EVALUATION OF THE ROLE OF FECAL CALPROTECTIN AS A BIOMARKER OF ENDOSCOPIC DISEASE ACTIVITY IN PATIENTS WITH CROHN'S DISEASE

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ABSTRACT

Introduction: Crohn's disease is a chronic inflammatory bowel illness with transmural inflammation and diverse clinical manifestations. Accurate assessment of disease activity is required to guide treatment and improve patient outcomes. This study assessed the diagnostic efficacy of fecal calprotectin as a biomarker of endoscopic disease activity in patients with Crohn's disease undergoing biologic therapy. **Methods**: We conducted this prospective cohort study of 70 patients at Baghdad Teaching Hospital/Medical City between January 2024 and January 2025. We measured disease activity using the Simple Endoscopic Score for Crohn's Disease (SES-CD). We classified endoscopic activity as remission (0-2), mild activity (3-6), moderate activity (7-15), or severe activity (≥16). **Results:** Among the 70 patients, 51 (72.8%) were in remission, while 19 (27.2%) had active disease after treatment. Active patients had significantly higher post-treatment fecal calprotectin levels than those in remission (367.89 vs. 111.83 µg/g, $P < .001$). ROC analysis showed an area under the curve of 0.835 ($P < .001$). A fecal calprotectin cutoff of ≥148.5 µg/g resulted in 89.4% sensitivity, 70.6% specificity, 53.1% positive predictive value, and 94.7% negative predictive value. **Conclusion:** Fecal calprotectin effectively detects endoscopic disease activity in patients with Crohn's disease. Its high sensitivity and negative predictive value suggest it could be useful as a noninvasive monitoring tool, but the results should be interpreted in the context of this single-center investigation.

Keywords: fecal calprotectin; Crohn's disease; biomarkers; endoscopic disease activity; biologic therapy

INTRODUCTION

Crohn's disease (CD) is an idiopathic inflammatory condition with unknown causes comprising genetic, immunologic, and environmental components. CD is distinguished by transmural inflammation and can affect any part of the gastrointestinal tract, from the mouth to the perianal region (Zeind et al., 2024). Approximately 40%-50% of Crohn's disease patients involve the ileum alone (ileitis), 40% include both the ileum and colon (ileocolitis), and 30% involve only the colon. One-third of patients had perianal illness, such as fistulas, fissures, or abscesses (Dulai et al. 2019).

Crohn's disease incidence rates vary by area, with estimates ranging from 4.1 to 22.78 per 100,000 in Europe, 0.09 to 3.6 per 100,000 in Asia and the Middle East, 13.23 to 26.0 per 100,000 in Oceania, and 0.04 to 0.64 per 100,000 in South America. These estimates reflect different study periods and regions (Caron et al., 2024).

Prevalence estimates ranged from 61.6 to 178 per 100,000 in Europe, 0.34 to 14.9 per 100,000 in South America, and 146 to 201 per 100,000 in North America. In children and adolescents, incidence rates ranged from 1.7 to 6.8 per 100,000 in Europe, 0.19 to 1.53 per 100,000 in Asia and the Middle East, and 6.0 to 7.9 per 100,000 in North America (Zhang et al., 2023).

A recent meta-analysis of 2,145 patients, 1,059 of whom had inflammatory bowel disease, found pooled fecal calprotectin sensitivity and specificity of 88% (95% CI, 80%-93%) and 72% (95% CI, 59%-82%), respectively, for distinguishing inflammatory bowel disease from irritable bowel syndrome (Bencardino et al., 2024). Several fecal biomarkers have been proposed; however, fecal calprotectin remains one of the most thoroughly researched markers for discriminating between inflammatory and functional gastrointestinal disorders (Vernia et al., 2020; Di Ruscio et al., 2018).

FC is an effective fecal marker in the care of CD, optimizing the use of endoscopic procedures (Vernia et al., 2020). FC is a consistent predictor of disease activity in CD patients, including those with ileal CD. FC is thus advised for routine follow-up in CD patients (Li et al., 2023). Fecal calprotectin is highly effective in detecting endoscopic ulcers regardless of CD location; however, it requires a lower threshold value in patients with pure ileal involvement (Buisson et al., 2021). Normalizing FC within 12 months of diagnosis is associated with a lower risk of Crohn's disease development (Plevris et al., 2021).

The purpose of this study was to assess fecal calprotectin's diagnostic efficacy in detecting endoscopic disease activity in Crohn's disease patients on biologic therapy.

