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ORIGINAL ARTICLE

Diagnostic Accuracy of Low-Cost Blood Test Inflammatory Markers in Severe Ulcerative Colitis

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ABSTRACT

Background: Ulcerative colitis (UC) is a long-standing inflammatory disease with remission and exacerbation courses. Early detection of relapses, flares, disease activity changes, and treatment responses is key to optimizing patient management. The evidence about the usefulness of low-cost blood test inflammatory markers concerning UC disease activity is still limited. This study aimed to evaluate the diagnostic accuracy of low-cost serum inflammatory markers in monitoring UC activity.

Methods: This cross-sectional study was conducted in the inflammatory bowel disease (IBD) clinic, Zagazig University Hospital, Egypt. Fecal calprotectin and low-cost serum inflammatory markers including C-reactive protein (CRP), C-reactive protein-albumin ratio (CAR), lymphocyte-monocyte ratio (LMR), mean platelets volume-lymphocyte ratio (MLR), mean platelets volume-platelets ratio (MPR), neutrophil-lymphocyte ratio (NLR), platelets-lymphocyte ratio (PLR), red cell distribution width-platelet ratio (RPR), and systemic immune-inflammation index (SII) were measured.

Results: The area under the curve (AUC) of CRP, CAR, Fecal calprotectin, LMR, SII, and MPR in the diagnosis of severe UC were 0.85, 0.85, 0.84, 0.81, 0.83, and 0.80, respectively. CRP, CAR, Fecal calprotectin, NLR, LMR, SII, Albumin, MPR, and RPR were independent predictors for Mayo score grade 3.

Conclusions: low-cost serum inflammatory markers such as CRP, CAR, LMR, SII, and MPR showed diagnostic accuracy in monitoring severe UC activity.

Keywords: Low-cost, Inflammatory Markers, Ulcerative Colitis.

INTRODUCTION

Ulcerative colitis (UC) is a chronic heterogeneous idiopathic inflammatory disorder of the colorectum characterized by remission and exacerbation course **[1]**. UC is affecting a growing number of patients worldwide with an overall incidence and 1.2-20.3 and 7.6-245 instances per 100,000 people annually, respectively, are the prevalence rates**[2].**Additionally, the incidence is rising across the Middle East; nevertheless, assessing the current situation remains hampered by a lack of reliable registry and epidemiological studies **[3].**

Accurately determining the disease activity in UC patients is crucial for evaluations and treatment outcome prediction **[4]**. As a result, establishing mucosal repair rather than only a

clinical remission is now the therapeutic goal of UC **[5]**; because mucosal healing lowers the risk of hospitalization and surgery, improves prognosis, and enhances quality of life, all of which are linked to long-term clinical remission **[6].**

Colonoscopy is still the gold standard for determining the degree of UC disease activity as a result. Nevertheless, this method has the disadvantages of being costly, time-consuming, and invasive. It is also painful and necessitates an uncomfortable preparatory regimen in addition to a professional operator. These restrictions frequently cause UC patients to suffer and hinder the regular assessment of UC **[7].**

Therefore, in order to diagnose and treat UC, noninvasive, low-cost ways of predicting mucosal repair using helpful biomarkers are clinically necessary. Numerous studies have indicated that fecal calprotectin is a dependable noninvasive marker for assessing mucosal healing in this regard; yet most places still do not routinely use it in clinical practice due to its excessive cost, lengthy duration, and influence of intestinal movement. Additionally, some patients have poor compliance as a result of the difficult fecal sample collection and processing **[8].**

Comparable sensitivity and specificity in a serum biomarker would make it easier, less costly, more frequent, and less intrusive to evaluate disease activity than it is now possible **[9].**

Due to its great sensitivity and accuracy as well as its correlation with the clinical and even endoscopic activity of inflammatory bowel disease (IBD), high-sensitivity C-reactive protein (hs-CRP) has recently drawn attention in UC **[10].**Additionally, some research has shown that an effective blood diagnostic for UC is the C-reactive protein (CRP) to albumin ratio (CAR) **[1, 10].** Furthermore, it has been observed that a few inflammatory markers associated with complete blood count (CBC), such as the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and lymphocyte-monocyte ratio (LMR), are indicative of the clinical disease activity of UC **[10, 11].**

However, the evidence about the usefulness of these inflammatory markers in UC remains scarce and represents an unmet need. Thus, the purpose of this study was to evaluateCRP, CAR, and CBC-related inflammatory markers asinexpensive, non-invasive, and independent indicators of endoscopic activity.

METHODS

Thiscross-sectional study was conducted in the Internal Medicine Department, Zagazig University Hospital, IBD outpatient clinic on 106 patients aged over 18,at the time of the first endoscopy, diagnosed with UC. Patients were categorized into the mild to moderate group (75) and the severe group (31) based on Mayo endoscopic sub-score grades.

Inclusion criteria: Those who were18 at the time of the endoscopy and who had been diagnosed with UC based on endoscopy, laboratory, radiography, histology, and clinical evaluation were included in the study.

Exclusion criteria: Those with a history of gastrointestinal surgery, other autoimmune diseases, blood system diseases, cancer, or serious medical complications, such as chronic kidney disease and cardiovascular disease, acute intestinal infection (stool cultures with Clostridium Difficile toxin assay), other systemic infections, long-term

and short-term (within 3 months) use of anticoagulants, antiplatelet aggregation drugs, anticoagulants, hormones, immune-suppressants, and biologics.

