Role of Neutrophil Lymphocyte Ratio in Prediction of Disease Activity in Ulcerative Colitis Disease

Ahmed El-Sayed Taha[1], Dina Fathy AbdElsayed Mohamed[1], Menna-t-Allah Gamal Saad El Dine[2], Fady Fadl Zaki Rizk[1], Ahmed Bahaa Eldin Abbas[3], Mennatallah Ali Rashwan[3], Tamer Mahmoud ElTantawy ELbaz[1], Mohamed Ibrahim Negm[3]

[1]*Endemic medicine department, Faculty of medicine, Cairo university, Cairo, Egypt.*
[2]*Pathology department, Faculty of Medicine, Cairo University.*
[3]*Integrated clinical and research center for intestinal disorders (ICRID), Faculty of Medicine, Cairo University.*

Corresponding Author
Ahmed El-Sayed Taha El-Sayed
ORCID 0000-0003-1597-8303

Mobile: +201002928158
Email: a.tahaa85@cu.edu.eg

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Background and study aim: None of Serum biomarkers that are utilized for diagnosis and evaluating ulcerative colitis (UC) disease activity is specialized for intestinal inflammation. Thus, it is preferable to have access to simple, low-cost techniques for evaluating disease activity. Aim of the study is to examine whether neutrophil lymphocyte ratio (NLR) levels are changed in UC patients and to know its potential as a simple, affordable, and accessible predictor of ulcerative colitis patients' disease activity.

Patients and Methods: This cross-sectional analytic study involved 62 UC patients and 31 volunteers as a control group. All degrees of disease activity and severity were included. Physician global assessment as well as patient's overall Mayo Score. Colonoscopy with a confirmation biopsy and Mayo endoscopic score was calculated. NLR, serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cell count (WBC), and Fecal calprotectin (FC) were measured in all subjects.

Results: NLR was significantly higher in active patients (4.3±2.4) compared to inactive patients (1.7±1.1) and control group (1.8±0.7) with P-value of <0.001. NLR threshold of greater than 2.1 is indicative of active UC with AUC of 0.878. NLR is higher in patients with higher endoscopic activity with median value of 1.4, 2.6, 4.1 in mayo endoscopic scores 1, 2, 3 respectively. NLR was positively correlated with platelets, CRP and FC among all the study subjects, P-values were 0.004, <0.001 and 0.04 respectively.

Conclusion: NLR is strongly correlated with disease activity in patients having UC, and it is more accessible and affordable than many other non-invasive indicators.

INTRODUCTION

One of the two incapacitating, recurrent types of inflammatory bowel disease (IBD) that has no definite treatment is ulcerative colitis (UC). The prevalence of UC is rising quickly on a global scale. UC is an immune-mediated disease which causes chronic colonic inflammation and substantially bloody diarrhea, frequent bowel movements, and tenesmus. Multifactorial immunological, genetic, environmental, and microbial components all participate in the etiology of ulcerative colitis [1]. While endoscopy accompanied with pathological biopsy is an effective method. Evaluating UC, its invasiveness, expense, and the problems that come with intrusive surgery restrict its application and make it difficult to use for continuous monitoring [2]**.** Immunosuppressants like thiopurines, cyclosporin as well as tumor necrosis factor (TNF) antagonists like vedolizumab, ustekinumab, as well as Janus kinase (JAK) inhibitors like tofacitinib are all used for moderate to severe active UC.

There are currently new therapeutic goals for IBD as clinical remission that lasts longer, reduced hospitalization duration, the avoidance of surgical intervention, and repair of the mucosa or prevention of disease development [3]. Among individuals with severe UC, endoscopic evaluation of

mucosal activity may be unnecessary due to its high cost, inconvenience, and risk of infection.

White blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are noninvasive mediators of IBD utilized in the clinical setting. However, due to their lack of specificity, the biomarkers now utilized to evaluate mucosal activity in IBD have not been found. As a result, the identification of biomarkers that can serve as substitutes for endoscopy in evaluating mucosal disease activity represents an unmet clinical need [4].

Circulating white blood cell (WBC) counts are known to change in response to systemic inflammatory diseases like UC. In response to systemic inflammation, circulating neutrophil numbers rise while lymphocyte numbers fall, as is widely recognized. It has been suggested to use the neutrophil lymphocyte ratio (NLR) as a useful biomarker for systemic inflammatory responses, and there is currently growing evidence to support this idea [5].

