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Role of Fecal and Blood Markers in The Assessment of Severity of Ulcerative Colitis

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Abstract:

Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease with varying severity, making accurate assessment critical for effective management. Fecal and blood markers have emerged as probable non-invasive tools for evaluating disease activity in UC. **Aim:** This study aimed to evaluate the effectiveness of combined fecal and blood markers in assessing UC severity. **Methods:** In a cross-sectional study, 50 UC patients and 25 matched healthy controls were analyzed. Clinical data, along with albumin, complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fecal calprotectin, and serum matrix metalloproteinase 9 (MMP-9) levels, were measured. Disease activity was assessed using the Mayo score and correlated with these biomarkers. **Results:** UC patients had significantly higher levels of ESR, CRP, and fecal calprotectin compared to controls ($p < 0.001$). MMP-9 levels were also significantly elevated in UC patients (1231.92 ± 612.93 ng/ml) versus controls (653.24 ± 265.17ng/ml, $p < 0.001$). MMP-9 showed a positive correlation with bowel movements per day ($r = 0.347$, $p = 0.013$), bowel movements per night ($r = 0.279$, $p = 0.050$), SCCAI score ($r = 0.408$, $p = 0.003$), and CRP level ($r = 0.281$, $p = 0.050$). The optimal MMP-9 cut-off to distinguish UC patients from controls was > 471 ng/ml, with 78% sensitivity and 66% specificity. **Conclusion:** Serum MMP-9 levels in UC patients correlate with disease activity with 70% NPV, 82% PPV, and AUC of 0.772 ($p< 0.001$), serum MMP-9 and fecal calprotectin levels could be useful non-invasive markers for evaluating UC activity and severity.

Keywords: Ulcerative colitis; fecal calprotectin; matrix metalloproteinase 9; disease severity; inflammatory marker

Introduction

Inflammatory bowel diseases (IBD), which include Crohn's disease (CD) & ulcerative colitis (UC), are chronic, relapsing conditions that significantly impact both the gastrointestinal tract and overall quality of life. These disorders lead to debilitating symptoms that affect patients' quality of life & place substantial burdens on society and healthcare systems. Although the specific etiology of UC remains unknown, it is commonly considered to stem from an improper immune reaction to environmental factors, such as luminal & microbial antigens, especially in people with genetic predisposition [(1)].

Epidemiological data suggest that UC is more prevalent in developed countries, particularly in colder and urban environments [(2)]. However, the incidence rates of UC in regions like Asia & the Middle East show significant increase over recent decades [(3)]. The spread of UC globally correlates with shifts toward Western dietary patterns and lifestyles, indicating a connection between industrialization and increased disease incidence [(4)].

Despite the stabilization of UC incidence rates in Western countries, the prevalence continues to grow, with projections showing a dramatic rise in the number of affected individuals from 2015 to 2025. This trend is largely due to improvements in diagnostic capabilities and relatively low mortality rates associated with the disease [(5)].

Severe episodes of UC can be highly debilitating and potentially life-threatening, underscoring the importance of effective disease monitoring and management [(6)].Traditionally, the corner stone in evaluating disease activity in inflammatory bowel diseases has been colonoscopy with histopathologic analysis of biopsy samples. This approach, however, is costly and invasive, with inherent risks such as perforation [(7)].

As such, there is growing interest in identifying non-invasive biomarkers like fecal calprotectin (FCT) and matrix metalloproteinases (MMPs), particularly MMP-9, which have shown potential in monitoring intestinal inflammation more safely and cost-effectively. These biomarkers offer a less invasive alternative for assessing disease activity, providing critical insights without the risks associated with traditional endoscopic methods. [(8,9)]

The purpose of this research was to assess the role of combined fecal & blood parameters in assessing UC activity and severity.

Patients and methods:

Patients:

This cross-sectional research was conducted on cases referred to Benha University Hospital and Mahalla Hepatology Teaching Hospital, Egypt, throughout the period from February 2023 to November 2023. The research involved 75 subjects divided into 2 groups: Group I (Cases group): Involved 50 cases having UC & Group II (Control group): Involved 25 age & sex matched apparently healthy controls. The ethical committee of the Faculty of Medicine, Benha University Hospitals granted approval for this investigation. Parents provided informed written consent. The ethical approval code number is {M.S.23.12.2022}.