The sample size was calculated using Open Epi info according to the following the frequency of severe UC was 22.9% **[12]** and total number of UC cases coming to ZUH in 6 months expected to be 180 cases so 95% CI, the estimated sample was 106 cases.

Approval was obtained from the Zagazig University Institutional Review Board (IRB # 1247-25/10/2023). The work presented was completedfollowing the World Medical Association's (WMA) Declaration of Helsinki, which governs human experimentation ethics. All patients involved in the trial gave their informed consent in accordance with the study protocol.

All patients enrolled in the study underwent a comprehensive review of their medical history, a thorough clinical examination, and an endoscopic evaluation. The endoscopic findings were assessed and classified based on the Mayo Endoscopy Score (MES), following the methodology described by **Magro et al. [13]**. This scoring system was employed as an indicator of disease severity. The score is created by combining clinical characteristics, physician evaluation, and endoscopic findings. Higher scores indicate that patients have a more serious condition. The score runs from 0 to 12. Mayo endoscopic sub-score grades were as follows: Grade 0: normal or inactive (0-2), grade 1: mild (3-5), grade 2: moderate (6-10), and grade 3: severe (11-12) **[14].** Before consuming the prescribed drugs for colonoscopy preparation, a stool sample was collected to examine fecal calprotectin. Fasting blood samples were collected in the morning at the time of endoscopy and were sent to the laboratory test for examination of CBC, serum albumin, and CRP. From laboratory results, the following ratios were calculated: NLR (neutrophil-lymphocyte ratio), PLR (platelets-lymphocyte ratio), The CRP to-albumin ratio (CAR), MLR (Mean platelets volume-lymphocyte ratio), MPR (Mean platelets volume-platelets ratio), RPR (red cell distribution width-platelet ratio) and Systemic Immune-Inflammation Index (SII) calculated according to the following formula: SII=Platelets count x Neutrophil count/lymphocyte count.

The cost of various blood tests, including inflammatory markers and ratios such as NLR, PLR, CAR, MLR, MPR, RPR, and SII, can vary based on factors like location, laboratory, and whether the tests are covered by insurance. These inflammatory markersare often included as part of CBC with differential. A typical CBC costs approximately $2-4. CAR is not usually offered as a standalone test; it is calculated from separate CRP and albumin tests. CRP test costs approximately $4-5. Albumin costs $4-5.The combined cost for CRP and albumin tests would be roughly $8-10.

The fecal calprotectin test costs approximately $30-40.The price of an endoscopy for UCtypically ranges from $70-100.

Statistical Analysis

The data were loaded into the statistical package for the social sciences (SPSS version 27.0) [14] program to be analyzed.The Shapiro–Wilk testwas used to determine the normality of data distribution.The following tests were used to determine whether

differences were significant based on the type of data qualitative data is represented as numbers and percentages, whereas quantitative data is generally represented by mean ± SD. Find out how the qualitative variable differs and is associated by using the Chi-square test (X2) in conjunction with Mc Nemar or sign. P values were set at less than 0.05 and less than 0.001 for outcomes that were considered highly significant. Comparing differences between more than two examined groups, use the Mann Whitney or t-test for quantitative independent groups, followed by a paired t-test or the Kruskal Wallis test for quantitative variables that are not normally distributed. A significant threshold of $P < 0.05$ was established.

RESULTS

The age of the studied cases ranged from 18 to 36 years with a mean of 32.7 years. Regarding sex, 62.3% were female. More than half of the cases (59.4%) were from rural areas and 31.1% were smokers. DM and HPT were found in 20.8% and 29.2% of the studied cases, respectively (Table 1).

The median platelet count, neutrophil count, and lymphocyte count were 290, 4.27, and2.27, respectively. The mean of MPV was 10.14, NLR was 2.85, LMR was 11.13, MLR 0.26, and RDW 13.34. The mean MPR was 0.034 of RPR 0.045 while the median of the Systemic Immune-Inflammation Index was 552.69. This table shows that Albumin levels among the studied cases ranged from 2.17 to 5.1 mg/dl with a mean of 4.35 mg/dl. CRP ranged from 0.6 to 9.7 mg/dl with a median of 8.05 mg/dl, while CAR ranged from 0.13 to 22.06 mg/g with a median of 1.86 mg/g Regarding fecal calprotectin, it ranged from 220 to 392µg/g with mean 303.33µg/g (Table 1).About 37% of the cases had mild disease, 34% and 29.2% had moderate and severedisease, respectively. Mayo's score ranged from 3 to 12 with a mean of 7.57 (Table 1).

There was a statistically significant relation between severity and smoking, HTN, and DM among the studied cases. There was a statistically significant increase in CRP, CAR, fecal calprotectin, Platelets, neutrophil, NLR, PLR, LMR, MLR, and SII and a decrease in albumin, lymphocyte, MPR, and RPR among severe cases compared to mild and moderate (Table 2).

