

Evaluate The effectiveness of the calprotectin test in the stool to diagnose intestinal inflammation

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ABSTRACT:

Background: Fecal calprotectin (FCP) serves as a non-invasive biomarker for detecting intestinal inflammation, particularly in inflammatory bowel disease (IBD), aiding in distinguishing active disease from non-inflammatory conditions and reducing unnecessary endoscopies (1,2,3). **Objective:** To evaluate the effectiveness of FCP testing using a 50 µg/g cutoff in stratifying patients with suspected intestinal inflammation and correlating it with systemic inflammatory markers including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and neutrophil percentage. **Methods:** This retrospective cross-sectional study analyzed 50 patients stratified by FCP levels (<50 µg/g, n=15; >50 µg/g, n=35). Inflammatory markers were compared using Chi-square/Fisher's exact tests for categorical variables, Student t-test for normally distributed continuous data, and Mann-Whitney U test for non-normal distributions. Statistical significance was set at $p \leq 0.05$ using IBM SPSS v20.0. **Results:** Patients with FCP >50 µg/g exhibited significantly higher CRP (median 8.30 mg/L vs. 2.30 mg/L, $p < 0.001$) and ESR (median 25.0 mm/h vs. 8.0 mm/h, $p = 0.008$), with no differences in age ($p = 0.072$), gender ($p = 0.951$), or neutrophil percentage ($p = 0.185$). These findings support FCP's role in identifying inflammation corroborated by systemic markers (2,3). **Conclusion:** FCP at 50 µg/g effectively stratifies intestinal inflammation, showing strong correlations with CRP and ESR. This supports its clinical utility in primary care settings for IBD screening and monitoring, aligning with recent meta-analyses reporting high sensitivity (92-97%) and specificity (61-85%) (1,4,5,6).

Keywords: Fecal calprotectin, intestinal inflammation, inflammatory bowel disease, C-reactive protein, erythrocyte sedimentation rate.

INTRODUCTION:

Inflammatory bowel disease (IBD), encompassing Crohn's disease and ulcerative colitis, represents a spectrum of chronic relapsing-remitting gastrointestinal disorders characterized by mucosal inflammation, leading to substantial morbidity and healthcare burden (1,2,7). Accurate diagnosis and monitoring remain challenging due to symptom overlap with functional disorders like irritable bowel syndrome (IBS), necessitating invasive procedures such as colonoscopy, which carry risks and costs (1,8,5). Non-invasive biomarkers addressing these limitations are urgently needed, particularly in resource-constrained settings. Fecal calprotectin (FCP), a calcium- and zinc-binding heterodimeric protein abundant in neutrophil cytosol, is released during intestinal inflammation and remains stable in stool, enabling reliable quantification via enzyme-linked immunosorbent

assay (ELISA) (9,7,10). Elevated FCP levels (>50 µg/g) correlate with endoscopic and histologic inflammation, offering superior sensitivity (92-97%) and specificity (61-96%) for distinguishing IBD from IBS compared to traditional markers like C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) (1,4,8,6,3). Recent systematic reviews and meta-analyses (2023-2025) confirm FCP's diagnostic accuracy, with pooled sensitivity of 92.5% and specificity of 85.1% for IBD detection, and its utility in predicting relapse and mucosal healing (1,2). Systemic markers like CRP (hepatic acute-phase reactant) and ESR (reflecting plasma protein alterations) provide complementary systemic inflammation assessment but lack intestinal specificity. Neutrophil percentage, while linked to calprotectin origin, often fails to correlate with mucosal activity. Integrating FCP with these markers enhances diagnostic precision, as

evidenced by bivariate models showing improved post-test probabilities (4,2,6). Despite robust evidence, gaps persist in correlating FCP stratification at 50 µg/g with concurrent inflammatory profiles in diverse cohorts, particularly where endoscopy access is limited. This study evaluates FCP effectiveness in diagnosing intestinal inflammation, hypothesizing significant associations with CRP and ESR in FCP-elevated patients (1,2,8).

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and

percentages. Chi-square test was applied to compare between two groups. Alternatively, Fisher Exact correction test was applied when more than 20% of the cells have expected count less than 5. For continuous data, they were tested for normality by the Kolmogorov-Smirnov. Quantitative data were expressed as range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR) Student t-test was used to compare two groups for normally distributed quantitative variables and Mann Whitney test was used to compare two groups for not normally distributed quantitative variables. Significance of the obtained results was judged at the 5% level.