METHODS

We conducted the study at Baghdad Teaching Hospital/Medical City, Baghdad, Iraq. We collected data from January 2024 to January 2025 using a prospective cohort design.

Inclusion criteria were a histopathologically confirmed diagnosis of moderate-to-severe Crohn's disease, treatment with biologic therapy, complete clinical records, and commitment to follow-up.

Patients with the following conditions were excluded from the study:

- History of colorectal malignancy.
  Use of medications that may alter intestinal mucosal integrity, such as non-steroidal anti-inflammatory drugs (NSAIDs) or proton pump inhibitors (PPIs) within four weeks prior to sample collection.
- Patients with decompensated heart failure, pulmonary, or renal disease.
- Pregnant or lactating women.

A total of 70 patients were included using purposive sampling. Before initiation of biologic therapy, baseline characteristics (age, sex, BMI, and comorbidities) were recorded. Fecal calprotectin and serum CRP were measured, and colonoscopy was performed to confirm the diagnosis and evaluate disease extent and activity. Disease activity was assessed using the SES-CD, which generates a total score from 0 to 56 based on four variables recorded across five segments: terminal ileum, right colon, transverse colon, left colon, and rectum.

1. Size of ulcers: (0) None; (1) aphthous ulcers: 0.1–0.5 cm; (2) large ulcers:
0.5–2 cm); (3) very large ulcers: >2 cm).
2. Ulcerated surface: (0) None; (1) 10%; (2) 10%–30%; (3) >30%.
3. Affected surface: (0) Unaffected segment; (1) 50%; (2) 50–75%; (3)
>75%.
4. Presence of narrowings: (0) None; (1) Single, can be passed; (2) Multiple,

can be passed; (3) Cannot be passed.

We calculated the total SES-CD as the sum of the segmental scores. We categorized endoscopic disease activity as remission (0–2), mild (3–6), moderate (7–15), or severe (≥16).

We collected stool samples early in the morning before bowel preparation or endoscopy and transported them to the institutional research laboratory under controlled temperature conditions within 2 hours of collection. We stored samples at −20°C until analysis. Fecal calprotectin concentrations were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Aeskulisa) designed for quantitative detection of human calprotectin in fecal samples. We performed the assay according to the manufacturer's protocol.

Results were expressed as micrograms of calprotectin per gram of stool (μg/g). According to the ELISA kit, the reference range was:

Negative: <35 μg/g

Positive: ≥35 μg/g

The Iraqi Board for Medical Specializations approved the study. We obtained written informed consent from all participants before enrollment.

Statistical analysis included comparison of baseline and post-treatment fecal calprotectin and C-reactive protein concentrations between the remission and active-disease groups. We used receiver operating characteristic (ROC) analysis to assess the ability of fecal calprotectin to discriminate active endoscopic disease from remission. We calculated the area under the ROC curve (AUC), sensitivity, specificity, positive predictive value, and negative predictive value, and selected the cutoff with the highest combined sensitivity and specificity.

RESULTS

Among the 70 patients, 51 (72.8%) achieved remission, whereas 19 (27.2%) had active disease after treatment, as shown in Figure 1.

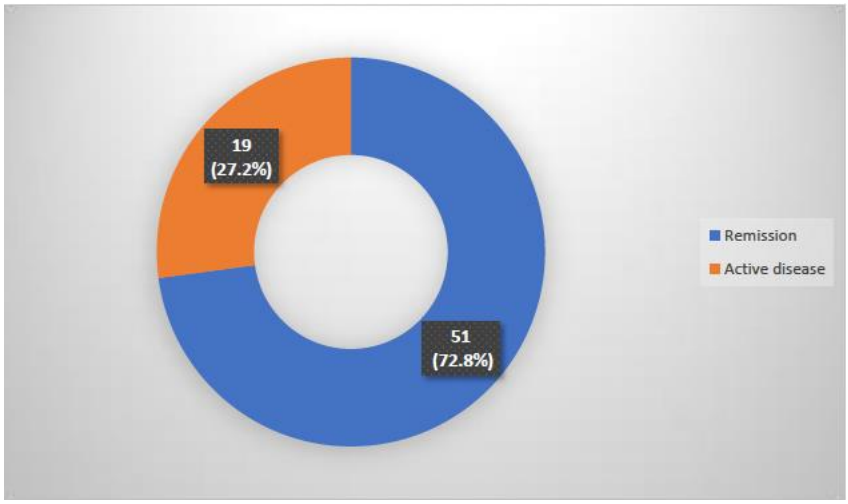

Figure 1: Distribution of patients according to remission rate after 1 year of treatment.

