Al-Azhar International Medical Journal

Volume 4 | Issue 7 Article 6

2023

Fecal Calprotectin as a Disease Activity and Prognostic Marker in Ulcerative Colitis

Mohamed Abdelrashed AbdelKhalik
Gastroenterology, Hepatology and infectious diseases department, Faculty of Medicin, Al-Azhar University, Cairo, Egypt

Mohamed Ghareeb Mohamed
Gastroenterology, Hepatology and infectious diseases department, Faculty of Medicin, Al-Azhar University, Cairo, Egypt

Amr Ahmed Rezk
Gastroenterology, Hepatology and infectious diseases department, Faculty of Medicin, Al-Azhar University, Cairo, Egypt

Ahmed Elsherbiny Ibrahim Gomaa
Gastroenterology, Hepatology and infectious diseases department, Faculty of Medicin, Al-Azhar University, Cairo, Egypt, a.elsherbiny168@gmail.com

How to Cite This Article

AbdelKhalik, Mohamed Abdelrashed; Mohamed, Mohamed Ghareeb; Rezk, Amr Ahmed; and Gomaa, Ahmed Elsherbiny Ibrahim (2023) "Fecal Calprotectin as a Disease Activity and Prognostic Marker in Ulcerative Colitis," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 7, Article 6.
DOI: https://doi.org/10.58675/2682-339X.1910

ORIGINAL ARTICLE

Fecal Calprotectin as a Disease Activity and Prognostic Marker in Ulcerative Colitis

Ahmed Elsherbiny Ibrahim Gomaa [a,*], Mohamed Abdelrashed AbdelKhalik [a], Mohamed Ghareeb Mohamed [a], Amr Ahmed Rezk [b]

[a] Gastroenterology, Hepatology and Infectious Diseases Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[b] Clinical Pathology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Abstract

Background: **Ulcerative colitis (UC) is identified through endoscopy and biopsies. Endoscopy assesses a disease's severity. Calprotectin is a 24 kDa dimer of S100A8 and S100A9 calcium-binding proteins. Inflammatory bowel illnesses, celiac disease, and viral colitis elevate calprotectin levels in feces.**

Aim: **To examine the fecal calprotectin (FC) level in UC as a predictor of disease activity and prognosis as well as its correlation with other blood inflammatory markers.**

Patients and methods: **This cohort prospective study involved 150 cases who were subjected to colonoscopy at Al-Azhar University Hospitals endoscopy units.**

Patients were equally classified after colonoscopic examination into three groups: Group I consists of 50 patients with free colonoscopic examination. Group II 50 patients confirmedly diagnosed as UC after histopathological examination and Group III consists of 50 patients with colonoscopic disease rather than UC. Further subgrouping of Group II: Group II (A):50 patients confirmedly diagnosed as UC after histopathological examination before treatment. Group II (B): 50 patients confirmedly diagnosed as UC after histopathological examination after 3 months of specific treatment.

Results: **Group II had considerably more FC than group III, while FC was significantly lowest in group I than the other two groups. In group II, there is a significant positive correlation among FC with C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and total leukocyte count (TLC). Meanwhile, there is a significant positive correlation among FC with CRP and ESR in group III. FC yielded significance at a cut-off level of 184 μg/g with an AUC of 0.845 with 87.5% sensitivity and 76.8% specificity.**

Conclusion: **FC is considered a quick, reasonably priced, noninvasive diagnostic marker for UC disease activity and prognosis with high accuracy, sensitivity, and specificity. FC levels is a reliable indicator of UC severity due to their correlation with other markers (ESR, CRP, and TLC).**

Keywords: Fecal calprotectin, Prognostic marker, Ulcerative colitis

1. Introduction

Inflammatory bowel disease (IBD) is a worldwide health issue with an increasing prevalence.[1]

It consists of two basic types, ulcerative colitis (UC) and Crohn's disease (CD), both are distinct relapsing chronic inflammatory colon diseases.[2]

According to a research done over 15 years by Mostafa et al.[3] in Egypt, UC is much more prevalent than CD. The ratio of patients identified with UC to those diagnosed with CD was approximately 6:1.