Cancer patients, especially those with colorectal, biliary system, bladder, and breast cancer, may also use NLR as a predictor of mortality [6]. The NLR is a simple biomarker that is inexpensive and widely available. Many studies indicate that NLR may be a valuable new measure of UC disease severity [7].

PATIENTS/MATERIALS AND METHODS

This cross-sectional analytical study comprised 62 UC patients. They were recruited in a time frame from April 2022 to February 2023 from the following sites: Endemic Medicine Department, Faculty of Medicine, Cairo University, Integrated Clinical and Research Center for Intestinal Disorders (ICRID), Cairo university and Gastrointestinal Endoscopy and Liver Unit Kasr Alainy University Hospital (GIELUKA). Another 31 apparently healthy sex as well as age matched volunteers were asked to join as a control group in the research. Written consent was obtained from each patient involved in our research.

Patients aged greater than 18 years of both genders with UC confirmed by histopathology of colonic biopsies taken during colonoscopy procedures were a part of the research. All degrees of disease activity and severity were included.

Patients younger than 18 years, pregnant females, patients with other autoimmune diseases, patients with neoplastic disorder and patients receiving chemotherapy or immunosuppressive therapy were excluded from the research.

Following the Cairo University Hospitals' approval by the Institutional Review Board with a code of MS-279-2022, the study subjects were distributed to three groups: Group (1): Thirty-one healthy volunteers as a control group, group (2): Thirty-one UC patients in remission, Mayo score less than 3 and group (3): Thirty-one UC patients in active condition, Mayo score more than 3.

Activity of UC was calculated according to Mayo score. The Mayo Score evaluates the severity of UC using both endoscopic and clinical factors. This score has been employed in several clinical trials and practices since it was first suggested for use by Schroeder et al., in a study for UC treatment by 5-ASA medications. A patient's overall Mayo Score, which can vary from 0 to 12, is influenced by a number of factors, such as frequent stools, bleeding per rectum, abnormalities found during a flexible proctosigmoidoscopy or colonoscopy and physician global assessment [8].

Mayo score less than 3 indicates clinical remission. A score of 0 is assigned to normal mucosa or inactive UC. on the endoscopic portion of the Mayo Score, whereas mild disease characterized by mild friability, diminished vascular pattern, as well as mucosal erythema receives a score of 1. A score of 2 shows a mild disease with mild degree of friability and erosions but no ulceration or spontaneous bleeding; a score of 3 implies ulceration as well as spontaneous bleeding [9].

All the participants were subjected to comprehensive history taking concerning age, residency, occupation, history of pregnancy as well as lactation, special habits, family history of UC, associated medical or surgical conditions, history of drug intake, presence of diarrhea, stool frequency, blood in stools, abdominal pain, weight loss, fever, bleeding per rectum, urgency, extra intestinal manifestations e.g. ophthalmological symptoms, rheumatological symptoms and dermatological symptoms. Complete general and abdominal examination

were done. CBC was done for every participant in the study: Haemoglobin, platelets, total leucocytic count, neutrophil count, lymphocyte count. Inflammatory markers were done for patients having UC: CRP, ESR, and albumin. The NLR was calculated by dividing the total neutrophil count by the total lymphocyte count [10].

Colonoscopy was done for patients having UC at Gastrointestinal Endoscopy and Liver Unit Kasr Alainy University Hospital (GIELUKA), Cairo University and Integrated Clinical and Research Center for Intestinal Disorders (ICRID), Cairo University. According to the Montreal classification of IBD, ulcerative proctitis (E1), left-sided UC (E2), as well as severe UC (E3) were determined by the extent of colitis during the initial colonoscopy [11]. Colonoscopic biopsies were taken and sent for histopathology.

Statistical analysis

Upon entering the data onto a computer, statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) version 27. The Fisher Exact Test or Chi Square Test were used to compare categorical data as necessary.The terms mean and standard deviation, or median and range, were used to characterize numerical data. Numerical and percentage data were defined as categorical data. The Shapiro-Wilk and Kolmogrov-Smirnov tests were used to examine the normality of the data. The independent t test and the Mann-Whitney test were used to compare numerical variables between the two groups when they weren't regularly distributed. Spearman's correlation tests were employed. A statistically significant p-value was defined as one that was less than 0.05. All tests were two tailed.

