[3] With rising life expectancy and greater re tention of natural teeth, the prevalence of periodontal disease will continue to increase.[4] As numerous epidemiological studies have demonstrated significant associations between periodontitis

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and various systemic diseases, the impact of periodontal diseases on public health remains substantial.[5,6,7]

The extent and severity of periodontitis are dependent on multiple factors, including smoking, systemic diseases, stress, genetic predisposition, and the host's inflammatory profile.[8] Among these, diabetes is a significant risk factor that warrants special consideration, and the association between the two is firmly supported by extensive evidences.[9] Individuals with uncontrolled diabetes typically present with deeper periodontal pockets, greater attachment loss, and increased risk of tooth loss.[10] Chronic hyper glycemia in diabetes amplify the systemic inflammatory response and increases the pathogenicity of periodontal microbiota.[11] The accumulation of advanced glycation end products contributes to periodontal tissue destruction and adversely affects wound healing.[12]

Another factor that strongly influence the susceptibility to periodontitis is the individual host response, specifically the intensity of the inflammatory process and the selective activation of innate and adaptive immune pathways.[13] Periodontal lesions act as endogenous sources of infection, and recurrent bacteraemia perpetuates a systemic pro-inflammatory state, as evidenced by elevated total leukocyte counts and plasma C-reactive protein (CRP).[14] The roles of neutrophils, T and B lymphocytes, monocytes, and macrophages in the inflammatory process are well established. Neutrophils are the most common cell type and are recruited in large number in response to bacteria laden plaque. They form a barrier against periodontopathic bacteria by virtue of their secretory as well as phagocytic activity.[15] Lymphocytes on the other hands are the main effector cells of adaptive immunity. High inflammatory cytokine levels in periodontal diseases increases insulin resistance further worsen the diabetic status.[16] Successful periodontal treatment positively influence insulin sensitivity and contribute to better glycemic control.[17] Nonsurgical periodontal treatment (NSPT) is associated with reduction in the levels of white blood cells and biomarkers of inflammation.[18,19]

Along with other traditional markers of inflammation, Neutrophil to Lymphocyte Ratio (NLR) has recently gained recognition. NLR is calculated as the simple ratio of neutrophils to lymphocytes in peripheral blood. NLR is considered a superior diagnostic and prognostic marker of inflammation compared with either parameter alone in many diseases including peripheral arterial diseases, inflammatory bowel diseases and breast cancer. [20,21,22] It predicts patient survival more accurately and demonstrates the relationship between the innate response driven by neutrophils and the adaptive response supported by lymphocytes.[23]

Although NLR is a readily available and cost-effective biomarker of systemic inflammation, its role in monitoring the inflammatory response to periodontal therapy in diabetic individuals has not been adequately explored. The chronic low-grade inflammation characteristic of both type 2 diabetes mellitus and periodontitis underscores the need for markers that can capture systemic inflammatory changes following treatment. Therefore, this study investigated the effect of NSPT on NLR levels in controlled type 2 diabetic patients with periodontitis.

MATERIALS AND METHODS

The longitudinal clinical study was conducted in the Outpatient Department of Periodontics, Government Dental College, Kottayam, India over a period of 18 months from November 2023 to April 2025. The study was conducted in accordance with the ethical principles of Declaration of Helsinki, as revised in 2013. The Institutional Ethical Committee approved the study protocol (Approval number: IEC/M26/2023/R507 /DCK dated 21-09-2023). Based on previously published literature, assuming a mean reduction in NLR of 0.3 with a standard deviation of 0.5, a two-tailed α of 0.05, and 80% power, the minimum required sample size was calculated as 22 participants. We recruited a total 45 patients for the study.

The inclusion criteria were as follows: (1) patients diagnosed with type 2 diabetes mellitus for more than 1, but less than 5 years and under oral hypoglycemic agents with glycated hemoglobin levels(HbA1c) ≤ 7 (2) with age between 40─60 years (3) diagnosed with periodontitis as per 2017 classification of periodontal diseases and conditions (interdental clinical attachment level (CAL) ≥ 2 mm in ≥ 2 non-adjacent teeth or buccal CAL ≥ 3 mm with probing depth > 3 mm in ≥ 2 teeth, with CAL not attributable to non-periodontitis related causes) (3) with more than twenty natural teeth (4) Body mass index ≤ 30.

The exclusion criteria were (1) patients with type 2 diabetes mellitus with HbA1c level > 7, (2) under insulin (2) previous history of periodontal therapy for last 6 months, (3) antibiotic anti-inflammatory therapy for past 3 months, (4) patients with other systemic diseases like hypertension, cardiovascular diseases, rheumatoid arthritis etc, and (5) smokers.