Usually, UC begins in the rectum and proximally extend without interruption to involve the entire colon. UC mostly result from interplay between several genetic and environmental risk factors.[4]

Endoscopy and mucosal biopsies for histopathology provide the most accurate diagnosis of UC. In addition, laboratory research and imaging examinations aid in establishing an accurate diagnosis.[5]

Accepted 2 January 2023.
Available online 7 November 2023

* Corresponding author at: Gastroenterology, Hepatology and Infectious Diseases Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.
E-mail address: a.elsherbiny168@gmail.com (A.E.I. Gomaa).

https://doi.org/10.58675/2682-339X.1910

Nevertheless, it is a challenging problem and a significant topic of attention. Endoscopic and histological examinations, notwithstanding their practical success, are intrusive, expensive, and fraught with problems.[6]

Based on what a clinician observes during an endoscopy, an endoscopic scoring index evaluates disease activity. Common endoscopic indices consist of the UC Endoscopic Index of Severity, the Baron Score, the Mayo Clinic Endoscopic Score, and the UC Endoscopic Index.[7]

With sensitivities and specificities ranging from 50 to 60%, different studies have utilizing laboratory indicators as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) for UC activity assessment.[8] Although, a perfect test has not yet been established. Therefore, the supplementary use of additional blood markers contributes significantly to illness severity prediction and diagnostic accuracy.[9]

Calprotectin is a 24 kDa dimer of S100A8 and S100A9 calcium-binding proteins. The complex, which contains more than 60% of the soluble protein content of neutrophil cytosol, can serve as an indicator of intestinal inflammation.[10] In vitro research demonstrates that calprotectin exhibits bacteriostatic and fungistatic capabilities due to its capacity to bind manganese and zinc.[11]

IBD, untreated celiac disease, necrotizing enterocolitis, infectious colitis, colorectal cancer, and intestinal cystic fibrosis are the primary causes of the higher fecal calprotectin (FC) excretion, and high FC is a frequent observation among hospitalized coronavirus disease 2019 (COVID-19) cases, particularly those with SARS-CoV-2 fecal shedding.[12] This research objects to examine the FC level in UC as a predictor of disease activity and prognosis, as well as its association with other blood inflammatory indicators.

2. Patients and methods

This cohort prospective research involved 150 cases who were subjected to colonoscopy at Al-Azhar University Hospitals endoscopic units. An informed written consent was obtained from the case or relatives of the cases. The research was performed after approval from the Ethics Committee at Al-Azhar University Hospitals (79) from March 2022 to September 2022.

Pregnant female, breast feeder, and/or patients younger than 18 years were excluded and patients with a history of colonic malignancy, surgery, or history of UC treatment for last 3 months were excluded.

Patients were equally classified after colonoscopic examination into three groups: Group I: Consist of 50 patients with free colonoscopic examination. Group II: 50 patients confirmedly diagnosed as UC after histopathological examination and Group III: 50 patients with colonoscopic disease rather than UC. Further subgrouping of Group II: Group II (A): 50 patients confirmedly diagnosed as UC after histopathological examination before treatment. Group II (B): 50 patients confirmedly diagnosed as UC after histopathological examination after 3 months of specific treatment.

Using the UC activity index (UCAI) scoring method, we obtained baseline case information and assessed illness severity by subjective patient interviews. After applying a tourniquet to each case, blood specimens were obtained to determine the blood cell count and ESR.

A single expert gastroenterologist performed ileocolonoscopy with numerous mucosal biopsies on cases who were eligible. Evaluation of colonoscopic disease activity utilizing the Mayo Disease AI (0: normal mucosa, 1: erythema, 2: erosion, 3: ulcer). Those with Mayo disease AI scores $\geq$2 were deemed to have active UC.

On the day of colonoscopy, stool specimens were also obtained in screw-capped plastic containers and stored at −70 °C. FC was determined utilizing calprotectin ELISA kits (Demeditec Diagnostics GmbH, Germany). Regarding the manufacturer's recommendations, stool extracts were produced and tested for FC. The FC concentration was represented as ng/ml. The diagnostic value of the FC compared with Mayo disease AI as the gold standard approach was then evaluated.

The selected cases underwent full history taking, general examination and local abdominal examination, and **Laboratory investigations** to detect FC (CRP, ESR, and the complete blood count), and stool specimens were tested. **Radiological investigations were performed** to rule out the presence of additional disorders using abdominal ultrasonography.

Also, colonoscopy and histopathology was performed to determine the severity of the disease using the Mayo score; a complete colonoscopy with effective intubation of the terminal ileum was applied. Several specimens were obtained.