A statistically significant positive connection was observedbetween the Mayo score and CRP, CAR, fecal calprotectin, Platelets, neutrophil, NLR, PLR, LMR, MLR, and SII, and a statistically significant negative correlation between the Mayo score and albumin, lymphocyte, MPR, and RPR (Table 3).

CRP at cut-off>10.25 with AUC 0.85 had 87.1% sensitivity and 76% specificity. Forecasting that both positive and negative values were 60% and 93.4%, respectively with an overall accuracy of 79.2% in the diagnosis of severe UC. CAR at cut-off>2.18 with AUC 0.85 had a sensitivity of 90.3% and specificity of 74.7%. Positive and negative predictive values were 71.8% and 94.9%, respectively with an overall accuracy of 79.2% in the diagnosis of severe UC. Fecal calprotectin at cut-off>304 with AUC 0.84 had a 72% specificity and 80.6% sensitivity. The relative positive and negative predictive scores were 54% and 90% with an overall accuracy of 74.5% in the diagnosis of severe UC. LMR at cut-off <4.41 with AUC 0.81 had a sensitivity of 77.4% and specificity of

71.7%. Positive and negative predictive values were 86.6% and 56.4%, respectively with an overall accuracy of 75.5% in the diagnosis of severe UC (Table 4).

SII at cut-off>649.13 with AUC 0.83 had a sensitivity of 80.6% and specificity of 74.7%. Positive and negative predictive values were 56.8% and 90.3%, respectively with an overall accuracy of 76.4% in UCdiagnosis. MPR has a 77.4% sensitivity and a 72% specificity at cut-off <0.032 and AUC 0.80. The diagnosis of UCwas made with an overall accuracy of 73.6%, with positive and negative predictive values of 53.3% and 88.5%, respectively. RPR exhibited a sensitivity of 80.6% and specificity of 64% at cut-off <0.044 with an AUC of 0.78. About 48% of the predicted values were positive, negative,and 88.9% respectively with an overall accuracy of 68.9% in the diagnosis of severe UC (Figure 1, Table 4).CRP, CAR, Fecal calprotectin, NLR, SII, Albumin, MPR, and RPR were independent predictors for Mayo score grade 3 (Table 5).

Table 1: Demographic, laboratory, and endoscopic characteristics among the studied cases

Variable		**(n=106)**	
Age: (years)	Mean ± SD Range	32.7±10.4 18-63	
Variable		**No**	**%**
Sex	Male Female	40 66	37.7 62.3
Residence	Rural Urban	63 43	59.4 40.6
Smoking	No Yes	73 33	68.9 31.1
Co-morbidity	DM	22	20.8
	HTN	31	29.2
Laboratory investigations			
Platelet	Median Range	290 2.6-567	
Neutrophil absolute count	Median Range	4.27 1.17-13.6	
Lymphocyte absolute count	Median Range	2.27 0.37-6.4	
MPV	Mean ± SD Range	10.14±0.84 9-12	
NLR	Mean ± SD Range	2.85±1.07 1.02-4.79	
PLR	Mean ± SD Range	224.41±14.94 197-245	
LMR	Mean ± SD Range	4.53 0.67-24.38	
MLR	Mean ± SD Range	0.26±0.08 0.13-0.4	
RDW	Mean ± SD	13.34±0.90	

Variable		(n=106)	
	Range	11.65-15.42	
MPR	Mean ± SD Range	0.034±0.011 0.02-0.07	
RPR	Mean ± SD Range	0.045±0.015 0.02-0.08	
SII	Median Range	552.69 27.6-9841.08	
Albumin: (g/dl)	Mean ± SD Range	4.35±0.48 2.17-5.1	
CRP: (mg/dl)	Median Range	8.05 0.6-97	
CAR: (mg/g)	Median Range	1.86 0.13 – 22.06	
Fecal Calprotectin: (µg/g)	Mean ± SD Range	303.33±37.87 220-392	
Endoscopy		**No**	**%**
Severity	Mild (Mayo 3-5) Moderate (Mayo 6-10) Severe (Mayo 11-12)	39 36 31	36.8 34 29.2
Mayo score	Mean ± SD Median Range	7.57±3.25 7 3-12	

SD: Standard deviation, **MPV**: Mean platelets volume, **NLR**: Neutrophil lymphocyte ratio, **PLR**: Platelets lymphocyte ratio, **LMR**: Lymphocyte monocyte ratio, **MLR**: Mean platelets volume Lymphocyte ratio, **RDW**: Red Cell Distribution Width, **MPR**: Mean platelets volume platelets ratio, **RPR**: Red cell distribution width platelets ratio, **SII**: Systemic Immune-Inflammation Index, **CRP**: C Reactive protein, **CAR**: C reactive protein albumin ratio.