Data collection

After applying the inclusion and exclusion criteria, eligible participants were provided a detailed explanation about the study procedures and enrolled after obtaining written informed consent. Demographic data, height, weight, BMI and HbA1C were recorded. Participants were subsequently referred to the hematology laboratory, where a complete blood count analysis was performed using standard laboratory procedures.

Blood collection

Blood was drawn and collected from the antecubital fossa of the arm using a 21-gauge syringe by a hematology laboratory staff into a vacutainer incrementally in small volumes. The hematological parameters were estimated using an automated hematology analyzer, Mindray BC-21s Auto Hematology Analyzer (Mindray Medical International Limited, Shenzhen, China) according to the manufacturer's instructions. NLR is calculated as the ratio of neutrophils to lymphocytes.

Clinical Parameters

This is followed by recording of following clinical periodontal parameters.

Probing pocket depth (PPD): Measured as the distance from the base of the pocket to the gingival margin. CAL: Measured as the distance from cementoenamel junction (CEJ) to the base of the pocket. These were recorded using a University of North Carolina-15 probe (UNC-15 probe; Hu-Friedy® Manufacturing Inc., Chicago, IL, USA). Measurements were recorded at six sites per tooth, excluding the third molars. The mean PPD and mean CAL for each patient were calculated.

Full mouth plaque score (FMPS) and full mouth bleeding score (FMBS): Presence or absence of plaque (O'Leary's plaque index [1972]) and bleeding were recorded. Scores were assigned as 0 (absent) or 1 (present). Measurements were made at four sites per tooth, and sum total of scores from all surfaces with plaque and bleeding was divided by sum total of all surfaces separately.

Intervention and follow-up

A thorough NSPT (Steps 1 and 2) was performed for all participants in two appointments in two consecutive days using standard Gracey curettes (Hu-Friedy, Chicago, IL, USA) and ultrasonic scalers (Model UDS-E, Guilin Woodpecker Medical Instrument Co., Ltd., Guilin, China). They were instructed to strictly follow the oral hygiene instructions provided. Participants were recalled after 8 weeks. Post-treatment clinical parameters were reassessed. NLR was determined by the same method as described before.

Statistical analysis

The collected data were entered into Microsoft® Excel® 2019 (Version 2403 Build 16.0.17425.20176; 64-bit) and subsequently exported to SPSS software, version 29.0 (IBM Corp., Armonk, NY, USA) for statistical analysis.

The Shapiro–Wilk test was used to assess the distribution of data. Since most of the parameters demonstrated a normal distribution, parametric tests were used for statistical analysis. The level of significance was set at 5% (p value < 0.05) with a 95% confidence interval.

RESULTS

The demographic characteristics of study participants represented in Table 1. The study included a total of 45 participants, of whom 26 (57.8%) were female, and 19 (42.2%) were male. The mean age of the participants was 51.82 ± 4.76 years, with an age range of 44 to 60 years, indicating a predominantly middle-aged study population. The mean body mass index (BMI) was 26.87 ± 1.61 kg/m², indicating that most participants fell within the overweight category. The mean baseline HbA1c level was 6.55 ± 0.29%, reflecting controlled glycemic status among the study participants.

Table 1: Demographic characteristics of study participants

Variables	N	Percent		
Male	19	42.2		
Female	26	57.8		
	N	**Minimum**	**Maximum**	**Mean ±Std. Deviation**
Age	45	44	60	51.82±4.759
BMI (kg/m²)	45	22.9	29.8	26.869±1.612
HbA1c (%)	45	5.9	7.0	6.551± 0.288

Baseline and post treatment neutrophil count, lymphocyte count and NLR represented in table 2. Neutrophil counts showed no statistically significant change following non-surgical periodontal therapy, with mean values of 5726.67 ± 556.12 cells/mm³ at baseline and 5746.67 ± 577.06 cells/mm³ post-treatment (p = 0.807). In contrast, lymphocyte counts demonstrated a statistically significant increase after therapy, rising from a baseline mean of 2944.44 ± 478.90 cells/mm³ to 3211.11 ± 430.76 cells/mm³ at follow-up (p < 0.001). The neutrophil-to-lymphocyte ratio (NLR) showed a significant reduction from 1.98 ± 0.30 at baseline to 1.81 ± 0.25 post-treatment (p = 0.002). This finding may be attributable to a decrease in systemic inflammatory burden following non-surgical periodontal therapy.