Inclusion Criteria were adult patients diagnosed with UC. The diagnosis of UC has been determined using a combination of clinical characteristics, lab outcomes, radiological outcomes, endoscopic outcomes, & histopathology.

Exclusion Criteria were patients with history of Crohn's disease, infectious intestinal disease, pregnancy, age less than 18 years or over 65 years, active malignancy, chronic inflammatory conditions (e.g., Rheumatoid arthritis) and cardiovascular diseases.

Methods:

Detailed methodology and patient evaluation:

Comprehensive history taking, laboratory investigations & clinical investigations, have been performed. History includes personal details, medical complaints, comorbidities, and surgical history. Clinical examination evaluates general appearance, vital signs, and local abdominal findings, including per rectal examination when necessary. Laboratory investigations encompass complete blood count, ESR, CRP, fecal calprotectin, & serum matrix metalloproteinase 9 levels, aiding in disease evaluation.

Assessment of Clinical symptoms using the SCCAI: It is a scoring system that rates general well-being from 0 (very well) to 4 (terrible), evaluates daily and nightly bowel frequency, and measures urgency of defecation from 0 (none) to 3 (incontinence). It also scores blood in the stool, notes the presence of mucus and abdominal pain, and includes points for complications like joint pain, eye inflammation, erythema nodosum, and skin ulcers, providing a comprehensive index of disease activity [10].

Assessment techniques: Erythrocyte sedimentation rate has been detected from complete blood samples using the Westergren technique (Padova, Alifax, Italy). C-reactive protein was evaluated utilizing the nephelometric technique (Beckman Coulter, Fullerton, CA, USA).

Detection of fecal calprotectin (FC): Fresh fecal samples weighing 50-100 milligram were gathered from all subjects into clean containers and inoculated into Epitope Diagnostics Fecal Sample Collection Tubes using a calibrated loop. To obtain a clear supernatant, the samples were diluted 1:40 with Extraction Buffer & subsequently centrifuged at 3000 x g for five min. A new tube was utilized to transfer 0.15 milliliters of this supernatant, which was then mixed with 1.2 milliliters of Extraction Buffer & prepared for Fecal Calprotectin measurement using the ELISA technique.

Assessment of serum matrix metalloproteinase 9 level: The Human MMP-9 (Matrix Metalloproteinase 9 Gelatinase B) levels were determined using the BT lab ELISA Kit [Catalog No: E0936Hu], an enzyme-linked immunosorbent assay designed for specificity to MMP-9. In the assay, samples containing MMP-9 bind to pre-coated antibodies on the plate wells, followed by the addition of biotinylated MMP-9 antibodies and Streptavidin-HRP, which binds to the biotinylated antibodies. After washing away unbound Streptavidin-HRP, a substrate solution is added, causing a color change proportional to the MMP-9 concentration. The reaction is stopped with an acidic solution, and the absorbance is measured at 450 nm. The assay involves setting up samples and reagents at room temperature, adding and mixing various components per specific steps, and concludes with a reading of the color intensity to quantify MMP-9 levels.

Colonoscopy: Colonoscopies were performed by a single expert endoscopist using PENTAX EC-3890 TIK and LK colonoscope models to assess the mucosa of the colon & terminal ileum within all cases. Multiple biopsies were taken for histopathological examination. Ulcerative colitis (UC) extension was categorized using the Montreal classification, categorizing cases into four groups: ulcerative proctitis, left-sided UC, extensive UC, and pancolitis ([11, 12]. Sedation was administered intravenously using propafol and midazolam, with doses ranging from 25 to 100 μg of propafol & 5-10 milligram of midazolam. The technique involved a preliminary digital rectal examination followed by the insertion of the colonoscope through the anus to examine up to the terminal ileum, where biopsies have been obtained from any pathological lesions.

