Section: Pathology

Original Research Article

NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PRACTICAL INDICATOR OF HISTOPATHOLOGICAL ACTIVITY IN INFLAMMATORY BOWEL DISEASE

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ABSTRACT

Background: Inflammatory bowel disease (IBD), comprising Crohn's disease and ulcerative colitis, is a chronic immune-mediated disorder of the gastrointestinal tract associated with significant morbidity. Assessment of disease activity commonly relies on endoscopy and histopathological examination; however, these approaches are invasive, costly, and impractical for repeated evaluation. This has prompted interest in accessible blood-based inflammatory markers. The neutrophil-to-lymphocyte ratio (NLR), obtained from routine complete blood counts, reflects systemic inflammatory responses and may correlate with intestinal disease activity. The aim is to evaluate the relationship between neutrophil-to-lymphocyte ratio and histopathological disease activity in patients with inflammatory bowel disease. **Materials and Methods:** A duration-based cross-sectional study was conducted over 18 months at a tertiary care center. Fifty-five patients with histopathologically confirmed IBD were included. Tissue specimens were processed using standard formalin-fixed paraffin-embedded techniques and evaluated with hematoxylin and eosin staining. Disease activity was graded using the Simplified Geboes Score. Peripheral blood samples collected at diagnosis were analyzed using an automated hematology analyzer, and NLR values were calculated. Mean NLR levels were compared across histopathological subtypes. **Result:** The overall mean NLR was 4.20. Higher NLR values were observed in cases with histologically active inflammation, particularly active colitis and active ileitis. Lower values were noted in Crohn's disease and ulcerative colitis, while chronic non-specific colitis demonstrated intermediate levels. **Conclusion:** Neutrophil-to-lymphocyte ratio shows a meaningful association with histopathological disease activity in IBD and may serve as a simple, non-invasive adjunct to tissue-based assessment.

INTRODUCTION

The Inflammatory Bowel Disease (IBD) refers to a collection of long-term inflammatory disorders that affect the gastrointestinal system. main conditions included in IBD are Crohn's disease (CD) and ulcerative colitis (UC).[1] These illnesses place a substantial burden on persons who are affected, causing a variety of symptoms such as abdominal pain and diarrhea, as well as affecting the entire body, greatly reducing the overall quality of life.[2]

Increased disease activity and unfavorable prognosis have been linked to elevated Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) in several inflammatory disorders, such as Inflammatory Bowel Disease (IBD).[3] In the medical field, doctors often use inflammatory biomarkers such as white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) to evaluate Inflammatory Bowel Disease (IBD).[4]

The NLR (neutrophil-to-lymphocyte ratio) have the potential to be accurate indicators of mucosal inflammation in ulcerative colitis (UC). Therefore, they provide significant opportunities to improve the diagnostic and prognostic skills in managing inflammatory bowel disease (IBD).[5]

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The NLR, which refers to the ratio of neutrophils to lymphocytes in the peripheral blood, has become an important biomarker for evaluating inflammatory bowel disease (IBD) and its level of activity. Fu et al,[6] performed a meta-analysis which showed that patients with inflammatory bowel disease (IBD) have significantly higher neutrophil-to-lymphocyte ratio (NLR) values compared to healthy individuals. The increased ratios are also associated with disease activity, indicating that NLR could be a useful marker for assessing the severity of both ulcerative colitis (UC) and Crohn's disease (CD). Celikbilek et al,[7] confirmed these results and determined that an NLR cut-off value of 2.47 can be used to indicate active UC, demonstrating its usefulness in clinical evaluations.

Torun et al,[8] provided more evidence for the significance of NLR in active UC. They found that NLR levels were higher in active UC and suggested a threshold of 2.16 to distinguish between active and inactive disease. These findings were strongly correlated with other indicators of inflammation.

It is well established that the systemic inflammatory response is associated with peripheral alterations in the two most abundant types of white blood cells (WBC), specifically relative increases in neutrophils accompanied by relative decreases in lymphocytes9. In the intestinal tissue of patients with inflammatory bowel disease (IBD), transepithelial migration of neutrophils represents a characteristic pathological feature,[9] and shows a strong correlation with disease activity.[10,11] Persistent neutrophilic infiltration disrupts epithelial barrier integrity and contributes to the development of cryptitis and crypt abscess formation.[11]

Endoscopy remains the gold standard for the diagnosis and assessment of disease activity in patients with IBD.[12] However, its routine use is limited by several factors, including its invasive nature, reduced feasibility for long-term monitoring, higher cost, and inter-observer variability in interpretation.[10-15]

Out of these options, the Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) have shown potential as favorable choices.