The two study groups did not differ significantly in age, sex, or BMI, as shown in Table 1.

Table 1: Comparison of baseline characteristics between the study groups.

Variable	Group		P value
	Remission (N=51)	Active disease (N=19)	
Age			
12-17 years	8	2	0.381
	15.7%	10.5%	
18-39 years	33	16	
	64.7%	84.2%	
40 years and above	10	1	
	19.6%	5.3%	
Mean ± SD	29.04 ± 12.18	26.37 ± 8.25	

Sex			
Male	33	14	0.575
	64.7%	73.7%	
Female	18	5	
	35.3%	26.3%	
BMI			
Normal weight	36	8	0.070
	70.6%	42.1%	
Overweight	11	7	
	21.6%	36.8%	
Obese	4	4	
	7.8%	21.1%	

The study groups did not differ significantly in baseline SES-CD score, type of biologic therapy, or comorbidities (Table 2).

Table 2: Comparison of clinical characteristics between the study groups.

Variable	Group		P value
	Remission (N=51)	Active disease (N=19)	
Baseline SES			
Mean ± SD	11.57 ± 3.90	11.95 ± 4.42	0.607
Type of biologic therapy			
Infliximab	40	12	0.325
	78.4%	63.2%	
Ustekinumab	6	5	
	11.8%	26.3%	
Adalimumab	5	2	
	9.8%	10.5%	
Comorbidities			
DM	7	3	1.000

	13.7%	15.8%	
Hypertension	8	5	0.301
	15.7%	26.3%	
Cardiovascular disease	4	2	0.660
	7.8%	10.5%	

Before treatment, the active-disease and remission groups did not differ significantly in fecal calprotectin (258.26 ± 180.37 vs. 263.12 ± 210.81 μg/g, P = .436) or CRP (16.2 ± 5.8 vs. 15.7 ± 4.3 mg/L, P = .742) (Table 3).

Table 3: Comparison of fecal calprotectin and CRP between the study groups before treatment.

Variable	Group		P value
	Remission (N=51)	Active disease (N=19)	
Baseline Fecal calprotectin			
Mean ± SD	263.12 ± 210.81	258.26 ± 180.37	0.436
Baseline CRP			
Mean ± SD	15.7 ± 4.3	16.2 ± 5.8	0.742

After treatment, fecal calprotectin and CRP levels were significantly higher in the active-disease group than in the remission group. Mean fecal calprotectin was 367.89 ± 314.23 μg/g in the active-disease group versus 111.83 ± 99.12 μg/g in the remission group (P < .001). Mean CRP was 13.7 ± 7.0 mg/L versus 8.85 ± 4.35 mg/L, respectively (P < .001) (Table 4).

Table 4: Comparison of fecal calprotectin and CRP between the study groups after treatment.

Variable	Group		P value
	Remission (N=51)	Active disease (N=19)	
Fecal calprotectin			
Mean ± SD	111.83 ± 99.12	367.89 ± 314.23	<0.001

CRP			
Mean ± SD	8.85 ± 4.35	13.7 ± 7.0	<0.001

ROC analysis demonstrated good discrimination of active endoscopic disease by fecal calprotectin (AUC = 0.835, P < .001). A cutoff of ≥148.5 µg/g yielded 89.4% sensitivity, 70.6% specificity, a positive predictive value of 53.1%, and a negative predictive value of 94.7% (Figure 2).