Histopathological examination: The biopsy was referred to a single expert pathologist, who was responsible for the subsequent procedures: Sectioning,

embedding, processing, staining with hematoxylin and eosin, and fixation. Figure 1(A, B and C)

Evaluation of endoscopic disease activity: The endoscopic activity of UC has been estimated via the Mayo Endoscopic score (EMS). The scoring ranged from 0 to 3, where 0 =Normal mucosa, 1= Mild inflammation, erythema, and decreased vascular pattern, 2= Moderate inflammation, marked erythema, absent vascular pattern, friability, and erosions, and 3= Severe inflammation with spontaneous bleeding and ulceration. [13,14] Figure 2 (A, B and C)

Statistical analysis

Statistical analysis was done utilizing The Statistical Package for Social Science (IBM Corp., 2017. Version 25.0 of IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp. involving revision, coding, and tabulation. Normality has be) Figured utilizing the Kolmogorov-Smirnov test, with normality assumed if $p > 0.05$. Descriptive statistics involved means, standard deviations, ranges for numerical data, frequencies & percentages for categorical data. Analytical methods employed included the Student T Test & Mann-Whitney Test for comparing group means, Chi-Square & Kruskal-Wallis tests for categorical variables, & Spearman's association for assessing the association among non-parametric variables. ROC analysis has been utilized for detecting the test's accuracy through sensitivity, specificity, PPV, NPV, and optimal cutoff values based on the Youden index. Statistical significance was set at a p-value < 0.05, with values < 0.01 indicating high significance.

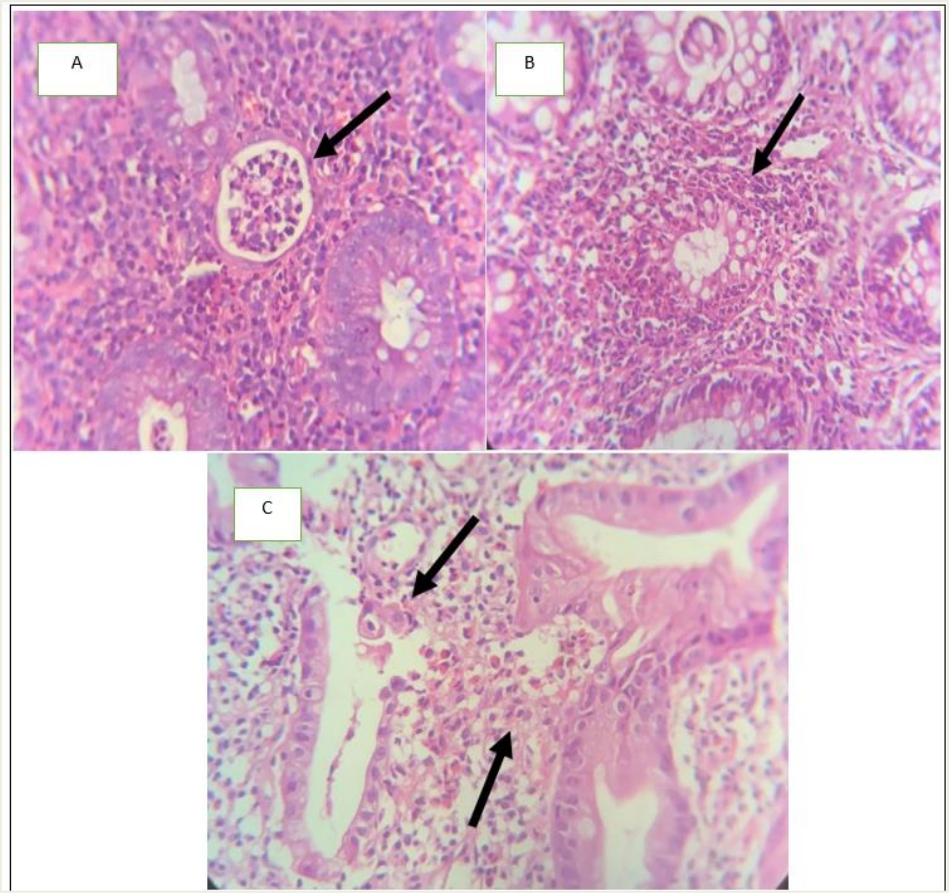

Figure 1: Histopathological examination of a colon tissue sample, showing:

A. Crypt abscess (Black arrow).
B. Neutrophilic infiltration forming cryptitis (Black arrow).
C. Distorted glands, neutrophilic and eosinophilic infiltration. (Black arrows).