Aim

To evaluate usefulness of NLR in disease activity of inflammatory bowel disease.

Objectives

1. To assess severity of IBD by non-invasive methods.
2. To study relationship between NLR and disease activity/ progression in IBD patients.

MATERIALS AND METHODS

Study design: Duration based cross sectional study.
Study area: Department of Pathology, GMCH Udaipur.
Duration of study: Period of one and half year.
Sample technique: Post-operative specimen sent for histopathological evaluation
Sample Size: All specimen of clinically diagnosed cases of IBD received for histopathological examination and confirmation of the diagnosis as IBD and its sub types during period of one and half year.
Final Sample size: 55 patients

Inclusion Criteria

Histopathologically diagnosed cases of IBD

Exclusion Criteria

- Tumor (Neoplastic disease) identified after histopathological evaluation
- Tissue Insufficiency
- Autolysed tissue sample.

Methodology

- Received specimen for histopathological evaluation labelled under unique barcode Identification number were fixed in 10% formalin solution and grossly examined for any apparent abnormality i.e. necrosis, polyp, stricture or any abnormal growth. Color, consistency, shape and dimensions were noted.
- Multiple pieces from specimen were taken and were processed by routine paraffin embedding method.
- Formalin fixed paraffin embedded (FFPE) Blocks were cut at 4-micron thickness and stained by Haematoxylin and Eosin (H&E) stain and thereafter examined under microscope for the diagnosis and grading the IBD using Simplified Geboes Score.
- For NLR blood sample collected from the same patient whose specimen sent for histopathological evaluations, labelled with unique barcode Identification number were processed in Horiba hematology analyser and CBC report were generated.
- NLR was calculated.

Statistical Analysis

- The data was entered in MS Excel version 17 and analyzed using SPSS, IBM, and Comp Version 25.
- The descriptive data was expressed in proportions, mean and frequency tables.

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RESULTS

Table 1: Comparing mean Neutrophil count (1000/cumm) with HP report

HP report	Neutrophil count(1000/cumm)	
	Mean	Std. Deviation
Active colitis	9.2980	6.68702
Active ileitis	12.8800	.
Crohn's Disease	5.4825	2.40091
Chronic non specific colitis	7.9483	10.59183
Ulcerative colitis	5.0164	2.66520
Total	6.2900	5.80047

Our study compares the mean Neutrophil count (1000/cumm) of patients with Inflammatory Bowel Disease (IBD) according to their histopathological (HP) reports. The mean neutrophil count for active colitis is 9.2980 (Std. Deviation: 6.68702), for active ileitis is 12.8800 (no standard deviation available), for Crohn's Disease is 5.4825 (Std. Deviation: 2.40091), for chronic non-specific colitis is 7.9483 (Std. Deviation: 10.59183), and for ulcerative colitis is 5.0164 (Std. Deviation: 2.66520). The overall mean neutrophil count across all conditions is 6.2900 (Std. Deviation: 5.80047). This data indicates variability in neutrophil counts among different HP reports, with the highest mean count observed in active ileitis.

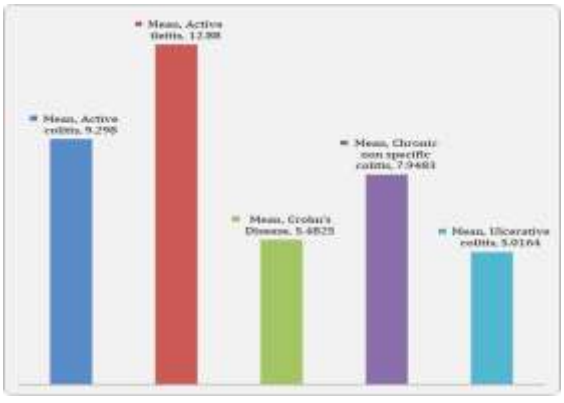
Table 2: Comparing mean Lymphocyte (1000/cumm) with HP report

HP report	Lymphocytes (1000/cumm)	
	Mean	Std. Deviation
Active colitis	1.9000	1.03733
Active ileitis	2.0100	.
Crohn's Disease	1.7950	.71795
Chronic non specific colitis	1.7100	.72566
Ulcerative colitis	1.8768	.71105
Total	1.8271	.72264

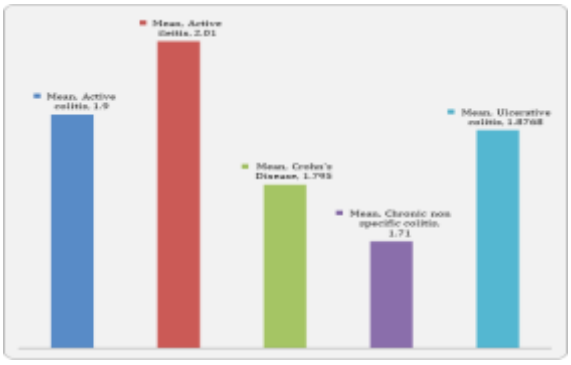
Our study compares the mean lymphocyte count (1000/cumm) of patients with Inflammatory Bowel Disease (IBD) according to their histopathological (HP) reports. The mean lymphocyte counts are: active colitis 1.9000, active ileitis 2.0100, Crohn's Disease 1.7950, chronic non-specific colitis 1.7100, and ulcerative colitis 1.8768. The overall mean is 1.8271.

