

## Fecal Calprotectin as a Noninvasive Marker of Intestinal Inflammation

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## Abstract

## Review Article

Fecal calprotectin (FC) is a noninvasive and reliable biomarker for identifying intestinal inflammation. It is commonly used to identify and monitor digestive inflammation, including Crohn's disease and ulcerative colitis. Calprotectin is a calcium-binding protein which is mainly derived from neutrophils and during an inflammatory process it is released into the intestinal lumen. Measurement of fecal calprotectin gives important information regarding mucosal inflammation and helps in differentiating IBD (Inflammatory bowel disease) from functional disorders such as irritable bowel syndrome (IBS) (Tibble JA *et al.*, 2000). This article reviews diagnostic applications of fecal calprotectin, its clinical interpretation, and limitations in diagnosing IBD.

**Keywords:** Fecal calprotectin (FCP), inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), biomarkers, intestinal inflammation, neutrophils.

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### INTRODUCTION

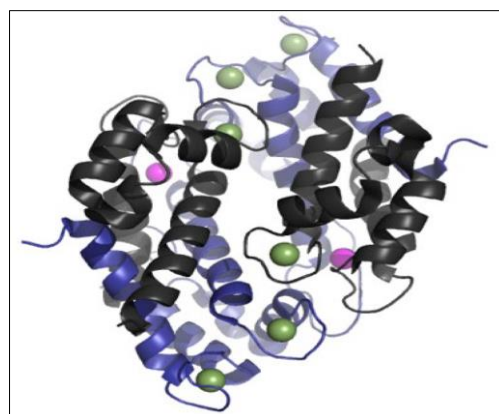
Assessment of intestinal inflammation has an important role in diagnosing and managing many gastrointestinal diseases. Endoscopic procedures with biopsy are considered diagnostic for the assessment of mucosal inflammation; however, they are invasive and expensive. It is also impractical to use repeated endoscopic methods to monitor the disease process. Because of these reasons the use of noninvasive biomarkers are becoming more valuable. (Van Rheenen *et al.*, BMJ. 2010)

Fecal calprotectin is one important fecal biomarker. Because calprotectin is released from activated neutrophils during inflammatory processes in the gastrointestinal tract, its presence in stool correlates with the inflammation of the mucosa. Therefore, measurement of fecal calprotectin has become an important screening tool in the evaluation of patients presenting with persistent gastrointestinal symptoms.

#### Biological Characteristics of Calprotectin

Calprotectin is made of two protein complexes, S100A8 and S100A9, belonging to the S100 family of calcium-binding proteins (Walsham NE, Sherwood RA. 2016). It is a cytosolic protein found in neutrophils and is also present in monocytes and macrophages.

During inflammation within intestinal mucosa, neutrophils migrate across the intestinal epithelium and release calprotectin into the gut. One important feature of this protein is that it is resistant to enzymatic degradation, which allows it to remain stable in faeces for several days. Because of this stability, faecal calprotectin can be measured reliably using methods such as enzyme-linked immunosorbent assays (ELISA) and other immunochemical techniques. (Walsham NE, Sherwood RA. 2016)



**Figure 1.** Crystal structure of calprotectin loaded with  $Mn^{2+}$  and  $Ca^{2+}$ , composed of two S100A8-S100A9 dimers. S100A8 and S100A9 chains are shown in grey and blue, respectively. Purple spheres indicate  $Mn^{2+}$ , and green spheres indicate  $Ca^{2+}$ . Each dimer binds only one manganese ion [6].

## Clinical Application

### Diagnosis of Inflammatory Bowel Disease

One of the main uses of fecal calprotectin is in presenting complaints where inflammatory bowel disease is suspected. Neutrophil infiltration of the intestinal mucosa causes fecal calprotectin to rise, which is characteristic of conditions such as Crohn's disease and ulcerative colitis. Studies have shown that fecal calprotectin testing has high sensitivity for detecting intestinal inflammation, making it a valuable screening tool for patients with suspected IBD.

### Differentiation of IBD from Functional Gastrointestinal Disorders

Patients with inflammatory bowel disease and those with irritable bowel syndrome may present with similar symptoms, including abdominal discomfort, diarrhea, and altered bowel habits. Fecal calprotectin measurement can help clinicians in distinguishing these conditions. Individuals with functional gastrointestinal disorders generally show normal or minimally elevated calprotectin levels, whereas significantly elevated

concentrations are seen in inflammatory pathologies that warrant further investigations.

### Monitoring Disease Activity

In patients with already diagnosed inflammatory bowel disease, fecal calprotectin levels are closely associated with disease activity. Serial measurement can be useful for monitoring response to treatment in such cases. If fecal calprotectin concentrations start to rise, it may indicate ongoing inflammation giving a chance to adjust therapy earlier. (Mosli MH *et al.*, 2015)

### Interpretation of Fecal Calprotectin Levels

When interpreting fecal calprotectin results both laboratory reference ranges and the patient's clinical presentation should be considered. Generally, values below 50 µg/g of stool are regarded as normal and are mostly not associated with significant intestinal inflammation. Levels between 50 and 200 µg/g may be considered borderline. In such cases often repeat testing or additional clinical correlation is required. Concentrations more than 200 µg/g usually means active intestinal inflammation. (Lin JF, *et al.*, 2014)

Fecal calprotectin > 50 µg/g	Normal
Fecal calprotectin 50 and 200 µg/g	Borderline
Fecal calprotectin > 200 µg/g	Needs further evaluation

Increased levels can be seen in other conditions such as gastrointestinal infections, colorectal cancer, celiac disease, and in patients taking non-steroidal anti-inflammatory drugs. Therefore, fecal calprotectin results must always be interpreted along with other clinical findings and other diagnostic tests.

### Limitations

Although fecal calprotectin provides valuable information about intestinal inflammation, it also has several limitations. FCP lacks disease specificity and may show raised results in many other gastrointestinal disorders, such as gastrointestinal infections, colorectal cancer, celiac disease, and in patients taking non-steroidal anti-inflammatory drugs. It is also seen that physiological factors such as age may affect calprotectin concentrations because higher levels are sometimes seen in infants and elderly individuals. In these cases, fecal calprotectin testing should not be used as a diagnostic tool.

## CONCLUSION

Fecal calprotectin has become an important noninvasive marker for assessing intestinal inflammation. It is clinically useful in detecting inflammatory bowel disease, differentiating inflammatory conditions from functional gastrointestinal disorders, and monitoring disease activity over time. It is understood that endoscopic assessment cannot be

replaced completely by fecal calprotectin. Yet it can still help clinicians in clinical decision-making and reduce the need for unnecessary invasive procedures.

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