A combination of clinical, endoscopic, radiographic, and histological evidence were required to diagnose UC. As infective colitis may mirror the symptoms of ulcerative colitis, this was often sought and eliminated.

Substantial numbers of activated granulocytes and monocytes/macrophages are extravasated

into the colonic mucosa in active UC. These infiltrating leukocytes might induce significant mucosal tissue damage through releasing degradative proteases, reactive oxygen derivatives, and proinflammatory cytokines; pathogens promote inflammation.

2.1. Sample size calculation

Sample size calculation was done by G*Power 3.1.9.2 (Universitat Kiel, Germany). The calculation depends on the following: 90% power, 5% confidence limit, the expected correlation coefficient was 0.73 between FC and total leukocyte count (TLC) according to the previous study.[13] Therefore, 150 patients should be included in the study.

2.2. Statistical analysis

Using SPSS 22.0 for Windows, all data were gathered, tabulated, and statistically examined (SPSS Inc., Armonk, IL, USA). The variance between the qualitative variables was calculated using the chi square test and Fisher's exact. Thus, to compare more than two dependent groups with normally distributed variables, one-way ANOVA test was used and the Kruskal–Wallis test was used to analyze variables with non-normal distribution. The paired *t*-test used to compare variables were not regularly distributed, whereas the Wilcoxon-signed ranks test was used to examine properly distributed data. Pearson correlation was done to estimate the degree of correlation among two quantitative variables. Overall diagnostic performance was evaluated using ROC curve analysis, where an ideal test would have a curve that starts in the bottom left, moves to the top left, and finishes in the top right. The total performance of the test is measured by the area under the curve (AUC), where an AUC greater than >50% indicates satisfactory performance and an AUC around 100% indicates optimal performance. A two tailed P value < 0.05 was considered statistically significant.

3. Results

Table 1 Shows no significant variance among the groups regarding age, Sex, and BMI.

Table 2 shows that there was a significant variance among the groups regarding mucous diarrhea, vomiting, nausea, weight loss, and severe bowel movement urgency was significantly higher in group II and group III than group I, while abdominal pain or cramps was insignificantly different among the groups.

Table 3 shows that there was a significant variance among the groups regarding Hb, TLC, ALT, AST, CRP, ESR and FC, which was significantly higher among group II than group III, while FC was significantly lowest among group I than the other two ones.

Fig. 1 shows that the prevalent grade was mild activity (48%), 40% of the patients were of moderate activity, and 12% were of severe activity.

Table 4 shows that there is a significant decrease in TLC, CRP, ESR, and FC after treatment among UC patients. Meanwhile, there is a significant increase in hemoglobin among UC patients.

Table 5 shows that FC before and after treatment were significantly higher among severe cases than moderate and mild ones. FC was significantly lower after treatment compared with before treatment according to severity of disease.

Table 6 shows that there is a significant positive correlation among FC with TLC, CRP, and ESR among group II. Meanwhile, there is a significant positive correlation among FC with CRP and ESR among group III.

Table 7, Fig. 2 shows that FC yielded significance at a cut-off level of 184 μg/g with an AUC of 0.845 with a sensitivity of 87.5% and a specificity of 76.8%.

Table 8, Fig. 3 shows that FC yielded significance in moderate to severe UC before treatment at a cut-off level of >864 μg/g with an AUC of 0.992 and $P < 0.001$with a sensitivity of 100% and a specificity of 95% and after treatment at a cut-off level of >148 μg/g with an AUC of 0.871 and $P < 0.001$with a sensitivity of 83.3% and a specificity of 75% and yielded insignificance in mild-moderate before and after treatment.

Table 1. Demographic characteristics and clinical data among the studied groups.

	Group I ($n = 50$)	Group II ($n = 50$)	Group III $n = 50$)	F	*P*
Age (years)	42.61 ± 10.75	43.91 ± 11.16	42.34 ± 11.62	0.281	0.755
Sex					
Female	23 (46%)	20 (40%)	19 (38%)	0.715	0.700
Male	27 (54%)	30 (60%)	31 (62%)		
BMI (kg/m^2)	26.49 ± 2.7	27.16 ± 3.68	26.73 ± 3.45	0.528	0.591

Data are presented as Mean ± SD or frequency (%), BMI: Body mass index.