Table 2: Comparison of baseline and posttreatment neutrophil count, lymphocyte counts and neutrophil lymphocyte ratio (NLR) in study participants

Parameter	Time point	Mean ±SD	Mean difference	SD difference	T	df	p value
Neutrophil count (cells /mm³)	BL†	5726.67 ±556.12	-20.000	546.726	-0.245	44	0.807*
	PT‡	5746.67 ±577.06					
Lymphocyte count (cells /mm³)	BL†	2944.44 ±478.89	-266.66	384.944	-4.647	44	<0.001*
	PT ‡	3211.11 ±430.76					
NLR§	BL†	1.97756 ±.29840	0.16666	0.3331	3.356	44	0.002*
	PT‡	1.81089 ±.24920					

*p value <0.05 was considered significant (Paired t test *).
†BL, baseline; ‡ PT, pos treatment; §NLR, neutrophil-lymphocyte ratio.

All assessed clinical periodontal parameters showed statistically significant improvement following non-surgical periodontal therapy. (Table 3)

Table 3: Changes in clinical periodontal parameters among study participants before and after non-surgical periodontal therapy

Parameter	Time point	Mean ±SD	Mean difference	SD difference	T	df	p value
FMBS (%)‖	BL†	78.36± 9.028	49.978	7.300	45.924	44	<0.001*
	PT‡	28.38± 7.439					
FMPS (%)**	BL†	78.91± 10.27	51.089	8.265	41.466	44	<0.001*
	PT‡	27.82± 6.833					
PPD (in mm)ᵽ	BL†	4.226± 0.664	0.8800	0.4530	13.029	44	<0.001*
	PT‡	3.346± 0.413					
CAL (in mm)£	BL†	4.280± 0.755	0.6755	0.4853	9.338	44	<0.001*
	PT‡	3.604± 0.588					

*p value <0.05 was considered significant (Paired t test *). †BL, baseline; ‡PT, post-treatment; ‖FMBS, full mouth bleeding score; **FMPS, full mouth plaque score; ᵽPPD, probing pocket depth; £ CAL, clinical attachment level.

Table 4: Baseline neutrophil-lymphocyte ratio and stage of periodontitis.

Stage of periodontitis	n	Mean ± SD	95% Cl of mean	F	P value
Stage I	8	1.751±0.101	1.66 - 1.83	6.538	0.003*
Stage II	22	1.937±0.319	1.79 - 2.07		
Stage III	15	2.157±0.298	2.02 - 2.28		

Statistically significant *p<0.05, ANOVA*

DISCUSSION

The present longitudinal clinical study evaluated change in NLR following NSPT in controlled type 2 diabetic individuals with periodontitis and demonstrated a significant post-treatment reduction in NLR, which probably attributed to reduction in systemic inflammatory burden following NSPT. These findings support the growing body of evidence that periodontitis is not merely a localized inflammatory condition but has profound systemic impact. Systemic inflammation is the key factor that mediates the association between periodontitis and impaired fasting glucose or diabetes.[24] Reduction in systemic inflammatory burden following NSPT can be objectively assessed using readily available hematological indices.

NLR was utilized as the surrogate marker to assess the low grade systemic inflammatory state in the present study. NLR is widely used across medical disciplines as a readily available and reliable marker of immune responses in diverse medical conditions.[25] This novel inflammatory marker was conceptualized based on observations of hemodynamic changes following endotoxemia experiments in healthy human volunteers.[26] Zahorec et al. observed simultaneous neutrophilia and lymphopenia in cancer patients admitted to the intensive care unit, which correlated with the severity of the clinical condition, and termed this phenomenon the neutrophil–lymphocyte stress factor (NLSF).[25] NLR is a highly sensitive indicator of acute critical states of infections, inflammation, and sepsis and post operative complications.[25] An elevated NLR is often associated with chronic conditions such as coronary artery disease, cancer, diabetes, and other low-grade inflammatory states. [25] It is also affected by age, race, stress and medications. [25] An NLR between 1 and 2 is generally considered normal in adults, while values below 0.7 and above 3 indicate pathological states.[25] Owing to its simplicity, low cost, rapid responsiveness, and wide availability, NLR serves as a practical marker of systemic stress and inflammation, with dynamic changes often preceding clinical deterioration, thereby facilitating early risk stratification in acute and critical care settings.

