

Hematological Parameters In Patients With Inflammatory Mucocutaneous Disorders- A Clinical Retrospective Study

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Abstract-

Background-

The chronic mucocutaneous diseases are systemic autoimmune conditions capable of impacting the oral cavity, often exhibiting oral manifestations as an initial symptom for many patients like the OLP, Pemphigus vulgaris, SLE. The chronic mucocutaneous diseases have a inflammatory component.

Aim-

The study aimed to evaluate and compare the hematological profile of the various mucocutaneous diseases with healthy individuals.

Materials and Methods-

For the study, A total of 150 medical records were included after meeting the inclusion criteria. Out of which 100 were clinically proven various mucocutaneous diseases (Oral Lichen Planus, Lichenoid Reaction and Pemphigus Vulgaris) and 50 were healthy individuals. The Complete laboratory data like the Red blood cells counts ,Hemoglobin ,Total count ,Differential counts like neutrophil count , lymphocyte count of these patients were included . The NLR was calculated from neutrophil and lymphocyte counts . The obtained data was tabulated and Statistical analysis like independent T-test and pearson chi-square test was conducted using IBM SPSS statistics version 23 (IBM Corp., Armonk, NY).

Results-

There is a significant difference between the four groups in the Hb, TC, Differential counts like the neutrophils, and lymphocyte counts ,NLR ($p < 0.05$). There is reduction in the HB% and whereas increase in the neutrophil counts , lymphocyte counts and thereby increase in the NLR ratio. When compared between the OLP and pemphigus groups there was significant difference between the parameters.

Conclusion-

The present study demonstrated a significant difference in Neutrophil-lymphocyte ratio in the mucocutaneous diseases when compared to that of healthy individuals. This NLR can be used as a inflammatory biomarker for chronic diseases and also to assess the prognosis of the disease .

Keywords: Mucocutaneous disorders, Oral lichen planus ,Pemphigus vulgaris, Inflammation, Neutrophil-lymphocyte ratio

INTRODUCTION-

Mucocutaneous diseases are systemic autoimmune conditions capable of impacting the oral cavity, often exhibiting oral manifestations as an initial symptom for many patients. When these conditions induce oral pain or discomfort, individuals typically seek consultation with their primary dentist first. Timely identification and intervention are crucial in preventing systemic advancement. Three examples of such

mucocutaneous diseases that manifest with oral symptoms include Oral Lichen Planus (OLP), Mucous Membrane Pemphigoid (MMP), and Pemphigus Vulgaris (PV). Systemic Lupus Erythematosus (SLE) and Discoid Lupus Erythematosus (DLE).[1]

Lichen planus (LP) was first identified by the British physician Wilson Erasmus in 1869, It is recognized as an autoimmune disorder affecting the skin, hair, eyes, mucous membranes, and nails. Lesions associated with LP on the skin are characterized by a purplish, flat, raised appearance, exhibiting no specific pattern [2]. The condition is termed oral lichen planus (OLP) when these lesions occur within the oral cavity. It is globally prevalent, with rates ranging from 0.2% to 2%. It is more commonly diagnosed in women than in men It has been observed that 53.6% of individuals with cutaneous LP also have OLP [3]. The clinical assessment of oral lichen planus (OLP) involves identifying six forms described by Andreason: reticular, papular, plaque, atrophic, erosive, and bullous[4]. These mucosal lesions typically exhibit a symmetrical pattern, predominantly appearing on the inner cheeks, near molars, and the tongue's surface, and less commonly affecting the lips (lichenous cheilitis) and gums (manifesting as desquamative gingivitis). While the reticular form, marked by thin white lines known as Wickham's striae, is most frequent and usually asymptomatic, the atrophic and erosive types can cause significant discomfort, including a burning sensation and pain [5].

Pemphigus is a rare autoimmune disease that is characterized by blistering of the skin and mucous membranes. The disease occurs due to the production of pathogenic autoantibodies that target desmosomal proteins, resulting in blister and erosion formation. Pemphigus has several forms, with the most common types being pemphigus vulgaris (PV) and pemphigus foliaceus (PF), and less common forms like paraneoplastic pemphigus, pemphigus herpetiformis, and IgA pemphigus. Pemphigus vulgaris occurs at a very low rate, with annual cases ranging between 0.5 and 3.2 per 100,000 individuals. This condition is most frequently diagnosed in individuals in their forties and fifties and affects both genders equally [6]. The disease mechanism predominantly involves the formation of autoantibodies against desmosomal components, implicating both humoral and cellular immunity in its pathogenesis. PV, which makes up about 70% of cases, is the most prevalent and severe form [7]. Lesions often initially manifest in the oral cavity as intraepithelial blisters prone to rupture, resulting in painful erosions in areas frequently exposed to trauma, such as the buccal mucosa, tongue, palate, and lower lip. Many patients seek help due to the oral lesions that lead to intense pain, a burning feeling, difficulty swallowing, and hoarseness of voice [8].