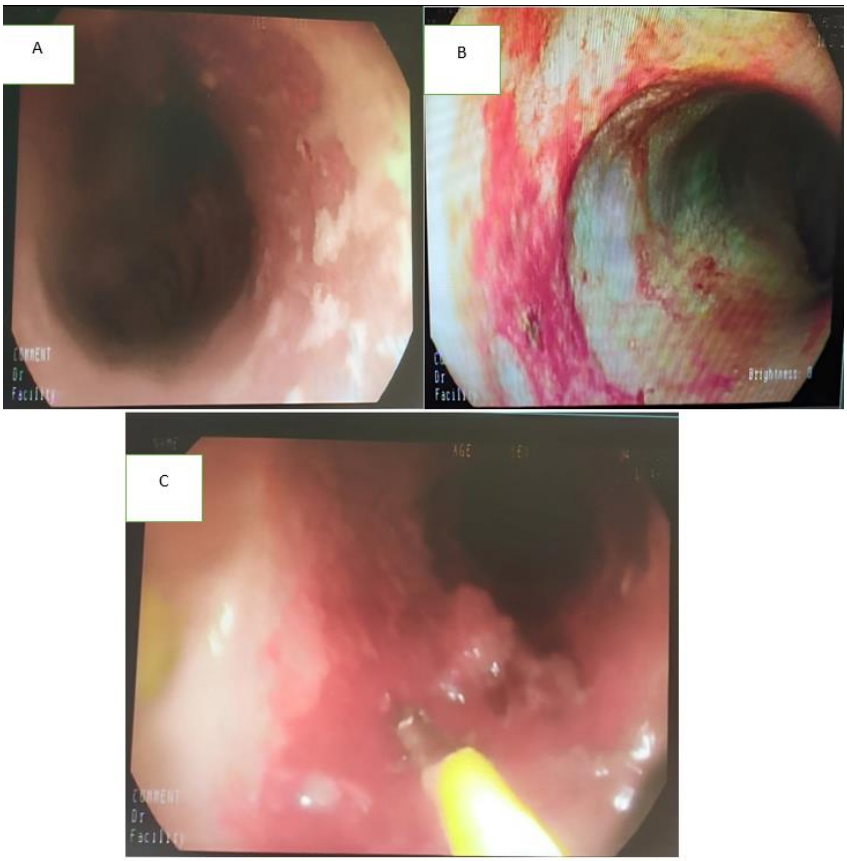

Figure 2: Colonoscopy picture of patient with active UC, showing:

A. Hyperemia and multiple linear ulcers.
B. Significant hyperemia and bleeding.
C. Pseudo polyps, hyperemia, and bleeding.

Results:

The current study included 50 patients with ulcerative colitis (the cases group) as well as 25 healthy participants as a control group.

The average age within the cases group was 32.90 ± 9.40 years, and there was a predominance of female gender. There was no statistically significant variance among the cases & the control group according to the basic demographic data. Demographic data of the two study groups is shown in Table 1.

The mean SCCAI sore among patients was 5.22± 4.14, baseline clinical data of the cases is shown in Table 1.

Regarding laboratory investigations, there was no statistically significant difference between UC patients & controls in haemoglobin level (p = 0.071), WBCs count (p= 0.231), platelets count (p= 0.866) and albumin level (p= 0.624). Table 2

The mean ESR at first hour and second hour, and CRP levels were significantly higher in UC patients than controls (P < 0.001). Mean Fecal calprotectin level in the UC patients was (448.84 ± 713.39) which was statistically significantly greater than in control group (68.2 ± 28.26) (P < 0.001). Table 2

Mean serum Matrix Metalloproteinase 9 (MMP-9) levels in UC patients was (1231.92 ± 612.93) ng/ml which was statistically significantly greater compared to the control group (653.24 ± 265.17 ng/ml) (P < 0.001). Table 1

Regarding endoscopic findings, Hyperemia was reported in 90% of patients, Superficial ulceration in 44%,

Friability in 44%, Pseudo polyps in 14%, Loss of haustration in 18% & vascular pattern Loss in 68%. The most common disease extension was the left colon in 36% patients, proctitis in 22%, and pancolitis and extensive lesions in 20%. There were 12 patients (24%) with mayo score 1, 22 patients (44%) with mayo score 2 and 16 patients (32%) with mayo score 3. Regarding histopathological activity, there were 14 (28%) active UC cases, 29 (58%) cases of chronic active UC, 5 (10%) cases with chronic inactive UC, and 2 (4%) patients had Chronic active UC with atypia.