ROC curve was created to enable the comparison of various testing approaches and the determination of threshold values for test findings. A larger area under a ROC curve (AUC) is indicated by a greater area under the ROC curve (AUC), where 1 denotes 100% sensitivity and specificity and 0.5 denotes no discriminatory usefulness. If both false-positive and false-negative test results are equally unacceptable, the cutoff level for an abnormal test result that results in the point nearest the upper left corner of the ROC curve is ideal. The following were the requirements to meet in order to be eligible for AUC: 0.90 – 1 = excellent; 0.80 – 0.90 = good; 0.70-0.80 = fair; 0.60-0.70 = poor; and 0.50-0.6 = fail. At the point of maximum accuracy, the optimal cutoff point was determined.

RESULTS

In the current study, variations across the three groups with respect to demographic and clinical criteria were found not significant as shown in (Table 1).

Active UC patients had significantly lower haemoglobin level and lymphocyte count in contrast to the control group (p-value: 0.017) and the inactive patients (p-value: <0.001). Also, they had significantly higher serum WBC, platelet count and NLR compared to the control group and inactive patients with P- value of <0.001 as shown in (Table 1).

In comparison between patients having active UC and those having inactive UC, diarrhea, abdominal pain and blood with stools were discovered to be higher in active UC group with statistically significant difference (P-value of <0.001). However, other clinical, intestinal and extraintestinal manifestations were not significant between these two groups (Table 2).

Regarding clinical signs, when the two groups of UC were compared, the mean pulse and mean temperature were higher significantly in active UC group, while the mean systolic blood pressure was lower significantly in active UC group with different P-values as shown in (Table 2).

During colonoscopic examination, extent of the disease was not associated with significant P-value between active and inactive UC groups. About half of inactive UC patients had mayo endoscopic score 1 while only 2 patients of active UC group had mayo endoscopic score 1 that was statistically significant (P-value <0.001) as shown in (Table 2). In active UC patients, the mean CRP, mean ESR were statistically significant greater than in inactive UC, mean serum albumin was statistically significant lower than in inactive UC. The median FC was greater than in those with inactive UC as shown in (Table 2). At the time of the study no significance was detected between active and inactive UC groups regarding the type of treatment, as shown in (Table 2).

The mean of NLR was higher with higher Mayo score with no significant difference in active UC group as shown in (Table 3).

NLR wasn't statistically different according to the extent of disease in both UC groups as shown in (Table 3). NLR was greater in patients with higher endoscopic activity during colonoscopy that was statistically significant. The median of NLR is 1.4, 2.6, 4.1 in mayo endoscopic scores 1, 2, 3 respectively as shown in (Table 3) and this gave a good relationship between NLR and Mayo endoscopic score.

NLR showed varying p-values of negative correlation with albumin and hemoglobin in all cases. Platelets, CRP, and FC showed varying p-values of positive correlations with NLR. NLR and ESR didn't correlate. For active UC patients, NLR was correlated negatively with hemoglobin, albumin and FC with statistically insignificant P values, NLR was correlated positively with platelets, CRP and ESR, with statistically insignificant p-values. For inactive UC patients, NLR was positively correlated with hemoglobin, platelets, CRP and albumin with statistically insignificant P-values, NLR was negatively correlated with ESR with statistically insignificant P-values as shown in (Table 4).

Results of an examination of receiver operating characteristic curves, which established a NLR threshold of greater than 2.1 for active UC with AUC of 0.878, sensitivity of 90.3%, specificity of 78.1%, positive predictive value of 80%, as well as negative predictive value of 89.3% are shown in Figure (1A).

Analysis of receiver operating characteristic curves showed that a CRP value greater than 12 indicated active UC, with cut-off point curve (AUC) of 0.841 and a sensitivity of 74.2%. and specificity 90.6% as shown in Figure (1B).

The receiver operating characteristic curve analysis established a cut off of ESR greater than 41 for active UC, with an AUC of 0.686, sensitivity of 58.6%, and specificity of 77.4% as shown in Figure (1C).