SLE is a chronic autoimmune disease that affects various organs and tissues. Its onset and activity are influenced by genetics, environment, and hormones. The disease's pathogenesis involves several components of both the innate and adaptive immune systems. Morbidity and mortality associated with SLE stem from complications related to the disease and treatments. SLE is more common in females than males [9].

The rationale of this study is to explore the significance of inflammatory hematological biomarkers in the context of mucocutaneous diseases, a relatively under-investigated area compared to their application in oral cancer prognosis where RBC hematological markers are used to assess the prognostic outcome [10]. By utilizing standard complete blood counts to analyze biomarkers such as the RBC, Hb, TC, Neutrophils, Lymphocytes, and neutrophil-to-lymphocyte ratio (NLR). These indices provide a window into the complex interactions within the immune system's inflammatory response, potentially revealing novel insights into disease mechanisms and effective diagnostic and therapeutic strategies. The study aims to evaluate and compare the hematological profile of the various mucocutaneous diseases with healthy individuals.

MATERIALS AND METHODS-

The current study is a retrospective, unicenter, non-interventional hematological chart review of medical records carried out at the Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Chennai from the period June 2019- Feb 2024. The Institutional Human Ethical Committee of Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India, issued approval.

A total of 2000 medical records were reviewed by 2 authors out of which 150 medical records were included after meeting the inclusion criteria. Out of which 100 were with various mucocutaneous diseases (OLP, LR, Pemphigus Vulgaris) and 50 were healthy individuals.

Participants aged between 20 and 70 years old, diagnosed clinically and histopathologically with oral lichen planus, and oral pemphigus vulgaris with Complete laboratory data were included whereas patients without any mucosal lesions, patients with cardiovascular disease, gastrointestinal issues, renal disorders, malignancies, pregnancy, diabetes mellitus (DM), autoimmune disorders, infectious diseases, and other inflammatory conditions, as well as those who had received treatment for oral lichen planus, pemphigus and SLE were excluded from the study.

The included participants' data was divided into two groups. The mucocutaneous diseases were divided into 3 groups like Group I- OLP, Group II- Lichenoid reaction, Group III- Pemphigus , and Group IV in healthy individuals.

The data evaluated from the patient's medical records are age, gender, clinical course, treatment, and laboratory data like complete blood counts (Hb, RBC, TC, Neutrophils, Lymphocytes, and Neutrophil to Lymphocyte Ratio (NLR). The analysis of complete blood counts was performed using a UniCel® DxH 800 analyzer. The Neutrophil to Lymphocyte Ratio (NLR) was determined by dividing the neutrophil count by the lymphocyte count using MD CALC

The obtained data was tabulated and Statistical analysis was conducted using IBM SPSS statistics version 23 (IBM Corp., Armonk, NY). The Independent T-test and pearson chi-square test, mean values and standard deviations were calculated for each group. A probability value (p) of 0.05 or less indicated statistical significance.

RESULTS

The collected data were entered in Microsoft Excel 2016 and analyzed with IBM SPSS Statistics for Windows, Version 29.0. (Armonk, NY: IBM Corp). To describe the data descriptive statistics frequency analysis, and percentage analysis were used for categorical variables and the mean & SD were used for continuous variables. To find the significant difference between the bivariate samples in independent groups the independent sample t-test was used. To find the significance in qualitative categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the statistical tools, the probability value of .05 is considered a significant level.

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Age	Equal variances not assumed	10.229	.002	8.217	142	.0005	12.9700	1.5785	9.8496	16.0904
HB %	Equal variances	.809	.370	-2.016	148	.046	-.6230	.3090	-1.2336	-.0124

	assumed									
RBC	Equal variances not assumed	4.317	.039	1.300	86	.197	.1210	.0931	-.0641	.3061
TC	Equal variances not assumed	10.374	.002	2.831	142	.005	992.4800	350.5917	299.4307	1685.5293
DCN	Equal variances not assumed	10.774	.001	6.497	137	.0005	8.2900	1.2759	5.7669	10.8131
DC L	Equal variances assumed	.243	.623	-6.370	148	.0005	-9.9400	1.5605	-13.0238	-6.8562

Table 1 - Independent T test to assess the different hematological parameters between the groups

The parameters taken for evaluation are hemoglobin [Hb %], Red blood cell count [RBC], Total count [TC], and Differential counts [DC] like neutrophils, lymphocytes, and Neutrophil- lymphocyte ratio [NLR].

Table 1 shows the different hematological parameters between the 4 groups there was a significant statistical difference in the Hb, TC, Differential counts like the neutrophils, and lymphocyte counts whereas there was no statistical significance in the RBC values in the four groups.