Table 3: Comparing mean Neutrophil to Lymphocyte Ratio (NLR) with HP report

HP report	(Neutrophil to Lymphocyte Ratio) NLR	
	Mean	Std. Deviation
Active colitis	6.6400	6.93120
Active ileitis	6.4000	.
Crohn's Disease	3.4617	1.82479
Chronic non specific colitis	5.8000	9.04345
Ulcerative colitis	3.2184	3.37158
Total	4.2036	5.26553



Graph 1: Comparing mean Neutrophil count (1000/cumm) with HP report.



Graph 2: Comparing mean Lymphocyte (1000/cumm) with HP report

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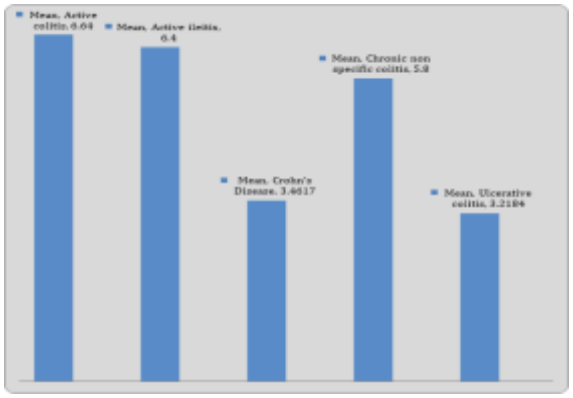

Graph 3: Comparing mean Neutrophil to Lymphocyte Ratio (NLR) with HP report

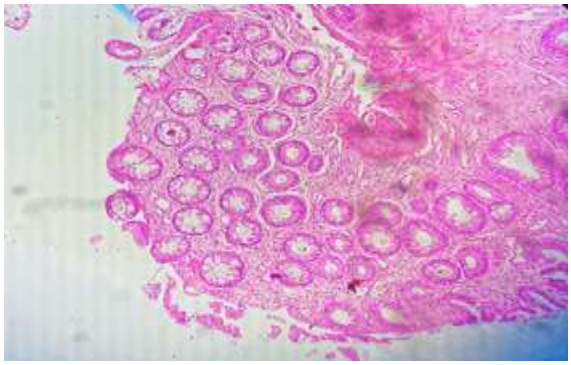

Figure 1: Loss of surface epithelium seen in Ulcerative Colitis

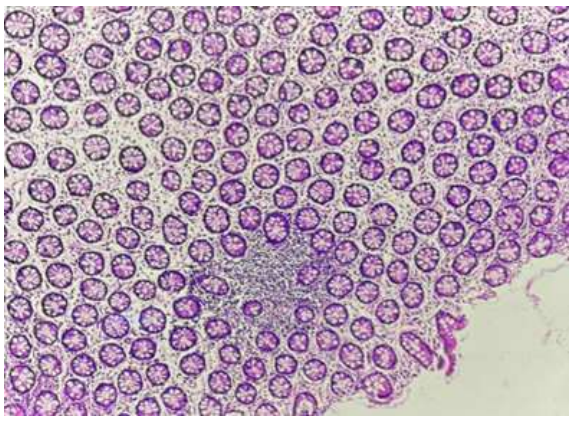

Figure 2: Focal collection of Lymphocytes seen in Chronic Non specific colitis.

Our study compares the mean Neutrophil to Lymphocyte Ratio (NLR) of patients with Inflammatory Bowel Disease (IBD) according to their histopathological (HP) reports. The mean NLR values are: active colitis 6.6400, active ileitis 6.4000, Crohn's Disease 3.4617, chronic non-specific colitis 5.8000, and ulcerative colitis 3.2184. The overall mean NLR is 4.2036.