Table 2. Demographic characteristics and clinical data among the studied groups.

	Group I (n = 50)	Group II (n = 50)	Group III (n = 50)	X^2	P
Mucous diarrhea	0 (0%)	30 (60%)	31 (62%)	51.45	<0.001
Abdominal pain or cramps	15 (30%)	20 (40%)	22 (44%)	2.22	0.332
Vomiting	10 (20%)	35(70%)	30 (60%)	28.0	<0.001
Nausea	17 (34%)	36 (72%)	20 (40%)	16.70	0.002
Weight loss	14 (28%)	34 (68%)	37 (74%)	25.47	<0.001
Severe bowel movement urgency	0 (0%)	25 (50%)	30 (60%)	44.50	<0.001

P value < 0.05 as considered significant.

Table 3. Laboratory parameters between the three groups.

	Group I (n = 50)	Group II (before treatment) (A) (n = 50)	Group III (n = 50)	F	P
Hb (g/dl)	13.18 ± 1.22	10.87 ± 1.67	11.19 ± 1.81	31	<0.001
TLC (x 10^3/l)	6.58 ± 1.69	13.75 ± 2.42	9.13 ± 1.83	164	<0.001
PLT (x 10^3/l)	288.35 ± 52.23	275.32 ± 48.51	269.85 ± 46.15	1.88	0.156
ALT (U/l)	22.94 ± 5.86	27.32 ± 6.31	25.46 ± 5.54	6.91	0.001
AST (U/l)	21.17 ± 5.34	25.48 ± 5.84	23.36 ± 5.33	7.65	0.001
Total bilirubin (mg/dl)	0.59 ± 0.181	0.625 ± 0.173	0.647 ± 0.168	1.36	0.259
Albumin (g/dl)	4.23 ± 0.382	4.06 ± 0.367	4.15 ± 0.321	2.83	0.062
INR	1.03 ± 0.065	1.01 ± 0.055	1.01 ± 0.062	1.8	0.168
Creatinine (mg/dl)	0.853 ± 0.182	0.937 ± 0.179	0.911 ± 0.185	2.79	0.065
Urea (mg/dl)	20.1 ± 4.21	22.82 ± 8.24	21.54 ± 6.51	2.17	0.118
CRP (mg/l)	4.45 ± 1.56	23.76 ± 4.2	16.37 ± 3.21	184	<0.001
ESR (mm/h)	19.62 ± 8.71	48.54 ± 12.63	36.47 ± 10.8	89	<0.001
FC (μg/g)	63.7 ± 14.52 40–82	562.9 ± 237.2 231–884	387.3 ± 154.65 125–692	120	<0.001

Data are presented as mean ± SD.
ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FC, fecal calprotectin; Hb, hemoglobin; INR, international normalized ratio; PLT: platelets; TLC: total leukocyte count.
P value < 0.05 as considered significant.

4. Discussion

Clinical management of UC requires accurate assessment of disease activity. Colonoscopy and biopsy are now the most reliable methods for determining the severity of UC and the degree of inflammation.[14]

During inflammation, FC is a common neutrophil protein that infiltrates the mucosa.

Fig. 1. Activity grade distribution among group II.

Table 4. Clinical characteristics before and after treatment among group II.

	Group II ($n = 50$)		Pt	P
	Before treatment (II A)	After treatment (II B)		
Hb (g/dl)	10.87 ± 1.67	12.35 ± 1.19	5	<0.001
TLC (x 10^3/l)	13.75 ± 2.42	6.87 ± 1.22	16	<0.001
PLT (x 10^3/l)	275.32 ± 48.51	293.7 ± 30.62	1.3	0.319
ALT (U/l)	27.32 ± 6.31	26.41 ± 4.87	1.3	0.215
AST (U/l)	25.48 ± 5.84	24.16 ± 4.72	1.6	0.168
Creatinine (mg/dl)	0.937 ± 0.179	0.921 ± 0.156	0.476	0.648
CRP (mg/l)	23.76 ± 4.2	6.53 ± 2.16	27	<0.001
ESR (mm/h)	48.54 ± 12.63	23.45 ± 9.24	12	<0.001
FC (μg/g)	562.9 ± 237.2	136.7 ± 54.6	15	<0.001

Data are presented as mean ± SD.
ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FC, fecal calprotectin; Hb, hemoglobin; INR, international normalized ratio; PLT, platelets; TLC, total leukocyte count.
P value < 0.05 as considered significant.