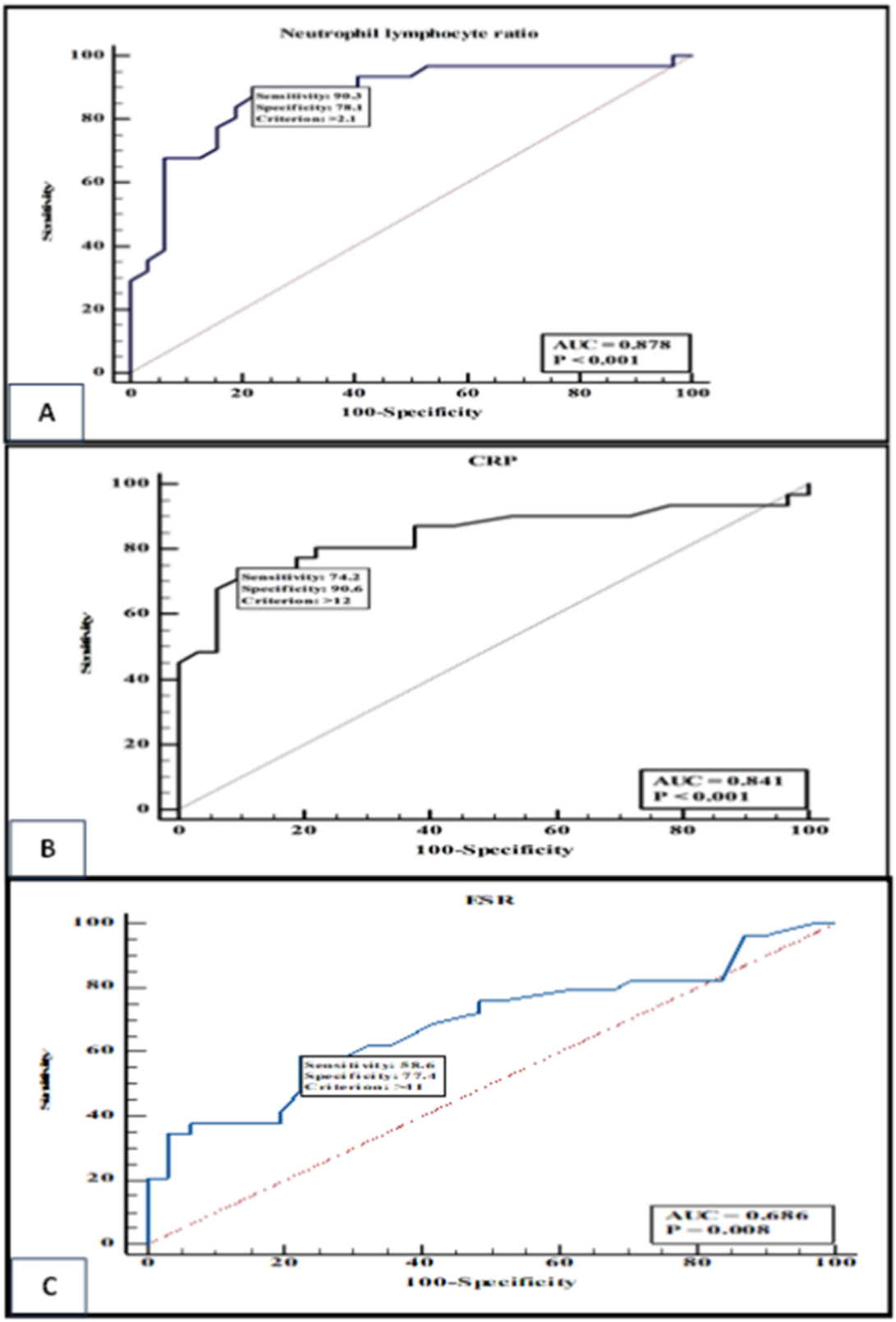

Figure 1. A: Cut off value, sensitivity, specificity of NLR as a marker of activity in UC patients
B: Cut off value, sensitivity, specificity of CRP as a marker of activity in UC patients
C: Cut off value, sensitivity, specificity of ESR as a marker of activity in UC patients
AUC: area under curve

Table 1. Comparison between three groups of study subjects with active and inactive UC regarding demographic data, chronic illness, NLR and laboratory values