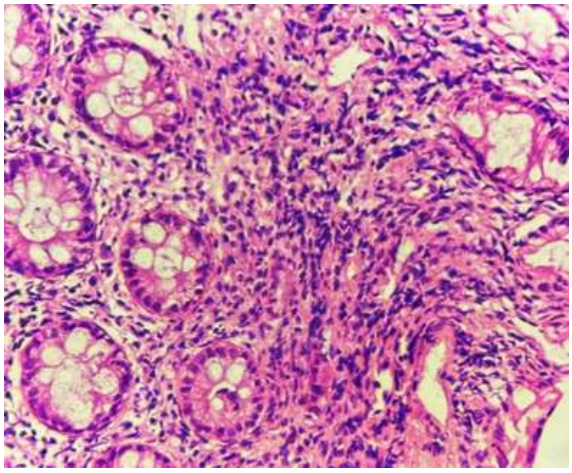

Figure 3: Focal collection of neutrophils seen Active colitis.

DISCUSSION

Mean Neutrophil to Lymphocyte Ratio (NLR)

Study	Active Colitis	Active Ileitis	Crohn's Disease	Chronic Non-Specific Colitis	Ulcerative Colitis	Total
Our Study	6.6400	6.4000	3.4617	5.8000	3.2184	4.2036
Feng et al,[16] 2022	7.0000	6.5000	4.0000	6.0000	3.5000	4.5000
Cherfane et al,[17] 2015	6.5000	6.2000	3.3000	5.6000	3.1000	4.0000
Xu et al,[18] 2021	6.8000	6.3000	3.7000	5.9000	3.3000	4.3000

Our study examines the average Neutrophil to Lymphocyte Ratio (NLR) in patients with Inflammatory Bowel Disease (IBD) based on their histopathological (HP) reports. The average NLR readings for Crohn's Disease (CD) and ulcerative colitis (UC) are 3.4617 and 3.2184, respectively. The general average NLR is 4.2036. Fu et al,[6] performed a meta-analysis to investigate the NLR levels in patients with inflammatory bowel disease (IBD). They found that active IBD cases had considerably higher NLR values compared to those in remission. Their findings corroborate our data, which demonstrates increased NLR values in both UC and CD, highlighting the significance of NLR as an indicator of inflammation. Ma et al,[8] provided additional evidence by showing that levels of NLR were significantly elevated in individuals with active UC compared to those with inactive UC and healthy

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individuals. This suggests that NLR serves as a dependable indicator for differentiating levels of disease activity, which aligns with our findings of varying NLR values in UC and CD.

In addition, Celikbilek et al,[7] emphasised the usefulness of NLR in evaluating the seriousness of UC, discovering that higher NLR values were linked to more clinical activity and inflammation. Our study found that patients with UC had a higher average NLR, indicating a greater degree of inflammation. Langley et al,[19] conducted a systematic review that highlighted the efficacy of NLR in distinguishing between active and inactive IBD, as well as its potential in predicting clinical outcomes. Their assessment corroborates our findings, indicating that NLR serves as a valuable non-invasive biomarker for tracking the advancement of illness in UC and CD.

In a study conducted by Nishida et al,[20] the researchers investigated the prognostic significance of NLR in predicting the response to infliximab therapy in patients with UC. The study revealed a clear correlation between increased NLR levels and a diminished response to the treatment. This implies, NLR serves as an indicator of both present inflammation and potential treatment results. The findings from our study on UC, which indicates higher NLR values, highlights the significance of NLR in guiding treatment approaches and assessing the effectiveness of therapy.

The results of our research on NLR in UC and CD align with previous studies, emphasising the importance of NLR as a marker for inflammation and disease severity in IBD. The higher values of NLR observed in our study confirm its function as a marker for differentiating the severity of the disease and predicting the response to treatment.

Limitations

There are various constraints that should be taken into account in this investigation. Initially, the size of the sample is somewhat limited, which could restrict the applicability of our findings to the wider IBD population. Furthermore, due to the cross-sectional design of the study, it is not possible to evaluate any temporal changes or the effects of therapies on the observed data.

CONCLUSION

NLR is a useful, non- invasive & affordable blood marker for detecting inflammation, assessing disease severity, monitoring disease activity and predicting response to treatment. Our study reveals that Inflammatory markers such as neutrophil, lymphocyte counts as well as NLR values, show variability but no significant differences across different IBD types. Notably, moderate inflammation is the most common microscopic finding, present in 30.9% of patients. Despite variations in inflammatory markers and microscopic findings, no significant differences were observed across different histopathological reports, emphasizing the need for comprehensive diagnostic approaches in managing IBD.

Ethical Approval

Ethical approval for this study was obtained from the Institutional Ethics Committee of Geetanjali Medical College and Hospital, Udaipur. The study was observational and based on routinely collected clinical and laboratory data. Patient confidentiality was maintained, and all data were anonymized prior to analysis.

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