Table 5. Fecal calprotectin among group II according to disease activity.

FC (μg/g)	Mild ($n = 24$)	Moderate ($n = 20$)	Severe ($n = 6$)	KW	P
Before treatment					
Mean ± SD	424.71 ± 189.6	597.7 ± 164.9	1101.3 ± 157.8	24.3	<0.001
Range	220–867	397–964	845–1320		
After treatment					
Mean ± SD	100.75 ± 40.27	125.75 ± 28.77	197 ± 51.42	16.3	<0.001
Range	51–214	89–189	124–260		
	<0.001	<0.001	<0.001		

FC, fecal calprotectin, *P* value < 0.05 as considered significant.

Table 6. Correlation between fecal calprotectin level and inflammatory markers.

	Group II ($n = 50$)		Group III ($n = 50$)	
	R	P	r	P
Age	0.213	0.367	0.293	0.109
BMI	0.264	0.081	0.241	0.125
TLC	**0.473**	0.001	0.311	0.078
PLT	0.221	0.118	0.213	0.127
ALT	0.302	0.143	0.322	0.138
AST	0.293	0.381	0.206	0.177
Creatinine	0.241	0.163	0.387	0.154
CRP	0.602	<0.001	0.393	0.005
ESR	0.542	<0.001	0.376	0.009

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; PLT, platelets; TLC, total leukocyte count.
P value < 0.05 as considered significant.

Data support its utilization in differentiating irritable bowel syndrome (IBS) from IBD and measuring abdominal pain. According to extensive study, the FC level correlates closely with histological, endoscopic, and clinical indications of disease activity in instances of UC. As noted by some researchers, FC may better indicate disease activity in UC than in CD. FC assessment might be effective in expecting clinical relapse in CD and UC cases,

Table 7. Validity of FC as a predictor of ulcerative colitis activity.

Cut-off	AUC	S.E.	Sig.	95% CI	Sensitivity	Specificity
184	0.845	0.051	<0.001	0.771–0.989	87.5%	76.8%

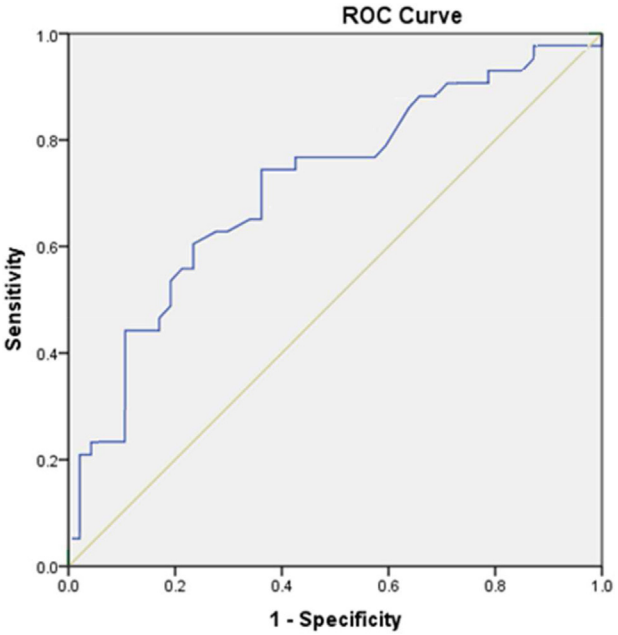

Fig. 2. ROC curve of fecal calprotectin as a predictor of ulcerative colitis activity.

Table 8. Validity of FC as a predictor of ulcerative colitis severity.

	Cut-off	AUC	*P* value	Sensitivity	Specificity
Moderate to severe before treatment	>864	0.992	<0.001*	100	95
Moderate to severe after treatment	>148	0.871	<0.001*	83.33	75
Mild to moderate before treatment	>557	0.660	0.052	75	54.17
Mild to moderate after treatment	≤167	0.244	0.244	80	33.33

particularly over the subsequent 3 months. FC may also be used to evaluate therapy response.[15]

To examine the relationship between the level of FC and other blood inflammatory markers as well as its predictive value for disease activity and prognosis in UC was the major goal of this research.