		Active UC T=31(%)	Inactive UC T=31(%)	Control T=31(%)	P value
Age(years.)	Mean ±SD	31.3±12.4	28.7±11.6	32.8±11.3	0.392
	Range	18-65	19-60	20-55	
Sex	Male	20(64.5)	18(58.1)	18(58.1)	0.836
	Female	11(35.5)	13(41.9)	13(41.9)	
Smoking	No	21(67.7)	26(83.9)	27(87.1)	0.129
	Yes	10(32.3)	5(16.1)	4(12.9)	
Diabetes	No	28(90.3)	31(100.0)	29(93.5)	0.364
	Yes	3(9.7)	0(.0)	2(6.5)	
Hypertension	No	30(96.8)	31(100.0)	28(90.3)	0.319
	Yes	1(3.2)	0(.0)	3(9.7)	
Family history of ulcerative colitis	No	27(87.1)	27(87.1)	0	1.000
	Yes	4(12.9)	4(12.9)	0	
Age of onset of illness (years) 'Mean±SD'		27.2±12	23.3±13	-	0.213
Duration of illness (years) 'Mean±SD'		3.9±4	5.6±5.9	-	0.178
Haemoglobin(g/dl) 'Mean ±SD'		10.4±1.7	12±2	12.2±1.8	<0.001
WBC (×1000/mm^3) 'Mean ±SD'		10.3±4.8	6.8±2.6	5.6±1.8	<0.001
Neutrophil (×1000/mm^3) 'Mean ±SD'		7.3±3.9	3.8±2	3.3±1.4	<0.001
Lymphocyte (×1000/mm^3) 'Mean±SD'		1.9±1.0	2.3±0.8	1.8±0.5	0.017
NLR 'Mean ±SD'		4.3±2.4	1.7±1.1	1.8±0.7	<0.001
Platelets (×1000/mm^3) 'Mean ±SD'		400.6±144.2	323.7±76.2	248.2±55.2	<0.001

T: TOTAL
SD: STANDARD DEVIATION
NLR: NEUTROPHIL LYMPHOCYTE RATIO

Table 2. Comparison between patients with active and inactive UC regarding clinical features, laboratory values, extent and treatment of disease

		ACTIVE UC N=31(%)	INACTIVE UC N=31(%)	P VALUE
DIARRHOEA	**NO**	**0(.0)**	**29(93.5)**	**<0.001**
	YES	**31(100.0)**	**2(6.5)**	
ABDOMINAL PAIN	**NO**	**1(3.2)**	**27(87.1)**	**<0.001**
	YES	**30(96.8)**	**4(12.9)**	
BLOOD WITH STOOLS	**NO**	**9(29.0)**	**28(90.3)**	**<0.001**
	YES	**22(71.0)**	**3(9.7)**	
HISTORY OF FEVER	**NO**	**22(71.0)**	**23(74.2)**	**0.776**
	YES	**9(29.0)**	**8(25.8)**	
HISTORY OF WEIGHT LOSS	**NO**	**10(32.3)**	**12(38.7)**	**0.596**
	YES	**21(67.7)**	**19(61.3)**	
HISTORY OF DERMATOLOGICAL SYMPTOMS	**NO**	**26(83.9)**	**26(83.9)**	**1.000[A]**
	YES	**5(16.1)**	**5(16.1)**	
HISTORY OF RHEUMATOLOGICAL SYMPTOMS	**NO**	**10(32.3)**	**9(29.0)**	**0.783**
	YES	**21(67.7)**	**22(71.0)**	
HISTORY OF OPHTHALMOLOGICAL SYMPTOMS	**NO**	**25(80.6)**	**22(71.0)**	**0.374**
	YES	**6(19.4)**	**9(29.0)**	
BLOOD PRESSURE DIASTOLE		**68.1±8.8**	**69.4±7.7**	**0.580**

BLOOD PRESSURE SYSTOLE		**108.9±10.9**	**116.5±8.5**	**0.004**
PULSE		**97.5±15.6**	**82.8±8.3**	**<0.001**
TEMPERATURE		**37.2±0.4**	**37.0±0.2**	**0.002**
WEIGHT		**66.8±16.8**	**64.5±17.5**	**0.614**
EXTENT OF ILLNESS*	**PROCTITIS**	**0**	**2(6.5)**	**0.278**
	LEFT SIDED COLITIS	**12(41.4)**	**15(46.9)**	**0.254**
	PANCOLITIS	**17(58.6)**	**14(45.2)**	**0.219**
MAYO ENDOSCOPIC SCORE**	**MAYO 1**	**2(6.4)**	**16(53.3)**	**<0.001**
	MAYO 2	**15(48.4)**	**14(46.7)**	
	MAYO 3	**14(45.2)**	**0**	
CRP (MG/L)		**19.0(0.4-140)**	**3.3(0.6-22.0)**	**<0.001**
ESR (MM/H)		**48.0(5.0-130.0)**	**22.0(3.0-105.0)**	**0.004**
ALBUMIN (G/DL)		**3.4±0.7**	**4.2±0.4**	**<0.001**
FECAL CALPROTECTIN/ MEDIAN		**926(264-994)**	**73(53-140)**	**<0.001**
CURRENT TREATMENT***	**BIOLOGIC**	**14(48.3)**	**9(29.0)**	**0.298**
	CONVENTIONAL	**14(48.3)**	**21(67.7)**	
	SURGERY	**1(3.4)**	**1(3.3)**	