Table 2: Relation between demographic data and laboratory investigations and disease severity among the studied cases

Variable		Severity				t	P
		Mild and moderate (n=75)		Severe (n=31)			
Age (years)	Mean ± SD Range	33.2±10.29 18-63		31.48±10.74 19-60		0.77	0.44 NS
Variable		**No**	**%**	**No**	**%**	χ^2	**P**
Sex	Male Female	31 44	77.5 66.7	9 22	22.5 33.3	1.41	0.24 NS
Residence	Rural Urban	48 27	76.2 62.8	15 16	23.8 37.2	2.22	0.14 NS
Smoking	No Yes	56 19	76.7 57.6	17 14	23.3 42.4	**4.02**	**0.04***
Co-morbidity	No DM DM	64 11	76.2 50	20 11	23.8 50	**5.77**	**0.02***
	No HTN HTN	58 17	77.3 54.8	17 14	22.7 45.2	**5.36**	**0.02***
Albumin: (mg/dl)	Mean ± SD Range	4.42±0.38 3.4-5.1		4.17±0.64 2.17-5.1		**2.45**	**0.02***
CRP: (mg/dl)	Median Range	5.3 0.6-75		18 4.7-97		0.17	0.87 NS

Variable		Severity		t	P
		Mild and moderate (n=75)	Severe (n=31)		
CAR: (mg/g)	Median Range	1.30 0.13-22.06	3.82 1.12-21.56	**5.72**	**<0.001 ****
Fecal Calprotectin: (µg/g)	Mean ± SD Range	289.41±30.56 220-342	337±32.54 297-392	**7.16**	**<0.001 ****
Platelet	Mean ± SD Range	296.08±92.06 151-567	405±100.74 188-567	**5.39**	**<0.001****
Neutrophil absolute count	Median Range	4.2 1.17-13.6	6.26 1.14-13.6	**4.35**	**<0.001 ****
Lymphocyte absolute count	Median Range	2.39 0.7-6.4	1.3 0.37-3.6	**5.79**	**<0.001****
MPV	Mean ± SD Range	10.15±0.85 9-12	10.13±0.85 9-12	0.10	0.92 NS
NLR	Mean ± SD Range	2.56±0.97 1.02-4.79	3.55±0.98 1.09-4.79	**4.77**	**<0.001****
PLR	Mean ± SD Range	221.6±13.46 197-253	231.19±16.32 201-254	**3.13**	**0.002***
LMR	Mean ± SD Range	5.24 1.58-24.38	3.25 0.67-8.57	**5.03**	**<0.001****
MLR	Mean ± SD Range	0.24±0.06 0.13-0.4	0.31±0.08 0.11-0.4	**4.81**	**<0.001****
RDW	Mean ± SD Range	13.31±0.91 11.72-15.42	13.40±0.86 11.65-14.88	0.42	0.67 NS
MPR	Mean ± SD Range	0.037±0.010 0.02-0.07	0.027±0.008 0.02-0.05	**5.03**	**<0.001 ****
RPR	Mean ± SD Range	0.049±0.014 0.03-0.08	0.036±0.012 0.02-0.08	**4.58**	**<0.001 ****
SII	Median Range	490 27.6-4173.14	1900.85 204.55-9841.08	**5.36**	**<0.001 ****

CRP: C reactive protein, **CAR**: C reactive protein albumin ratio, **MPV**: Mean platelets volume, **NLR**: Neutrophil lymphocyte ratio, **PLR**: Platelets lymphocyte ratio, **LMR**: Lymphocyte monocyte ratio, **MLR**: Mean platelets volume Lymphocyte ratio, **RDW**: Red Cell Distribution Width, **MPR**: Mean platelets volume platelets ratio, **RPR**: Red cell distribution width platelets ratio, **SII**: Systemic Immune-Inflammation Index. **SD**: Standard deviation**,** t: Independent t-test χ^2: Chi-square test, MW: Mann Whitney test, NS: Non-significant (P>0.05) *: Significant (P<0.05).

Table 3: Correlation between Mayo score and lab findings among the studied cases

Variable	Severity	
	r	P
Albumin: (mg/dl)	-0.21	0.03*
CRP: (mg/dl)	0.41	<0.001**
CAR: (mg/g)	0.40	<0.001**
Fecal Calprotectin: (µg/g)	0.52	<0.001**
Platelet	0.44	<0.001**
Neutrophil absolute count	0.34	<0.001**
Lymphocyte absolute count	-0.60	<0.001**
MPV	0.007	0.94 NS
NLR	0.44	<0.001**

Variable	Severity	
	r	P
PLR	0.34	<0.001**
LMR	-0.50	<0.001**
MLR	0.41	<0.001**
RDW	0.17	0.09 NS
MPR	-0.49	<0.001**
RPR	-0.44	<0.001**
SII	0.41	<0.001**

CRP: C reactive protein, **CAR**: C reactive protein albumin ratio, **MPV**: Mean platelets volume, **NLR**: Neutrophil lymphocyte ratio, **PLR**: Platelets lymphocyte ratio, **LMR**: Lymphocyte monocyte ratio, **MLR**: Mean platelets volume Lymphocyte ratio, **RDW**: Red Cell Distribution Width, **MPR**: Mean platelets volume platelets ratio, **RPR**: Red cell distribution width platelets ratio, **SII**: Systemic Immune-Inflammation Index. r: Correlation coefficient, NS: Non-significant (P>0.05), *: Significant (P<0.05), **: Highly Significant (P<0.001).