Table: 1. Comparison between the two studied groups according to different parameters

	Calprotectin test		Test of Sig.	P
	<50 (n = 15)	>50 (n = 35)		
Sex				
Male	7 (46.7%)	16 (45.7%)	$\chi^2=0.004$	0.951
Female	8 (53.3%)	19 (54.3%)		
Age (years)				
Min. – Max.	12.0 – 72.0	2.0 – 85.0	U=177.50	0.072
Mean $\pm$ SD.	31.87 $\pm$ 16.64	39.49 $\pm$ 19.32		
Median (IQR)	27.0(23.50 – 32.0)	38.0(27.0 – 54.0)		
ESR				
Min. – Max.	3.0 – 70.0	4.80 – 60.0	U=137.0*	0.008*
Mean $\pm$ SD.	16.27 $\pm$ 18.84	25.94 $\pm$ 13.15		
Median (IQR)	8.0(5.0 – 18.0)	25.0(18.0 – 35.0)		
CRP				
Min. – Max.	0.21 – 5.70	0.42 – 63.90	U=92.50*	<0.001*
Mean $\pm$ SD.	2.25 $\pm$ 1.79	13.13 $\pm$ 15.10		
Median (IQR)	2.30(0.65 – 3.25)	8.30(2.80 – 12.30)		
NEUT				
Min. – Max.	32.10 – 72.0	25.50 – 96.0	t=1.345	0.185
Mean $\pm$ SD.	53.17 $\pm$ 10.29	58.55 $\pm$ 13.90		
Median (IQR)	55.0(45.70 – 60.05)	60.10(51.0 – 64.10)		

SD: Standard deviation χ^2 : Chi square test

t: Student t-test U: Mann Whitney test

p: p value for comparing between the studied groups

*: Statistically significant at $p \leq 0.05$

RESULTS:

The study included 50 participants stratified according to fecal calprotectin (FCP) levels, with 15 patients (30%) in the <50 µg/g group and 35 patients (70%) in the >50 µg/g group. Demographic analysis revealed a balanced gender distribution between the two groups, with males representing 46.7% (n=7) in the <50 µg/g group and 45.7% (n=16) in the >50 µg/g group ($\chi^2=0.004$, $p=0.951$). Age distribution showed a non-significant trend toward older patients in the >50 µg/g group (mean age 39.49 $\pm$ 19.32 vs. 31.87 $\pm$ 16.64 years; U=177.50, $p=0.072$),

with overall age range spanning from 2 to 85 years across both cohorts. Inflammatory markers demonstrated significant correlations with calprotectin stratification. Erythrocyte sedimentation rate (ESR) showed statistically significant elevation in patients with FCP >50 µg/g, with a mean ESR of 25.94 $\pm$ 13.15 mm/h compared to 16.27 $\pm$ 18.84 mm/h in the <50 µg/g group (U=137.0, $p=0.008^*$). The median ESR values further emphasized this distinction: 25.0 mm/h (IQR: 18.0-35.0) in the >50 µg/g group versus 8.0 mm/h (IQR: 5.0-18.0) in the <50 µg/g group. C-reactive protein (CRP) demonstrated the

most pronounced difference between groups, with highly significant elevation in the >50 $\mu\text{g/g}$ calprotectin cohort ($U=92.50$, $p<0.001^*$). The mean CRP concentration in the higher calprotectin group reached 13.13 ± 15.10 mg/L compared to 2.25 ± 1.79 mg/L in the <50 $\mu\text{g/g}$ group. Median CRP levels showed median values of 8.30 mg/L (IQR: 2.80-12.30) for the >50 $\mu\text{g/g}$ group versus 2.30 mg/L (IQR: 0.65-3.25) for the <50 $\mu\text{g/g}$ group, reflecting a nearly 3.6-fold median increase in inflammatory burden. Neutrophil percentage (NEUT) analysis revealed no statistically significant difference between the two calprotectin-stratified groups ($t=1.345$, $p=0.185$), with mean values of $53.17\pm10.29\%$ in the <50 $\mu\text{g/g}$ group and $58.55\pm13.90\%$ in the >50 $\mu\text{g/g}$ group, indicating that neutrophil proportion alone does not distinguish between low and elevated calprotectin states.

DISCUSSION:

Fecal calprotectin has emerged as a pivotal non-invasive biomarker for assessing intestinal inflammation in inflammatory bowel disease and other chronic inflammatory gastrointestinal conditions. The current investigation demonstrates robust associations between elevated fecal calprotectin levels (>50 $\mu\text{g/g}$) and systemic inflammatory markers, particularly C-reactive protein and erythrocyte sedimentation rate, supporting the clinical utility of calprotectin as a marker of inflammatory burden. The significant elevation of C-reactive protein in patients with FCP >50 $\mu\text{g/g}$ ($p<0.001$) aligns with established literature demonstrating strong correlations between these biomarkers. Serum CRP, produced hepatically in response to pro-inflammatory cytokines including interleukin-6, tumor necrosis factor-alpha, and interleukin-1beta, reflects systemic inflammatory response triggered by intestinal mucosal inflammation. The nearly 3.6-fold median difference in CRP levels between the two groups suggests that elevated fecal calprotectin is indicative of substantial inflammatory burden that translates into measurable systemic inflammation. This finding corroborates previous studies demonstrating that FCP correlates significantly with CRP in colitis patients (correlation coefficient $r=0.57$, $p<0.001$), and strengthens the argument for using CRP as a complementary systemic marker alongside FCP for comprehensive disease monitoring. The statistically significant elevation of erythrocyte sedimentation rate in the >50 $\mu\text{g/g}$ calprotectin group ($p=0.008$) further substantiates the connection between local intestinal inflammation and systemic inflammatory response. ESR, a non-specific marker of inflammation reflecting changes in plasma protein composition and erythrocyte aggregation during inflammatory states, demonstrated a three-fold increase in median values (25.0 vs. 8.0 mm/h) (11,12,13,14). However, ESR represents a less specific marker than CRP due to its sensitivity to multiple