**IN TWO PATIENTS OF ACTIVE UC, EXTENT COULDN'T BE DETECTED DUE TO SEVERE DISEASE.*
*** ONE PATIENT IN THE INACTIVE UC GROUP HAD COMPLETE ENDOSCOPIC REMISSION AND NORMAL COLONOSCOPY.*
**** TWO PATIENTS FROM ACTIVE UC GROUP WERE NON-COMPLIANT ON TREATMENT.*
N: NUMBER OF PATIENTS

Table 3: NLR in patients with different degrees of total Mayo score, Mayo endoscopic score and different extent of the disease in study groups

NLR IN DIFFERENT DEGREES OF TOTAL MAYO SCORE IN ACTIVE UC GROUP						
MILD (N=2)		**MODERATE (N=19)**		**SEVERE (N=10)**		**P VALUE**
MEAN	**SD**	**MEAN**	**SD**	**MEAN**	**SD**	
2.3	**0.8**	**4.2**	**2.6**	**4.8**	**2.2**	**0.227**
NLR IN PATIENTS WITH DIFFERENT DEGREES OF MAYO ENDOSCOPIC SCORE IN ACTIVE AND INACTIVE UC GROUPS						
MAYO1 (N=18)		**MAYO 2 (N=26)**		**MAYO 3 (N=18)**		**P VALUE**
MEDIAN (RANGE)		**MEDIAN (RANGE)**		**MEDIAN (RANGE)**		
1.42(0.57-2.5)		**2.65(0.38-12.2)**		**4.1(0.5-7.3)**		**<0.001**
NLR IN PATIENTS WITH DIFFERENT EXTENT OF THE DISEASE IN COLONOSCOPY IN ACTIVE AND INACTIVE UC GROUPS *						
PROCTITIS (N=2)		**LEFT SIDED COLITIS (N=27)**		**PANCOLITIS (N=31)**		**P VALUE**
MEDIAN (RANGE)		**MEDIAN (RANGE)**		**MEDIAN (RANGE)**		
1.08(0.96-1.2)		**2.2(0.57-12.2)**		**2.5(0.38-7.8)**		**0.242**

*IN TWO PATIENTS OF ACTIVE UC, EXTENT COULDN'T BE DETECTED DUE TO SEVERE DISEASE
N: NUMBER OF PATIENTS
SD: STANDARD DEVIATION
NLR: NEUTROPHIL LYMPHOCYTE RATIO
UC: ULCERATIVE COLITIS

Table 4: Correlation between NLR & other variables among all patients, patients with active and inactive UC

NLR in		
All patients	**R**	**p value**
Haemoglobin	-0.304	**0.016**
Platelets	0.364	**0.004**
CRP	0.498	**<0.001**
ESR	0.218	0.097
Albumin	-0.390	**0.002**
Fecal calprotectin	0.377	**0.040**
Active UC patients	**R**	**p value**
Haemoglobin	-0.262	0.154
Platelets	0.227	0.219
CRP	0.301	0.1
ESR	0.028	0.885
Albumin	-0.099	0.603
Fecal calprotectin (if present)	-0.092	0.716
Haemoglobin	-0.262	0.154
Platelets	0.227	0.219
CRP	0.301	0.1
ESR	0.028	0.885
Albumin	-0.099	0.603
Fecal calprotectin (if present)	-0.092	0.716
Inactive UC patients	**R**	**p value**
Haemoglobin	0.237	0.199
Platelets	0.242	0.189
CRP	0.054	0.774
ESR	-0.178	0.346
Albumin	0.071	0.703
Fecal calprotectin (if present)	-0.002	0.996

NLR: NEUTROPHIL LYMPHOCYTE RATIO
UC: ULCERATIVE COLITIS

DISCUSSION

Although UC is typically diagnosed in the early stages of adulthood or late adolescence, it may take place at any stage of life, as shown in our study, the average patient age having active UC was 31.3 years while the mean patient age having inactive UC was 28.7 years. Cosnes et al., discovered that the most of people with UC are in their 30s and 40s. [12]