Serum Matrix Metalloproteinase 9 (MMP-9) showed a statistically significant positive correlation with BM/ Day, BM/ Night, SCCAI score and CRP level. Table 3

There was no statistically significant correlation between serum MMP-9 levels according and disease extension ($p = 0.365$) or the Mayo score ($p = 0.627$). However, there was statistically significant correlation of serum MMP-9 levels and histopathologic disease activity ($p < 0.001$) where he greatest level of serum MMP- 9 was found in the patients' whose biopsy showed active disease (1937 ng/ml), followed by chronic active (1074 ng/), and Chronic inactive (872 ng/ml). Table 3

The best cut-off points of Matrix Metalloproteinase 9 level to differentiate patients with UC from control was > 471 ng/ml with 78% sensitivity and 66% specificity. The AUC was 0.772 with statistically significant value ($p< 0.001$). Table 4, Figure 3

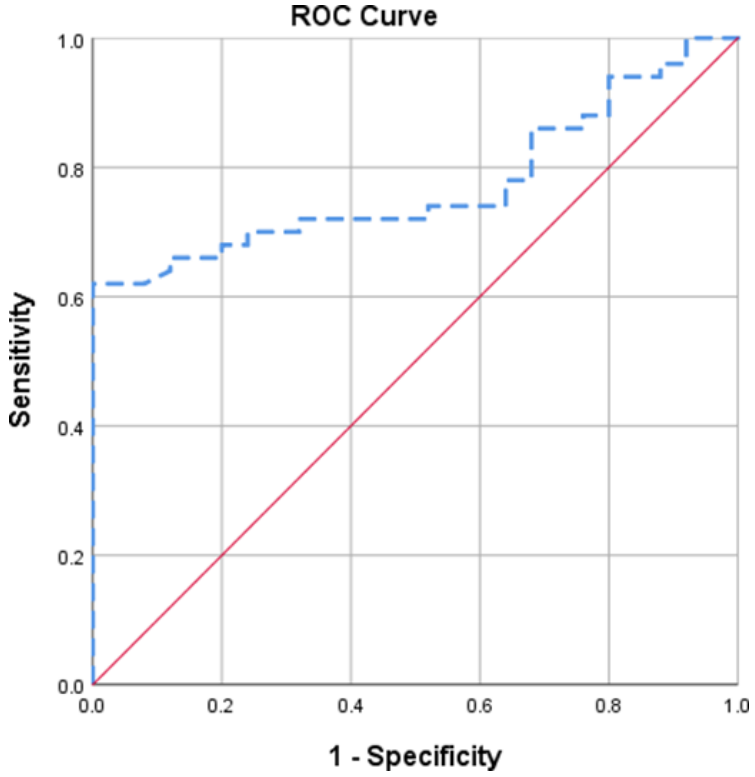

Figure 3: ROC Curve of MMP-9 (ng/ml) to distinguish cases from controls.

Table 1: Analysis of the demographic data, history, CBC, albumin, inflammatory markers and matrix Metalloproteinase 9 (ng/ml) in the two study groups and clinical data of the cases group.

		Groups				Test of significance
		Cases group (N=50)		Control group (N=25)		
Age (Years)		32.90 ± 9.40		33.86 ± 11.87		t = - 1.446 P = 0.253
Gender	Males	15	30%	11	44%	X^2 = 1.442
	Females	35	70%	14	56%	P = 0.230
Residence	Urban	34	68%	15	60%	X^2 = 0.471
	Rural	16	32%	10	40%	P = 0.493
Smoking	No	41	82%	21	84%	FET = 0.047
	Yes	9	18%	4	16%	P = 0.829
	Variables	**Ulcerative Colitis cases (N=50)**				
BM/ day		Mean ± SD				Range
BM/ Night		4.86 ± 3.2				1 - 13
SCCAI score		2.54 ± 2.33				0 - 13
				Number		Percent%
				Clinical manifestations		
Diarrhea				48		96%
Cramby abdominal pain				42		84%
Bleeding per rectum				35		70%
Weight loss				28		56%
Fever				22		44%
Anorexia				18		36%
Vomiting				5		10%
				SCCAI score		
Urgency						
None				22		44.0%
Immediately				7		14.0%
Hurry				21		42.0%
				Blood in stool		
None				15		30.0%
Trace				14		28.0%
Occasionally frank				15		30.0%
Usually, frank				6		12.0%
				General well being		
Very well				17		34.0%
Slightly below par				19		38.0%
Poor				11		22.0%
Very poor				2		4.0%
Terrible				1		2.0%
				Extra colic manifestations		
None				36		72.0%
arthropathy				13		26.0%
arthropathy/uveitis				1		2.0%