Table 4: Validity of blood test in the diagnosis of severe UC among the studied cases

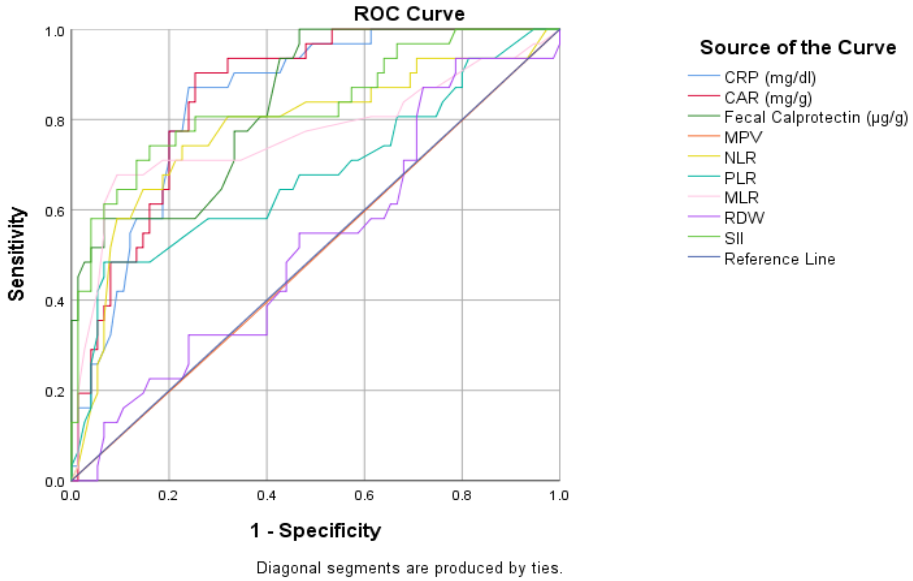
Marker	Cut off	AUC (CI 95%)	Sensitivity	Specificity	PPV	NPV	Accuracy	p
CRP	>10.25	0.85 (0.76-0.92)	87.1%	76%	60%	93.4%	79.2%	**<0.001 ****
CAR	>2.18	0.85 (0.78-0.93)	90.3%	74.7%	71.8%	94.9%	79.2%	**<0.001****
Fecal calprotectin	>304	0.84 (0.77-0.92)	80.6%	72%	54.3%	90%	74.5%	**<0.001 ****
MPV	>10.5	0.50 (0.37-0.62)	35.6%	67%	30.6%	71.4%	57.5%	0.94 NS
NLR	>3.02	0.78 (0.67-0.89)	74.2%	77.3%	57.5%	87.9%	76.4%	<0.001 **
PLR	>231.5	0.68 (0.56-0.80)	58.1%	72%	46.2%	80.6%	67.9%	0.004*
LMR	<4.41	0.81 (0.72-0.90)	77.4%	71.7%	86.6%	56.4%	75.5%	**<0.001 ****
MLR	>2950	0.77 (0.65-0.88)	71%	70.7%	50%	85.5%	70.8%	**<0.001 ****
RDW	>13.32	0.53 (0.41-0.65)	54.8%	53.3%	32.7%	74.1%	53.8%	0.69 NS
SII	>649.13	0.83 (0.74-0.93)	80.6%	74.7%	56.8%	90.3%	76.4%	**<0.001 ****
MPR	<0.032	0.80 (0.70-0.89)	77.4%	72%	53.3%	88.5%	73.6%	**<0.001 ****
RPR	<0.044	0.78 (0.68-0.88)	80.6%	64%	48.1%	88.9%	68.9%	**<0.001 ****

AUC: Area under curve, **CI**: Confidence interval, **PPV**: positive predicted value, **NPV**: negative predicted value, **: Highly Significant (P<0.001), **CRP**: C reactive protein, **CAR**: CRP albumin ratio, **MPV**: Mean platelets volume, **NLR**: Neutrophil lymphocyte ratio, **PLR**: Platelets lymphocyte ratio, **LMR**: Lymphocyte monocyte ratio, **MLR**: Mean platelets volume Lymphocyte ratio, **RDW**: Red Cell Distribution Width, **SII**: Systemic Immune-Inflammation Index, **MPR**: Mean platelet volume platelets ratio, **RPR**: Red cell distribution width platelets ratio.

Table 5: Liner regression analysis for predictors of Mayo sore among the studied cases

	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% CI for B	
	B	SE	Beta				
CRP (mg/dl)	0.039	0.018	0.175	2.176	**0.034***	**0.003**	**0.075**
Albumin (mg/dl)	-1.042	0.512	-0.155	-2.034	**0.045***	**-2.060**	**-0.024**
CAR (mg/g)	0.674	0.136	0.194	2.391	**0.038***	**0.395**	**2.267**
Fecal Calprotectin	0.023	0.007	0.271	3.135	**0.002***	**0.008**	**0.038**
Platelets	0.007	0.008	0.234	-0.932	0.354 NS	0.008	1.022
Neutrophil	0.057	0.136	0.043	0.418	0.677 NS	-0.214	0.328
Lymphocyte	0.876	0.293	0.294	-2.988	0.004 NS	-1.459	0.294
MPV	0.218	0.795	0.032	-0.274	0.785 NS	-1.798	1.362
NLR	0.150	0.305	0.050	0.492	**0.024***	**0.055**	**0.755**
PLR	0.023	0.017	0.107	1.347	0.056 NS	-0.011	0.058
LMR	-2.71	0.431	-0.189	-0.491	**0.006***	**-6.134**	**-1.327**
MLR	0.525	4.014	0.012	0.131	0.896 NS	-7.448	8.498
RDW	0.343	0.431	0.095	0.795	0.429 NS	-0.513	1.198
MPR	-7.947	0.498	-0.249	-0.592	**0.005***	**-10.219**	**-3.325**
RPR	-2.370	0.495	-0.120	-0.255	**0.009***	**-5.950**	**-1.210**
SII	0.043	0.009	0.116	1.303	**0.019***	**0.002**	**0.096**
Durbin Watson=1.21			R=0.75	R^2=0.57	F=8.55	P<0.001**	