Our findings were corroborated by research by Nouh et al.,[13] who found that GIa (active UC) had significantly lower mean hemoglobin values than the other groups while showing a highly significant rise in the mean TLC, platelet count (PLT), ESR, and CRP. According to the current study, compared with group III, group II showed noticeably higher amounts of FC.

Group I had significantly lower amounts of FC than the other two groups.

The FC concentration among UC and control cases differed significantly (*P* 0.05), according to the Chen et al. study's,[15] which is consistent with our findings.

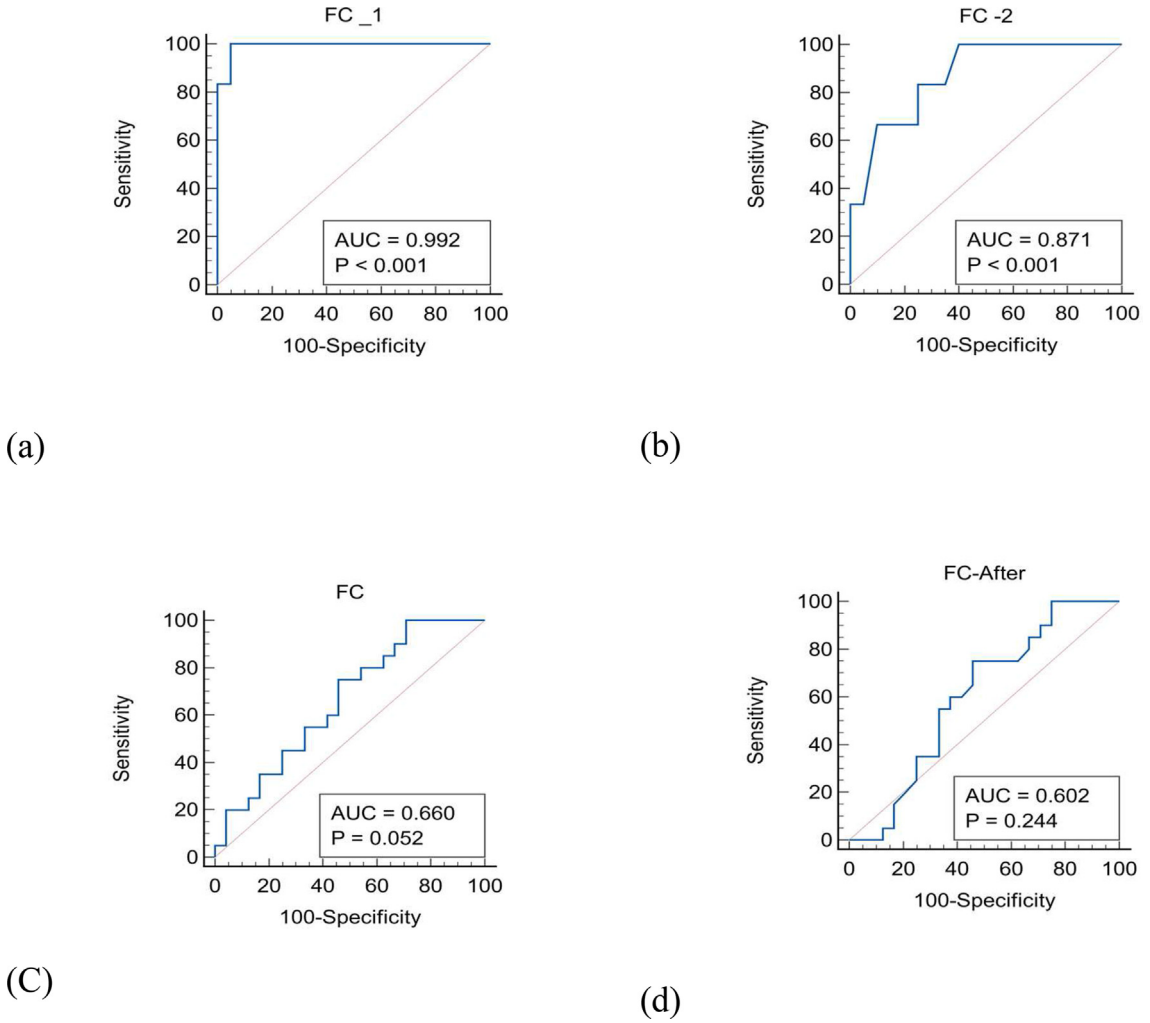

Fig. 3. ROC curve of fecal calprotectin as a predictor of ulcerative colitis severity (a) Moderate to severe before, (b) Moderate to severe after, (c) Mild-moderate before, (D) Mild-moderate after.