P: probability, t: Independent samples t-test, X^2= Chi-square test, FET: Fischer's exact test

Table 2: Analysis of CBC, albumin, inflammatory markers and matrix Metalloproteinase 9 (ng/ml in the two study groups.

	Groups				Test of significance
	Cases group (N=50)		**Control group (N=25)**		
Haemoglobin (gm/dl)					t = - 1.835
Mean ± SD	11.68 ± 1.59		12.38 ± 1.48		P = 0.071
Range	7.9 – 15.4		10.2 – 16.3		
WBCs (x10^3/fl)					z = - 1.197
Mean ± SD	7.68 ± 2.86		6.76 ± 1.93		P = 0.231
Range	3.2 – 16.3		4.2 – 10		
Platelets (x10^3/fl)					z = - 0.169
Mean ± SD	285.70 ± 104.84		277.60 ± 74.89		P = 0.866
Range	68 - 609		196 - 410		
Albumin (gm/dl)					t = 0.493
Mean ± SD	3.92 ± 0.38		3.88 ± 0.35		P = 0.624
Range	3 – 4.6		3.10 – 4.40		
ESR first hour (mm/hr)					z = - 6.553
Mean ± SD	22.92 ± 18.01		5.76 ± 1.13		P < 0.001*
Range	5 - 100		4 - 7		
ESR second hour (mm/hr)					z = - 6.247
Mean ± SD	41.34 29.23		11.96 2.34		P < 0.001*
Range	10 - 120		9 - 18		
CRP					
Negative	1	2%	25	100%	FET = 70.673
Positive	49	98%	0	0%	P < 0.001*
CRP level (ml/l)					
Mean ± SD	23.48 ± 38.71		3.8 ± 1.35		z = - 7.070
Range	6 - 192		1-5		P < 0.001*
Fecal calprotectin (mg/kg)					
Mean ± SD	448.84 ± 713.39		68.2 ± 28.26		z = - 3.327
Range	28 - 3920		29 - 157		P < 0.001*
Matrix Metalloproteinase 9 (ng/ml)					z = - 3.827
Mean ± SD	1231.92 ± 612.93		653.24 ± 265.17		P < 0.001*
Range	215 - 2339		143 – 1011		

P: probability, t: Independent samples t-test, X^2= Chi-square test, FET: Fischer's exact test

Table 3: Diagnostic value of MMP-9 (ng/ml) to distinguish cases from controls.

Diagnostic criteria	Matrix Metalloproteinase 9 (ng/ml)
AUC	0.772
Cut off point	> 471
Sensitivity	**78%**
Specificity	**66%**
NPV	**70%**
PPV	**82%**
Accuracy	**74%**
P	< 0.001*

AUC: area under the curve, NPV: Negative predictive value, PPV: Positive predictive value, P: probability, *: significant p value (< 0.05).

Table 4: Correlation between Matrix Metalloproteinase 99 (ng/ml) with clinical and laboratory data, disease extension, Mayo score and biopsy results of the cases group.

Clinical and laboratory parameters		MMP_9
Age	rs	0.045
	p	0.754
BM/ Day	rs	**0.347***
	p	**0.013**
BM/ Night	rs	**0.279***
	P	**0.050**
SCCAI score	rs	**0.408****
	P	0.003
HGB	rs	-0.146
	P	0.312
PLT	rs	0.053
	P	0.716
WBCs	rs	0.179
	P	0.214
albumin	rs	-0.212
	P	0.144
ESR (first hour)	rs	0.251
	P	0.078
ESR (second hour)	rs	0.170
	P	0.239
CRP level	rs	**0.281***
	P	**0.050**
Fecal calprotectin	rs	0.233
	P	0.104