B: regression coefficient, **SE**: Standard error, **CI**: Confidence interval, **NS**: Non-significant (P>0.05) *: Significant (P<0.05), **CRP**: C reactive protein, **CAR**: CRP albumin ratio, **MPV**: Mean platelets volume, **NLR**: Neutrophil lymphocyte ratio, **PLR**: Platelets lymphocyte ratio, **LMR**: Lymphocyte monocyte ratio, **MLR**: Mean platelets volume Lymphocyte ratio, **RDW**: Red Cell Distribution Width, **MPR**: Mean platelets volume platelets ratio, **RPR**: Red cell distribution width platelets ratio, **SII**: Systemic Immune-Inflammation Index.



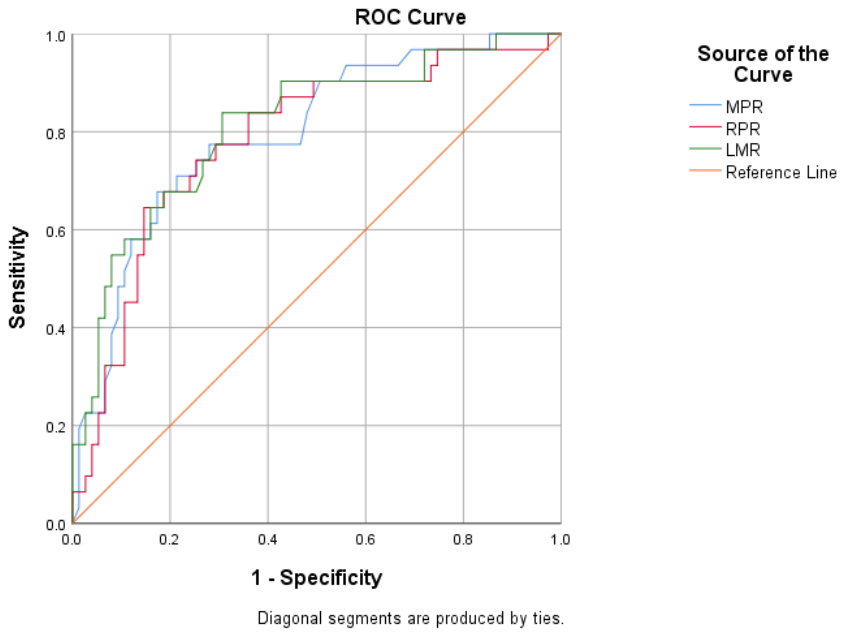


Figure 1: Roc curve for Validity of blood test in the diagnosis of severe UC among the studied cases.

DISCUSSION

The age range of the cases included in this study was 18 to 36 years, with a mean age of 32.7 years. Age, sex, place of residence, and disease severity did not significantly correlate with each other among the cases under study; nevertheless, there was a statistically significant rise in the frequency of smokers, diabetes, and high blood pressure in severe instances as compared to mild and moderate cases.

Akpinar et al. [15] revealed no statistically significant difference between the studied groups, which is consistent with our findings. Age, sex, BMI, and length of disease in remission and active periods were not statistically significant, according to **Cui et al. [10].**

The albumin levels in the cases under investigation in this study varied from 2.17 to 5.1 mg/dl, with a mean of 4.35 mg/dl. The median CRP was 9.7 mg/dl, with a range of 0.6 of 8.05 mg/dl while CAR ranged from 0.13 to 22.06 mg/g with a median of 1.86 mg/g. Regarding fecal calprotectin, it ranged from 220 to 392µg/g with a mean of 303.33µg/g.

These results were compatible with **Cui et al. [10]** who illustrated that the median CRP was 18.71 mg/dl while the median CAR was 0.588 mg/g. **Feng et al. [16]** reported that CRP ranged from 2.68 to 21.6 mg/dl with a median of 7.97 mg/dl. Regarding fecal calprotectin, it ranged from 212 to 433µg/g with a mean of 376.21µg/g.

According to our current findings, the median platelet count, neutrophil count, and lymphocyte count are firmly established at 290, 4.27, and 2.27, respectively. Means of MPV was 10.14, NLR was 2.85, LMR was 11.13, MLR 0.26, and that of RDW 13.34. The mean MPR was 0.034 of RPR 0.045 while the median of the Systemic Immune-Inflammation Index was 552.69. As far as we are aware, this is the first time we have used MRP in our study to evaluate its application. RPR, and the Systemic Immune-Inflammation Index as inflammatory markers in severe UC.

These findings unequivocally align with the previous results of **Cui et al. [10]**

whoillustrated that the means of MPV was 9.70, NLR was 2.19, and LMR was 3.52. **Feng et al. [16]** found that the median platelet count, neutrophil count, and lymphocyte count were 266, 5.16, and 1.6, respectively. The NLR mean was 3.