The goal of the study was to evaluate the NLR, as a good inflammatory marker, for its potential as a standalone, non-invasive technique to evaluate the disease activity in individuals with UC. When compared to controls as well as inactive UC patients, patients having active disease had higher NLR levels, and a cutoff value of 2.1 showed the existence of active disease with 90.3% sensitivity, 78.1% specificity, 80% positive predictive value, as well as 89.3% negative predictive value. Similarly, Torun et al., discovered an ideal cut-off value of 2.16 for indicating active disease with 81.8% sensitivity, 80.5% specificity, 86.8% positive predictive value, and 73.8% negative predictive value among 196 patients having UC (119 having active disease and 77 who did not) [13]. Also, our results are in line with the findings of Jeong et al., utilizing receiver operating characteristic analysis, we determined

that NLR of 2.3 is the optimal cutoff for identifying individuals with active UC [specificity: 66.7%, sensitivity: 61.2%, AUC: 0.650 (0.540-0.760), p = 0.01] [14]. Demir et al., as well reported that a 2.39 cut-off value confirmed a diagnosis of active illness, although with only 48.6% sensitivity and 77.5% specificity [15].

According to our research, the NLR value in UC patients was proportional to their disease activity. The mean of NLR was 2.3 in mild disease, 4.2 in moderate disease, 4.8 in severe disease, that agreed with Celikbilek et al., who also observed increased value of NLR with increased disease activity. However, the mean of NLR was 2.4 in mild disease, 3.17 in moderate disease and 3.85 in severe disease [16].

The Montreal classification was utilized to categorize the disease's severity in our study. 31 patients had severe disease, twenty-seven had left-sided colitis, and two had proctitis. We found that the median of NLR was 1.08 in patients with proctitis, the median of NLR was 2.2 in patients having left sided colitis and the median of NLR was 2.5 in patients with pancolitis with P value equals 0.242 that was statistically insignificant [17]. Our study demonstrated no relation between NLR and disease extent. Our results agree with those of Celikbilek et al., who compared NLR to disease progression in a group of 26 people with UC and 28 healthy controls and discovered no significant difference (P > 0.05) [16].

The endoscopic severity of UC was studied by Akpinar et al., who examined 105 healthy people, 104 patients having active UC, as well as the sensitivity of NLR for predicting endoscopic severity. When compared to the other study groups, the active group had significantly greater mean NLR (p<0.001) [7]. Our findings confirm these findings, showing that the median NLR was 1.42 in among patients with a Mayo endoscopic score of 1, 2.65 among those having a Mayo endoscopic score of 2, as well as 4.1 in patients having a Mayo endoscopic score of 3 (P <0.001). In contrast to these findings, Celikbilek et al., found no significant correlation (P > 0.05) between the NLR and disease activity in individuals with active condition, maybe it was contributing to small sample size of UC patients in his study (28 patients) and the cross sectional design of the study as he reported [16].

Also, our findings came in contradiction with those of Cherfane et al., who discovered no significant statistical difference in NLR values among patients having active and quiescent colonoscopy, this may be due to the large contribution of clostridium difficile infected patients (about two thirds of the total number) among the group of UC that they recruited and this confirms the confounding ability of infection on the NLR [18].

In line with the conclusions of Celikbilek et al., we discovered that WBC was greater in active UC when compared to inactive UC as well as healthy controls [16]. WBC was the strongest predictor of both clinical (e.g., PUCAI, total Mayo score) and mucosal endoscopic indices of disease severity [19].

NLR was found to have a significant association with WBC count (r = 0.474, P 0.001) as well as CRP (r = 0.498, P 0.001) in our study, but not with ESR (r = 0.218, p = 0.097). Demir et al., found associations that are statistically significant among NLR, ESR (r = 0.170, p = 0.043) and WBC count (r = 0.282, p = 0.001) in a sample of individuals with UC. Patients with UC showed no relationship between CRP and NLR (r = 0.102, P = 0.153) this may be related to the large number of control group in their study (140 individuals) in relation to UC groups (70 individuals) [15].

In individuals with active disease, there was no statistically significant association discovered regarding the NLR as well as CRP, ESR or WBC count. This contradicts the findings of Demir et al., who discovered NLR and WBC have an inverse relationship in patients with active UC. (r = -0.360, p = 0.002) this may be influenced by any infection or bacteremia in the active UC group in our study as we did not routinely check procalcitonin levels for infections, and determining bacteremia was difficult [15].