Disease extension	Number of patients	Matrix Metalloproteinase 9 (ng/ml) [median (range)]	Test of significance
Proctitis	11	961 (349 – 2271)	KW = 4.316
Sigmoiditis	3	1863 (1721 – 2005)	P = 0.365
Left side	18	1473 (290 – 2339)	
Extensive	10	1300 (232 – 2125)	
Pancolitis	10	1390 (215 – 2044)	
	Mayo score		
Mayo score 1	12	753 (215 – 1590)	KW = 0.148
Mayo score 2	22	1363 (290 – 2339)	P = 627
Mayo score 3	16	1528 (488 – 2247)	
Biopsy results			
Active	14	1937 (1191-2339)	KW = 21.291
Chronic active	29	1074 (215-1852)	P < 0.001*
Chronic inactive	5	872 (446 – 1453)	
Chronic active with atypia	2	(886 – 1023)	

P: probability, KW: Kruskal Wallis test, rs: Spearman's correlation, *: Statistically significant ($p < 0.05$).

Discussion:

Ulcerative colitis (UC) poses challenges in assessing disease severity, often relying on invasive procedures. Non-invasive biomarkers like FC, CRP, & MMP-9 offer potential alternatives. The purpose of the research was to assess the utility of combined fecal & blood parameters in gauging UC activity and severity. Through a cross-sectional case-control design, including clinical evaluation and laboratory tests, we sought correlations between these biomarkers and disease activity. This investigation aims to explore their role as non-invasive tools in guiding UC management.

Regarding demographics, the mean age of ulcerative colitis (UC) patients in our study was approximately 33 years, consistent with findings from previous studies. However, our study revealed a predominance of females, which contrasts with the typically reported male predominance in the existing literature. This difference may be due to regional variation [15].

Our study found no statistically significant variance among the cases & the control group regarding age or gender which is consistent with pervious literature [16,17]. However, no statistically significant difference was found between the case and control groups in terms of smoking prevalence. This finding contrasts with previous literature, which consistently reports a higher prevalence of ulcerative colitis among nonsmokers or recent ex-smokers [18]. These findings may be explained by the fact that the majority of patients in our study were women, and in this cultural context, smoking among women is often considered taboo, which could influence the overall smoking prevalence in the study population. [19]

In the current study, the most frequent clinical presentation of ulcerative colitis was chronic diarrhea within 48 (96%) patients, followed by crampy abdominal pain in 42 (84%) patients, and bleeding per rectum in 35 (70%), In another Egyptian study, the most prevalent presenting symptom was bleeding per rectum (50.5%), followed by chronic abdominal pain (20.5%) & chronic diarrhea (16.8%) [20]. Extraintestinal manifestations were reported in 14 patients, with arthropathy being reported in 13 patients (26%) and arthropathy/uveitis in 1 patient only (2%), which is consistent with previously reported percentages [21].

Regarding the extension of UC our study found that left side UC was the most frequent extension, followed by proctitis, which is line with pervious studies [22]. The most common endoscopic findings were hyperemia in 90% of patients, followed by loss of vascular pattern in 68% of patients. Regarding the histopathological disease activity among the included cases, 58% of patients had chronic active disease, 28% had active disease, and 10% had chronic inactive disease, only 2 patients had chronic active disease with atypia. Regarding laboratory investigations, our study found no statistically significant variance among UC patients and controls regarding the hemoglobin level ($p = 0.071$), WBCs count ($p= 0.231$), platelets count ($p= 0.866$), or albumin level ($p= 0.624$), these findings are similar to previously reported data in UC patients. [15]

UC patients in our study exhibited significantly elevated C-reactive protein levels in comparison to controls (13.9 vs. 3.02 mg/l, $p < 0.001$), they also exhibited significantly higher ESR levels (41.43 vs.11.9, $p < 0.001$), these findings are in accordance with previous studies [22].