Concerning Endoscopy findings, we found36.8% of the studied cases 34% of patients had a moderate condition, 29.2% a severe disease. Mayo's score ranged from 3 to 12 with a mean of 7.57.

Our findings were supported by those obtained by **Jeong et al. [12]** who demonstrated that 35.4% of the studied cases 58.3% had a moderate condition, 4.2% had a severe disease. The Mayo score average was 6.8±2.3.**Chen et al. [17]** reported that37.3%,52.4% of the cases in the study had a moderate condition, 10.25% had a severe disease.

Solem et al. [18]Elevated CRP levels were linked to increased endoscopic disease activity in IBD, according to research on the use of leukocytes and CRP for the detection of clinical, endoscopic, and radiographic activity in the disease. **Rosenberg et al. [19]**demonstrated that the likelihood of continued endoscopic activity in UC may be predicted by leukocytes and CRP, and that patients in need of treatment for active mucosal disease can be identified using these measures.

Our current findings clearly revealed that regarding MPV, there was no statistically significant distinction between mild, moderate, and severe instances and RDW but there was a statistically significant increase in CRP, CAR, fecal calprotectin, Platelets, neutrophil, NLR, PLR, MLR, and SII, and decrease in albumin, lymphocyte,LMR, MPR, and RPR among sever cases compared to mild and moderate. To our knowledge, the use of MRP, RPR, and the Systemic Immune-Inflammation Index as inflammatory markers in severe UCwas not investigated before.

These results were compatible with **Cui et al. [10]**who stated that all patients' MPV and LMR dramatically decreased, while the active group's hs-CRP, CAR, PLT, NLR, and PLR was greater. The UC endoscopic activity is highly correlated with these characteristics. **Ahmed et al. [20]** stated that fecal CPN and CRP were significantly higher in the moderate-severe group. **Xu et al. [21]**found that patients with active UC had significantly higher levels of monocytes and CRP in comparison to those with inactive UC, and that patients with active UC had significantly lower levels of lymphocytes and LMR. Additional multivariate analysis revealed that patients with active UC had significantly lower LMR.

According to **Feng et al. [16],** the median NLR for patients with active and remission UC was 3. (IQR 2.22–4.49) and 1.83 (IQR 1.41–2.51), respectively, which is consistent with our data. In clinically active UC patients, the median PLR value was 161.98 (IQR 116.87–222.25), but in the remission phase, it was 122 (IQR 96.78–147.92). Compared to patients in the remission period, PLR and NLR levels were found to be considerably higher in patients with active illness.

Jeong et al. [12] showed that NLR, PLR, and FC indicate intestinal mucosal abnormalities in UC, which is consistent with our findings. Stool tests like FC have been proposed as new biomarkers recently. Sixty percent of the cytosolic protein in neutrophils is made up of the calcium- and zinc-binding protein FC. Higher neutrophil migration into the intestinal mucosa and higher leukocyte turnover may be the cause of an elevated level of FC in patients with IBD. In contrast to NLR and

PLR, FC is more costly and necessitates stool sampling. PLR outperformed NLR, PLR, ESR, CRP, and FC in terms of AUC. These results indicate that a high PLR was more significant than FC in assessing the degree of mucosal inflammation, even if there were no significant differences. It is interesting to note that PLR was more significant in differentiating between mild to intermediate UC and severe UC, although NLR was a more important biomarker in separating UC patients from healthy controls. This discrepancy could result from contrasting various groups.

Analyzing blood composition is an easy and affordable way to gauge how active UC illness is **Okba al. [22]** observed that NLR and PLR are elevated while LMR is decreased in patients with active IBD, confirming the association between CBC parameters and disease activity in IBD patients.

The results of Akpinar et al. [15], who discovered that NLR increased in cases with endoscopically active illness and increased in correlation with mucosal injury, corroborated our findings. since there is little information available about how well NLR diagnoses UC. Clinically active colitis has been shown to increase NLR, and this rise has been linked to an increase in fecal calprotectin. Flares or activations of UC, in addition to its chronic character with lymphoplasmacytic infiltration, are linked to neutrophil-mediated epithelial damage. Neutrophils infiltrate the mucosa and/or crypts in cases of crypt abscesses and cryptitis. They believe that a higher peripheral neutrophil count in active illness is reflected in neutrophil-dominant intestinal infiltration. PLR dramatically rose in UC that was endoscopically active. Compared to NLR or PLR alone, the combination of the two can more correctly predict mucosal illness.

Ntolios et al. [23] add that it has been shown that MPV is connected to platelet activity in a diseased state. According to the study, larger platelets can be activated more quickly, contain more cell particles, and express more adhesion molecules. These characteristics may cause excessive platelet activity and raise the risk of clot formation. Simultaneously, these cells travel quickly to inflammatory regions where they would be eaten and activated, which could account for the drop in MPV in patients with chronic inflammation. This is comparable to the findings of **Polińska et al. [24],** who suggested that decreased MPV levels could be a sign of mucosal inflammatory activity in UC.