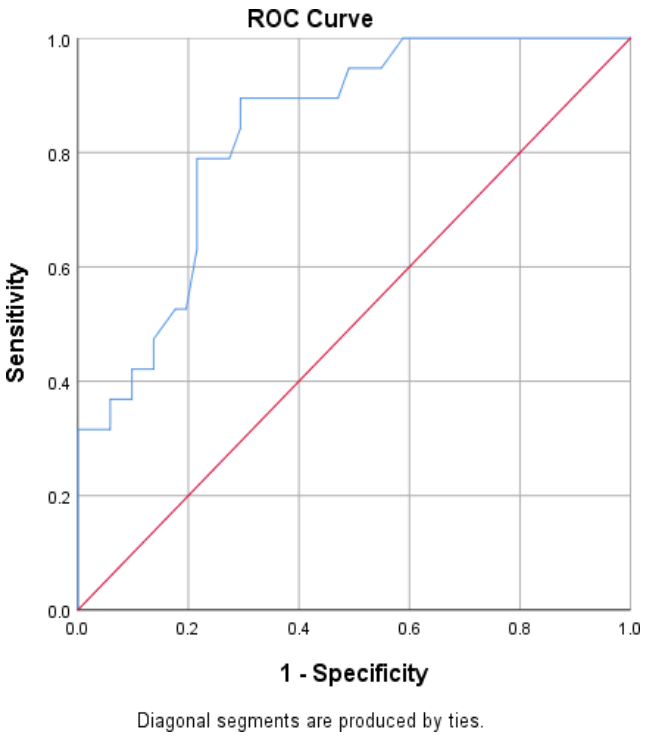

Figure 2: ROC analysis of fecal calprotectin for identifying active endoscopic disease according to colonoscopy.

DISCUSSION

The diagnosis and follow-up of patients with inflammatory bowel disease are complex and require integration of clinical, laboratory, endoscopic, histopathological, and radiological parameters (Gomollón et al., 2017; Lichtenstein et al., 2018; Peyrin-Biroulet et al., 2015). Recognition of inflammatory activity in Crohn's disease may be delayed or underestimated because some available methods are invasive or nonspecific. Noninvasive markers that reflect intestinal inflammation are therefore valuable in clinical practice (Sauter et al., 2014).

Colonoscopy with assessment of mucosal inflammation remains an important reference standard for evaluating endoscopic activity in Crohn's disease. Mucosal healing is a major therapeutic goal because it is associated with improved outcomes (Darr & Khan, 2017). However, colonoscopy is invasive and resource-intensive, supporting the use of noninvasive biomarkers for disease monitoring.

In the present study, we observed no significant differences between the study groups in baseline characteristics, baseline SES-CD score, type of biologic therapy, or comorbidities. Although this balance reduces concern about major measured group differences, the study was not designed to exclude residual or unmeasured confounding.

The present study found significantly higher fecal calprotectin concentrations in patients with active endoscopic disease than in those in remission. A fecal calprotectin cutoff of ≥148.5 μg/g showed 89.4% sensitivity and 70.6% specificity. Although CRP concentrations also differed significantly between groups, the present analysis emphasizes fecal calprotectin because the ROC analysis reported in this manuscript evaluated its performance.

In this cohort, a fecal calprotectin concentration ≥148.5 μg/g was associated with active endoscopic disease. The relatively high sensitivity and negative predictive value suggest potential usefulness for monitoring, whereas the lower positive predictive value indicates that an elevated result should not be interpreted in isolation. These findings support the role of fecal calprotectin as a monitoring tool rather than a standalone diagnostic test (Laharie et al., 2011).

These findings are broadly consistent with Penna et al. (2021), who studied 80 colonoscopies and reported that a fecal calprotectin cutoff of 155 μg/g had 96% sensitivity and 78% accuracy for detecting endoscopic activity. In that study, a CRP cutoff of 6.7 mg/L showed 75% sensitivity and 67% specificity.

Kopylov et al. (2016) reported substantial variation in diagnostic performance across fecal calprotectin thresholds in small-bowel Crohn's disease. A concentration of 50 μg/g yielded 83% sensitivity and 53% specificity, whereas 100 μg/g yielded 68% sensitivity and 71% specificity, and 200 μg/g yielded 42% sensitivity and 94% specificity. These findings illustrate that optimal thresholds may depend on disease location and clinical context.

Limitations of the Study

This study has several limitations. First, it was conducted at a single center and included a relatively small sample of 70 patients, which may limit generalizability and statistical precision. Second, the study included patients receiving different biologic therapies, which may introduce treatment-related heterogeneity. Third, dietary and preanalytical factors may influence fecal calprotectin measurements. Finally, the study did not report whether investigators assessing endoscopic activity were blinded to fecal calprotectin results. Consider these limitations when interpreting the findings.

CONCLUSION

In this study, fecal calprotectin demonstrated good discrimination between remission and active endoscopic disease after biologic treatment. Its high sensitivity and negative predictive value suggest that it may be useful as a noninvasive monitoring biomarker in patients with Crohn's disease.

A fecal calprotectin cutoff of 148.5 μg/g provided 89.4% sensitivity and 70.6% specificity for identifying active endoscopic disease in this cohort. External validation in larger, multicenter cohorts is required before this threshold can be recommended for routine clinical use.

Conflicts of Interest

The authors declare no conflicts of interest.

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