Fecal calprotectin is a well-established biomarker used in the diagnosis and monitoring of ulcerative colitis. It reflects intestinal inflammation and has been shown to correlate with both endoscopic and histological disease activity. Elevated fecal calprotectin levels are commonly observed in patients with active UC, making it a valuable non-invasive tool for distinguishing between inflammatory bowel disease and functional

gastrointestinal disorders. In our study, fecal calprotectin level was significantly higher in cases than in controls (140 vs. 17.5 – $p < 0.001$). The diagnostic accuracy for determining cases with UC of fecal calprotectin was 95.2%, with a sensitivity &specificity of 97.8 & 95.7%, respectively when a cut-off value of 53.95 µg/g was used; similar findings were document in pervious studies. [23,24]

Serum matrix metalloproteinase-9 (MMP-9) is a proteolytic enzyme involved in the degradation of the extracellular matrix and plays a key role in inflammation and tissue remodeling. In the context of ulcerative colitis, elevated levels of MMP-9 have been associated with disease activity, as it contributes to mucosal damage and inflammation. As a potential biomarker, MMP-9 can help differentiate between active disease and remission in UC patients [25].

In our study the mean serum MMP-9 level in UC patients was 1231.92 ± 612.93 ng/ml which was statistically significantly greater as compared to the control group (653.24 ± 265.17 ng/ml) (Range 143 – 1011 ng/m) ($P < 0.001$). Also, a high statistically significant variance was observed within the Matrix Metalloproteinase 9 level according to the histopathological disease activity ($p < 0.001$). The highest level of Matrix Metalloproteinase 9 was shown in the cases with active disease (1937 ng/ml), followed by cases with chronic active disease (1074 ng/ml), and cases with chronic inactive disease (872ng/ml). Our findings align with previous studies demonstrating a significant increase in MMP-9 levels in ulcerative colitis (UC) patients compared to controls, suggesting its role in facilitating UC progression. [26] Similarly, elevated serum MMP-9 levels have been observed in patients with active UC compared to those with inactive disease. [27] Additionally, it has been reported that baseline serum MMP-9 levels are significantly higher in UC patients than in healthy controls, even when CRP levels remain normal. [28]

In the current study, no statistically significant difference was observed in serum MMP-9 levels based on disease extent ($p = 0.365$). This contrasts with previous research, which reported significantly higher MMP-9 gene and protein expression in patients with extensive UC compared to those with disease confined to the left colon. [29]. This discrepancy could be attributed to differences in sample size, patient demographics, or disease activity between the studies. Additionally, variations in measurement techniques or study design may have influenced the results.

In the current study, serum MMP-9 showed a statistically significant positive correlation with BM/ Day, BM/ Night, SCCAI score and CRP level. Similar findings were shown by a study investigating MMP-9 levels in 35 children with UC which found that elevated serum levels of MMP-9 correlated with CRP levels and clinical scores, including the Mayo score and the Paris Classification of the Pediatric Ulcerative Colitis Activity Index (PUCAI). [30]

In the current study, the best cutoff point of serum MMP-9 level to differentiate cases with ulcerative colitis from control was > 471 ng/ml with 78% sensitivity and 66% specificity. The AUC was 0.772 with statistically significant value ($p< 0.001$).

Despite the obtained results, the study has some limitations; first, the cross-sectional nature of the study captures a single point in time, preventing conclusions about long-term disease progression, biomarker fluctuations, or causality. Second, lack of longitudinal and follow-up data makes it difficult to assess the predictive value of biomarkers over time or their utility in monitoring disease remission and relapse.

Additionally, the predominance of female participants and potential cultural influences, such as smoking being taboo among women, may have impacted the findings and limited their generalization to

other populations. Lastly, the relatively small sample size may limit the generalizability of the findings.

In summary, our study highlights the potential of combining non-invasive biomarkers, such as fecal calprotectin, CRP, and serum MMP-9, in assessing ulcerative colitis activity and severity. The significant correlations between these biomarkers and clinical parameters reinforce their utility as valuable tools in UC management. While our findings are consistent with much of the existing literature, the observed discrepancies, particularly regarding disease extent and smoking prevalence, suggest the need for further investigation into the influence of regional, demographic, and methodological factors. Overall, this research supports the role of these biomarkers in facilitating more personalized and less invasive approaches to ulcerative colitis diagnosis and monitoring

Conclusion:

Cases with ulcerative colitis exhibit significantly elevated levels of serum MMP-9 and fecal calprotectin, which are correlated with disease activity. These markers can serve as valuable non-invasive tools in evaluating the UC severity.

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