We discovered in our investigation that the Mayo score and CRP,fecal calprotectin, Platelets, neutrophil, NLR, PLR, MLR, and SII, had a statistically significant positive connection and a statistically significant negative correlation between Mayo score and albumin, lymphocyte, LMR, MPR, and RPR. Similar findings were obtained by **Cui et al. [10]**They showed that endoscopic activity was favorably linked with hs-CRP, CAR, NLR, and PLR in the MES-All group.However, there was a negative correlation between endoscopic activity and MPV and LMR. A statistically significant negative connection between the Mayo score and LMR was shown by **Cherfane et al. [25].**

In the current study, we found CRP at cut-off>10.25 with AUC 0.85 had a sensitivity of 87.1% and specificity of 76%. Positive and negative predictive values were 60% and 93.4% respectively with an overall accuracy of 79.2% in the diagnosis of severe UC. CARat cut-off>2.18 with AUC 0.85 had a sensitivity of 90.3% and specificity of 74.7%. Positive and negative predictive values were 71.8% and 94.9% respectively with an overall

accuracy of 79.2% in the diagnosis of severe UC. LMR at cut-off <4.41 with AUC 0.81 had a sensitivity of 77.4% and specificity of 71.7%. Positive and negative predictive values were 86.6% and 56.4% respectively with an overall accuracy of 75.5% in the diagnosis of severe UC. Fecal calprotectin at cut-off>304 with AUC 0.84 had a sensitivity of 80.6% and specificity of 72%. Positive and negative predictive values were 54% and 90% respectively with an overall accuracy of 74.5% in the diagnosis of severe UC.

To the best of our knowledge, this is the first time that we have used MRP, RPR in our investigation, and the Systemic Immune-Inflammation Index as inflammatory markers in severe UC. SIIat cut-off>649.13 with AUC 0.83 had a sensitivity of 80.6% and specificity of 74.7%. Positive and negative predictive values were 56.8% and 90.3% respectively with an overall accuracy of 76.4% in the diagnosis of UC. MPRhas a 77.4% sensitivity and a 72% specificity at cut-off <0.032 and AUC 0.80. The diagnosis of UCwas made with an overall accuracy of 73.6%, with positive and negative predictive values of 53.3% and 88.5%, respectively. RPR exhibited a sensitivity of 80.6% and specificity of 64% at cut-off <0.044 with an AUC of 0.78.Positive and negative predictive values were 48.1% and 88.9% respectively with an overall accuracy of 68.9% in the diagnosis of severe UC.

This was compliant with **Cui et al. [10]**who demonstrated that the AUC values for CAR and hs-CRP were higher than those of other laboratory indicators, at 0.853 (sensitivity 76.8%, specificity 84.8%) and 0.850 (sensitivity 77.6%, specificity 81.9%), respectively. The hs-CRP AUC (sensitivity 86.9%, specificity 85.4%), CAR AUC (sensitivity 81.8%, specificity 89.6%), and MPV AUC (sensitivity 77.1%, specificity 79.3%) were all 0.902, 0.904, and 0.838 in the MES-E3 group, respectively.

Posul et al. [26] and **Torun et al. [27]** claimed that NLR had a 61.2% and 81.8% sensitivity rate, respectively, for predicting clinically active UC illness. **Akpinar et al. [15]**found that the NLR had a 76.0% accuracy rate in predicting endoscopically active illness (AUC ± SE: 0.718 ± 0.039). Higher levels of the NLR and PLR combo were discovered to be the independent indicators of UC illness that were endoscopically active. Furthermore, an independent predictor of endoscopically active illness was ESR rather than CRP. In the study by **Celikbilek et al. [28],** NLR did not change between individuals with severe and non-extensive illness. Using multivariate logistic regression analysis, **Demir et al. [29]**showed that whereas NLR was higher in clinically active disease, CRP was the sole independent predictor for clinically active UC disease.

Ahmed et al. [20] reported that fecal calprotectin and CRP both had high sensitivity, but that fecal calprotectin had somewhat superior specificity (54%) and higher sensitivity (84.6%) in comparison to CRP (50%). These results are consistent with our findings.For the identification of disease activity in IBD, **Langhorst et al. [30]** demonstrated good specificity for both CRP and ESR, even though they were linked to a significantly lower sensitivity than fecal indicators.

Our current findings clearly revealed that CRP, CAR, Fecal calprotectin, NLR, LMR, SII, Albumin, MPR, and RPR were independent predictors for Mayo score grade 3. Obtained similar findings, demonstrating thatSII and CAR can significantly predict the Mayo score. **Moein et al. [31]** reported that

significant prediction of Mayo score can be made based on fecal calprotectin levels.

This study demonstrated some limitations. It was a cross-sectional study. Besides, it was conducted in a single place that might not be entirely representative of the population and could impact the precision of the diagnostic accuracy estimates.

Multicenter randomized clinical trials will be required to validate these markers before and after the treatment with conventional or biological therapy.

Conclusion

Low-cost serum inflammatory markers, such as CRP, CAR, LMR, SII, and MPR, have shown diagnostic accuracy in monitoring severe UC activity. These markers can be used as an alternative to expensive tests in low-income countries. This is particularly important since UC is a chronic disease that requires regular monitoring. However, it is crucial for these markers to be appropriately validated before widespread use.

Conflict of interest

The authors declared that they have no conflicts of interest with respect to the authorship and/ or publication of this article.

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