The FC values were 38 (30–102.5), 220.5 (87–367.75), 1138 (340.50–2699), and 2481 (1573–4067) g/g when each stage was categorized by Mayo scores. Patients with mild disease, moderate disease, and moderate and severe disease were all shown to have significantly different FC levels. In addition, according to Nouh et al.,[13] active UC cases had a mean FC value that was significantly elevated than that of controls and inactive UC cases.

Our results were in line with Chen et al.[15] who discovered that 49 patients (34.27%) had mild, 41 cases (28.67%) had moderate, and 7 cases (4.90%) had severe disease activity based on Mayo scores.

The present study showed that as regards clinical characteristics before and after treatment among group II, there is a significant decrease in TLC, CRP, ESR, and FC after treatment among UC patients. Meanwhile, there is a significant increase in hemoglobin among UC patients.

According to Ghweil et al.,[16] the levels of FC were statistically different in those with active UC compared with the control group and those with inactive UC. Cases with active UC exhibited significantly elevated CRP and ESR than those in the inactive or control groups.

Our findings exhibited waste FC, with an AUC of 0.845, responsiveness of 87.5%, and particularity of 76.8%, was a huge indicator of UC movement at an end level of 184 ng/g.

In the same context, the study by Garca-Sánchez et al.[17] found that FC may be a valuable measure for relapse prediction in IBD cases. Compared with ileal CD, its predictive value is higher in UC and CD with colon involvement and an inflammatory pattern.

The Nouh et al. research[13] review found that FC is a helpful, straightforward, readily administered, and cost-effective noninvasive marker for UC case assessment. It distinguished UC and other disorders generating colonic signs (cut-off of 131 μg/g) and among active and inactive UC (cut-off of 235 μg/g) with elevated accuracy, sensitivity, and specificity. It also correlates strongly with other markers for UC activity (UCAI, ESR, CRP, total leukocyte count, and PLT) and might be a reliable surrogate indicator for UC severity.

A recent systematic review[18] demonstrated that noninvasive fecal markers, such as FC, are potential MH biomarkers. It is essential that noninvasive indicators become accessible for regular clinical utilization. In other words, this might permit for a more frequent evaluation of inflammation, leading to more rapid clinical choices, and perhaps lessen the need for additional endoscopies. FC diagnostic efficiency was demonstrated in Schoepfer's study,[19] a cut-off of 50 μg/g is optimal for predicting mucosal inflammation. The correlation among FC with both Mayo endoscopic subscore 0 or Mayo endoscopic subscore 0 and 1 defining MH was described by Yamaguchi *et a*l.[20] Not unexpectedly, when the Mayo 0 score was utilized, specificity and PPV were higher. On the basis of the interpretations of the ROC graphs using UCEIS to define MH, a cut-off FC level of 154.5 g/g was determined to predict MH. It is not unexpected that no consensus has been reached about a suitable FC cut-off level for MH prediction.[1]

Moreover, Chen et al.[15] showed a significant connection between the FC levels, Mayo grades, and the UC Endoscopic File of Seriousness (UCEIS) scores. This was in line with Grgi et al.[21]

4.1. Conclusion

FC is considered a quick, reasonably priced, noninvasive diagnostic marker for UC disease activity and prognosis with high accuracy, sensitivity, and specificity. FC levels is a reliable indicator of UC severity due to their correlation with other markers (ESR, CRP, and TLC).

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors declared that there were no conflicts of interest.

References

1. Kristensen V, Klepp P, Cvancarova M, Røseth A, Skar V, Moum B. Prediction of endoscopic disease activity in ulcerative colitis by two different assays for fecal calprotectin. *J Crohns Colitis*. 2015;9:164–169.
2. Balderramo D, Trakal J, Herrera Najum P, et al. High ulcerative colitis and Crohn's disease ratio in a population-based registry from Córdoba, Argentina. *Dig Liver Dis*. 2021;53:852–857.
3. Mostafa EF, Metwally A, Hussein SA. Inflammatory bowel diseases prevalence in patients underwent colonoscopy in