No statistically significant association was discovered in patients in remission between the NLR and ESR, CRP or WBC count, according to our findings. These findings agreed with those of Demir et al., who observed no correlation between NLR and CRP, WBC count or ESR in those who are in remission [15].

Karoui et al., discovered a high correlation exists between the disease activity index and CRP. Furthermore, they stated that a 10 mg/l cut-off CRP level could identify the difference between active as well as inactive disease. These findings

were similar to our study, which showed patients with active UC had higher CRP levels than those with inactive UC. When the cut-off value of CRP was higher than 12, it indicated active disease with 74.2% sensitivity and 90.6% specificity [19].

Because of its high cost and difficulties with collecting stool samples, Calprotectin fecal marker is not commonly utilized. in clinical practice despite having a sensitivity of 93% as well as specificity of 96% for UC activity.[20] In our study, 18 patients having active UC and 12 patients having inactive UC were tested using FC alone. When comparing patients having active and inactive UC, the median value of FC was greater in the active UC group. The median FC was 926mg/L in patients having active UC while the median FC was 73mg/L in patients with inactive UC.

Our study had some limitations as the small number of patients regarding each group, so our results need to be independently validated in a larger group of UC patients in future studies.

Although medications including azathioprine, steroids, mesalamine, and anti-TNF can alter complete blood count (CBC) results (particularly absolute neutrophil counts), we didn't exclude patients using these medications. It was not possible to rule out the potential that infection could affect NLR. NLR may be impacted by cardiovascular disease, cancer, or infection, however no patients in this study presented with cardiovascular or cancer-related symptoms. We did not routinely check procalcitonin levels for infections, and determining bacteremia is difficult. Patients should ideally be divided into groups according to their present treatment in order to examine the predictive value of NLR.

CONCLUSION

In conclusion, NLR is strongly correlated with disease activity in patients having UC, and it is more accessible and affordable than many other non-invasive indicators. Since NLR is a simple and inexpensive test, we suggest using it as a useful instrument for the rapid assessment of UC disease activity.

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Authors' contributions: according to CRediT (Contributor Roles Toxonomy) Ahmed El-Sayed Taha, MD [1], (1) Conceptualization, (2) Data curation, (5) Investigation, (6) Methodology, (7) Project administration, (13) Writing-original draft. Dina Fathy AbdElsayed Mohamed, MSc [1], (2) Data curation, (3) Formal analysis, (5) Investigation, (6) Methodology. Menna-t-Allah Gamal Saad El Dine, MD [2], (5) Investigation, (6) Methodology, (10) Supervision, (11) Validation. Fady Fadl Zaki Rizk, MSc [1], (2) Data curation, (3) Formal analysis, (5) Investigation, (6) Methodology. Ahmed Bahaa Eldin Abbas, MSc [3], (5) Investigation, (6) Methodology, (13) Writing-original draft. Mennatallah Ali Rashwan, MSc [3], (2) Data curation, (3) Formal analysis, (5) Investigation, (6) Methodology. Tamer Mahmoud ElTantawy ELbaz, MD [1], (7) Project administration, (8) Resources, (10) Supervision, (11) Validation, (12) Visualization, (14) Writing-review and editing. Mohamed Ibrahim Negm, MD [3], (1) Conceptualization, (2) Data curation, (3) Formal analysis, (5) Investigation, (9) Software, (14) Writing-review and editing.

Availability of data and materials:

The data used and/or analyzed during the current study is provided within the manuscript or supplementary information files upon request.

HIGHLIGHTS

- Circulating white blood cell (WBC) counts are known to change in response to systemic inflammatory diseases like UC. In response to systemic inflammation, circulating neutrophil numbers rise while lymphocyte numbers fall, as is widely recognized. The neutrophil lymphocyte ratio (NLR) has been proposed as a beneficial biomarker of systemic inflammatory reactions, and there is currently growing evidence to support this idea.

- Assessment of disease activity is crucial in patients having UC and still challenging. Colonoscopy is important in assessing disease activity, but invasive. Hence, we need to search for noninvasive markers that have affordable costs.
- This study aimed to examine whether neutrophil lymphocyte ratio (NLR) levels were changed in UC patients and to investigate the impact of NLR as simple, cost efficient and accessible predictor of disease activity in UC patients.
- We demonstrated that in patients having UC, the NLR and disease activity were strongly associated. Since NLR is a simple and inexpensive test, we suggested using it as a useful instrument for the rapid assessment of UC disease activity.

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