Periodontitis patients consistently demonstrate significantly higher NLR values compared with periodontally healthy individuals. This finding supports the presence of a sustained low-grade systemic inflammatory burden, as confirmed by recent systematic reviews and meta-analyses. [27,28] Moreover elevated NLR is associated with increase in severity of periodontitis. [24] A study conducted by Lu et al. in Chinese population concluded a higher NLR in healthy individuals indicates a greater risk and severity of Generalized Aggressive Periodontitis.[29] Research on these novel biomarker sheds light on the link between periodontitis and systemic alterations and aids in prognostic assessment and disease grading.[28] Mishra.S et al. in their study concluded a cut off value of NLR of 2.5; more than 2.5 predict the severity of periodontitis.[30] In accordance with these findings, the present study demonstrated a significantly elevated baseline NLR across increasing severity of periodontitis. A recent study by Hu et al. likewise reported a significant increase in the neutrophil-to-lymphocyte ratio corresponding to greater severity grades of periodontitis.[31]

In the present study, neutrophil counts did not change significantly following NSPT, probably because of the

inclusion of controlled type 2 diabetes patients with HbA1c levels ≤ 7. This finding possibly reflects a relatively stable innate immune status at baseline in controlled diabetic individuals. Higher NLR values as the stage of periodontitis advances at baseline indicate increase in neutrophils leading to imbalance in the innate immunity. The lymphocyte counts increased significantly post-therapy, resulting in a net reduction in NLR, suggesting partial restoration of immune homeostasis following reduction of periodontal inflammatory burden. Similar to this result, a reduction in NLR following NSPT was reported in previous studies by Acharya et al., and Malik N et al.,.[32,33]

Diabetes mellitus and periodontal disease are interrelated chronic inflammatory conditions with overlapping pathogenic mechanisms. Failure to adequately manage either condition can amplify inflammatory cytokine production, leading to widespread systemic inflammation. Early diagnosis of periodontitis during its active phase is critically important, particularly in high-risk individuals, as it enables timely intervention and helps prevent further periodontal attachment loss. An elevated NLR in diabetic individuals not only reflects increased risk of systemic inflammation but also correlates with poorer glycaemic control. [34,35] NLR is a highly predictive biomarker in individuals with diabetes and periodontitis, demonstrating a clear and consistent association with the severity of periodontal tissue destruction. There are only few studies regarding change in NLR following NSPT in diabetic patients. A study by Mir et al. concluded, NSPT resulted in a significant reduction in neutrophil-to-lymphocyte ratio in chronic periodontitis patients with type 2 diabetes mellitus, indicating a decrease in systemic inflammatory burden.[36] Our study also demonstrated similar results, showing a significant reduction in NLR following NSPT.

The significant improvements observed in full-mouth plaque score, full-mouth bleeding score, probing pocket depth, and clinical attachment level following NSPT in the present study are consistent with established clinical evidence demonstrating the effectiveness of non-surgical periodontal therapy in controlling periodontal inflammation. Reduction in plaque accumulation and gingival bleeding likely contributed to decreased systemic dissemination of periodontal pathogens and inflammatory mediators. Earlier work by D'Aiuto et al. demonstrated that control of periodontal infection is associated with reductions in systemic inflammatory markers, providing mechanistic support for the observed decline in NLR.[37]

Collectively, these findings reinforce the bidirectional relationship between periodontitis and diabetes mellitus and support the use of NLR as a simple, inexpensive adjunctive biomarker for monitoring systemic inflammation and therapeutic response in diabetic patients undergoing periodontal therapy. Personalized periodontal care for patients with diabetes entails an individualized, risk-based framework that incorporates multiple factors; glycaemic control, duration of diabetes, and the patient's inflammatory profile into periodontal diagnosis and treatment planning. Tailoring periodontal therapy and maintenance to a diabetic patient's metabolic status optimizes periodontal outcomes and may modestly improve glycaemic control.

The inclusion of well-controlled diabetic patients, along with the exclusion of smokers and individuals with high body mass index, constitutes a major strength of the study by minimizing potential confounding factors. Standardized periodontal measurements performed by a calibrated single investigator minimized inter-examiner variability, while the use of automated hematological analysis enhanced the accuracy and reliability of the data. The small sample size, short follow-up period, and absence of a control group limit generalizability and long-term interpretation. Assessment was limited to NLR; inclusion of additional inflammatory biomarkers and post-treatment glycaemic parameters would have provided a more comprehensive evaluation.

CONCLUSION

Present study demonstrates NSPT leads to a significant improvement in systemic inflammatory status, as reflected by reductions in NLR. These findings highlight the potential role of periodontal treatment in modulating systemic inflammation in diabetic patients with periodontitis. Further longitudinal studies with larger sample sizes are warranted to confirm these observations and explore their clinical implications

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