Zagazig University Hospitals. *Afro Egypt J Infect Endem Dis*. 2018;8:81–87.
4. Călin R, Nuţă P. Therapeutic management in ulcerative colitis. *Med Int*. 2018;15:1–3.
5. Rodrigues BL, Mazzaro MC, Nagasako CK, Ayrizono MLS, Fagundes JJ, Leal RF. Assessment of disease activity in inflammatory bowel diseases: non-invasive biomarkers and endoscopic scores. *World J Gastrointest Endosc*. 2020;12:504–520.
6. Okba AM, Amin MM, Abdelmoaty AS, et al. Neutrophil/lymphocyte ratio and lymphocyte/monocyte ratio in ulcerative colitis as non-invasive biomarkers of disease activity and severity. *Auto Immun Highlights*. 2019;10:4.
7. Vashist NM, Samaan M, Mosli MH, et al. Endoscopic scoring indices for evaluation of disease activity in ulcerative colitis. *Cochrane Database Syst Rev*. 2018;1:125–130.
8. Soomro S, Venkateswaran S, Vanarsa K, et al. Predicting disease course in ulcerative colitis using stool proteins identified through an aptamer-based screen. *Nat Commun*. 2021;12:39–45.
9. Duijvestein M, Battat R, Vande Casteele N, et al. Novel therapies and treatment strategies for patients with inflammatory bowel disease. *Curr Treat Options Gastroenterol*. 2018;16:129–146.
10. Peretz A, Tkhawkho L, Pastukh N, Brodsky D, Halevi CN, Nitzan O. Correlation between fecal calprotectin levels, disease severity and the hypervirulent ribotype 027 strain in patients with Clostridium difficile infection. *BMC Infect Dis*. 2016;16:309–315.
11. Hoskin TS, Crowther JM, Cheung J, et al. Oxidative cross-linking of calprotectin occurs in vivo, altering its structure and susceptibility to proteolysis. *Redox Biol*. 2019;24:101–110.
12. Zerbato V, Di Bella S, Giuffrè M, et al. High fecal calprotectin levels are associated with SARS-CoV-2 intestinal shedding in COVID-19 patients: a proof-of-concept study. *World J Gastroenterol*. 2021;27:3130–3137.
13. Nouh MA, Ali AA, El Halim EF, Mohamed HI, El Ghany AM, Badawy AM. Calprotectin as a fecal marker for diagnosis and follow-up in patients with ulcerative colitis. *Menoufia Med J*. 2014;27:35–42.
14. Kucharzik T, Koletzko S, Kannengiesser K, Dignass A. Ulcerative colitis-diagnostic and therapeutic algorithms. *Dtsch Arztebl Int*. 2020;117:564–574.
15. Chen F, Hu Y, Fan Y-H, Lv B. Clinical value of fecal calprotectin in predicting mucosal healing in patients with ulcerative Colitis. *Front Med*. 2021;8:125–129.
16. Ghweil A, Khodeary A, Aziz SP. Diagnostic value of fecal calprotectin and serum MMP-9 in diagnosing disease activity of ulcerative colitis. *Open J Gastroenterol*. 2018;8:234–239.
17. García-Sánchez V, Iglesias-Flores E, González R, et al. Does fecal calprotectin predict relapse in patients with Crohn's disease and ulcerative colitis? *J Crohns Colitis*. 2010;4:144–152.
18. Boon GJ, Day AS, Mulder CJ, Gearry RB. Are faecal markers good indicators of mucosal healing in inflammatory bowel disease? *World J Gastroenterol*. 2015;21:11469–11480.
19. Schoepfer AM, Beglinger C, Straumann A, Trummler M, Renzulli P, Seibold F. Ulcerative colitis: correlation of the Rachmilewitz endoscopic activity index with fecal calprotectin, clinical activity, C-reactive protein, and blood leukocytes. *Inflamm Bowel Dis*. 2009;15:1851–1858.
20. Yamaguchi S, Takeuchi Y, Arai K, et al. Fecal calprotectin is a clinically relevant biomarker of mucosal healing in patients with quiescent ulcerative colitis. *J Gastroenterol Hepatol*. 2016;31:93–98.
21. Grgić D, Golubić K, Brinar M, Krznarić Ž. Predictive value of faecal calprotectin in ulcerative colitis - single centre experience. *Ann Med*. 2022;54:1570–1577.