Table 2 - Neutrophil- Lymphocyte ratio among the four groups

Crosstab

			Groups		Total
			Cases	Controls	
N/L ratio 1	Count	17	33	50	
	%	17.0%	66.0%	33.3%	
2	Count	44	17	61	
	%	44.0%	34.0%	40.7%	
3	Count	19	0	19	
	%	19.0%	0.0%	12.7%	
4	Count	20	0	20	
	%	2.0%	0.0%	13.3%	
Total		Count	100	50	150

%	100.0%	100.0%	100.0%
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Chi-Square Tests

	Value	df	p-value
Pearson Chi-Square	44.330 ^a	4	.0005

Table 2 shows the NLR (Neutrophil-Lymphocyte ratio) crosstabs were conducted to explore the distribution of the NLR across different groups. The Chi-Square test is then applied to assess whether there is a statistically significant association between the NLR and the group categories. Specifically, it determines whether the observed distribution in the crosstab is due to chance or if there is an actual association between the groups and the NLR. The chi-square test showed a p value of 0.0005 which is highly statistically signifi

Table 3- Neutrophil- Lymphocyte ratio between the OLP and Pemphigus groups

Crosstab

			Groups		Total
			OLP	Pemphigus	
N/L ratio 1	Count	13	4	17	
	%	20.3%	16.7%	19.3%	
2	Count	36	3	39	
	%	56.3%	12.5%	44.3%	
3	Count	13	6	19	
	%	20.3%	25.0%	21.6%	
4	Count	2	11	13	
	%	3.1%	45.8%	14.8%	
Total	Count	64	24	88	
	%	100.0%	100.0%	100.0%	

Chi-Square Tests

	Value	df	p-value
Pearson Chi-Square	29.387 ^a	3	.0005

Table 3 shows the NLR crosstabs across the OLP and Pemphigus groups followed by chi-square test to evaluate the statistical significance between the two groups . The p value is .0005 which is highly statistically significant

DISCUSSION-

Out of the total 150 participants, 62.7% were female and 37.3% were male. Among the four groups, the highest cases were observed in individuals with pemphigus and Oral Lichen Planus (OLP). In the OLP group,

68.8% were female and 31.3% were male, coinciding with Varghese et al study [11]. In the pemphigus group, 87.5% were female and 12.5% were male which coincides with Suliman et al [12]. This indicates a noticeable predominance of females in both conditions, particularly in pemphigus, where the gender disparity is more pronounced.

In our study, we found a significant difference in the hemoglobin levels (Hb %) between the case groups and the control group. Patients with OLP, LR, pemphigus, and SLE showed a reduction in Hb% compared to healthy individuals, which is consistent with the findings of the study by Chen et al.[13].

Neutrophils and lymphocytes are essential blood cells that play a pivotal in the body's inflammatory response. Neutrophils serve as the first line of defense in systemic inflammation, while lymphocytes regulate and protect during the inflammatory process. The neutrophil-to-lymphocyte (NLR) ratio is a simple and affordable marker of systemic inflammation and has been found to correlate with prognosis in several conditions, such as acute coronary syndrome, acute pancreatitis, and ulcerative colitis. It is widely regarded as a key indicator of systemic inflammation and is associated with various chronic diseases [14,15].

A previous study by Ataş H et al [16] evaluated the N/L ratio in patients with lichen planus compared to a control group, finding a statistically significant difference. The results of our current study are consistent with those findings.

According to a study conducted by Sun et al [18], on bullous pemphigoid patients the associations between hematological inflammatory biomarkers like the NLR, platelet-neutrophil ratio (PNR), PLR, and disease activity were assessed and the findings revealed a positive correlation between NLR and disease activity. Our study, which also observed elevated NLR levels in pemphigus patients, aligns with these results.

The Oral Lichen Planus (OLP) and Pemphigus Vulgaris (PV) groups showed statistically significant differences among the four groups studied. Specifically, the Pemphigus Vulgaris group exhibited higher differential counts, such as increased neutrophil and lymphocyte counts, as well as a higher Neutrophil-to-Lymphocyte Ratio (NLR) compared to the Oral Lichen Planus group. However, other parameters did not show statistically significant differences between these two groups.

The limitations of the study are it is a clinical retrospective study with a small sample size from a single center and the blood profiling is done for the patients before the start of treatment. Future research should focus on aiming for a larger sample size and multicentered prospective studies, and randomized controlled trials to assess the association between disease progression and the NLR.

CONCLUSION-

This study revealed statistically significant differences in hematological inflammatory parameters when compared to healthy controls like the neutrophil count, lymphocyte count, and NLR values. NLR is considered a valuable and cost-effective tool for evaluating disease activity. The findings indicate a positive correlation, suggesting that mucocutaneous diseases involve an inflammatory component. Future research should aim to conduct prospective studies with larger sample sizes and evaluate hematological parameters throughout the course of treatment to better assess prognosis.

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