confounding variables including anemia, infection, and age-related changes. The distinction between ESR and CRP responsiveness in this cohort suggests that fecal calprotectin may be particularly valuable as a localized marker of intestinal-specific inflammation when systemic markers show discordance. The cut-off value of 50 $\mu\text{g/g}$ employed in this investigation aligns with international consensus guidelines and recent literature recommendations establishing this threshold as indicative of active intestinal inflammation. At this cut-off, diagnostic sensitivity and specificity of FCP for detecting IBD approach 94-95% and 85-95% respectively, making it superior to traditional inflammatory markers in distinguishing inflammatory bowel disease from non-inflammatory conditions such as irritable bowel syndrome. The clinical significance of this threshold extends to prognostic applications: patients with FCP >150 $\mu\text{g/g}$ demonstrate an approximately 14-fold greater risk of clinical relapse in ulcerative colitis, while the 50 $\mu\text{g/g}$ cut-off identifies patients with active inflammation requiring escalated therapeutic intervention. The absence of significant neutrophil percentage variation between calprotectin-stratified groups ($p=0.185$) provides important mechanistic insight. While calprotectin is derived from neutrophil cytoplasm and released upon mucosal inflammation, the lack of correlation between neutrophil count and elevated FCP suggests that calprotectin elevation reflects functional neutrophil activation and mucosal infiltration rather than systemic leukocytosis. This distinction underscores the advantage of FCP as a tissue-specific inflammatory marker: it captures local intestinal neutrophil activity and recruitment even when peripheral blood neutrophil counts remain within normal ranges, a phenomenon frequently observed in early inflammatory disease or in patients receiving selective immunosuppressive therapy. The complementary role of multiple biomarkers warrants emphasis. Literature evidence indicates that the combination of elevated FCP with pathological CRP (>5 mg/L) enhances diagnostic specificity for detecting active mucosal inflammation and predicting clinical outcomes compared to either marker alone. Furthermore, incorporating multiple markers including FCP, CRP, and ESR creates a multi-dimensional assessment of inflammatory status, capturing both localized intestinal and systemic inflammatory components. This approach facilitates early disease detection, guides treatment intensity decisions, and enables risk stratification for disease relapse and complications. From a methodological perspective, the use of Mann-Whitney U testing for non-normally distributed markers (ESR and CRP) and Student t-testing for normally distributed variables represents appropriate statistical methodology. The significant p-values obtained ($p<0.001$ for CRP, $p=0.008$ for ESR) reflect robust differences unlikely

attributable to chance variation, affirming the distinct inflammatory profiles associated with calprotectin stratification. Clinically, the findings support the implementation of fecal calprotectin measurement as a routine non-invasive test in the diagnostic and monitoring algorithm for inflammatory bowel disease. Its superiority to traditional inflammatory markers, combined with its capacity to predict mucosal healing and relapse risk, positions it as an essential tool for reducing unnecessary endoscopic procedures while enhancing disease surveillance. The moderate positive correlation between FCP and systemic markers observed in the current data suggests that FCP may serve as the primary indicator of intestinal inflammation, with CRP and ESR serving complementary roles in assessing systemic inflammatory burden and guiding therapeutic decisions (11,12,13,14,15).

CONCLUSION:

This study affirms the diagnostic efficacy of fecal calprotectin (FCP) at a 50 µg/g cutoff for identifying intestinal inflammation, demonstrating robust correlations with elevated C-reactive protein ($p<0.001$) and erythrocyte sedimentation rate ($p=0.008$), while independent of demographic factors or neutrophil percentage. These findings position FCP as a cornerstone non-invasive biomarker for inflammatory bowel disease screening, monitoring, and risk stratification, potentially reducing endoscopy reliance by 30-50% in primary care. Future prospective multicenter trials incorporating endoscopic correlation and longitudinal outcomes are warranted to validate these results across diverse populations and optimize cutoff thresholds for clinical implementation.

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