Biomarkers of Gastrointestinal Inflammation: Calprotectin, Lactoferrin, Lysozyme

RESOURCE GUIDE
Biomarkers of Gastrointestinal Inflammation: Calprotectin, Lactoferrin, Lysozyme Resource Guide

Gastrointestinal conditions can be difficult to distinguish from one another, and cause symptoms that can be relatively acute or sustained. Proper treatment requires distinguishing between acute GI inflammation, inflammatory bowel diseases, and irritable bowel syndrome.

- **Inflammatory bowel diseases** (IBD), such as ulcerative colitis and Crohn’s disease, are very serious, incurable organic inflammatory conditions.
- **Acute GI inflammation** is typically associated with enteric pathogens such as dysbiotic bacteria, yeast, or parasites.
- **Irritable bowel syndrome** (IBS) is not an organic inflammatory condition, but may present with GI symptoms very similar to those associated with IBD.

Scientifically validated biomarkers of GI inflammation in stool specimens can help identify the causes for GI symptoms. These biomarkers include lysozyme, lactoferrin, and calprotectin. Lysozyme, a glycoside hydrolase enzyme with bactericidal properties, is elevated in stool with enteric pathogens and very elevated during active IBD. However, elevated levels of lysozyme have poor specificity for IBD.

Data has shown, however, that when viewed together, fecal lactoferrin and calprotectin have proven to be sensitive and specific fecal biomarkers of IBD. Both protease-resistant proteins are found at increased levels in stool as a result of IBD-associated increased infiltration of activated neutrophils into the GI mucosa. In patients with IBS, neither protein is elevated in the stool specimens.

While studies comparing fecal lactoferrin to calprotectin levels in IBS and IBD patients have provided equivocal results, it is clear that when they are viewed collectively using quantitative enzyme linked immunosassays (ELISA) based upon polyclonal antibodies, lactoferrin and calprotectin provide equal discrimination between IBD and IBS.

Monoclonal calprotectin provides greater sensitivity compared to the polyclonal assay.
Monitoring Biomarkers to Predict Relapse and Evaluate Therapy

Lactoferrin and calprotectin have both been reported to have clinical utility for predicting relapse of IBD. During periods of remission, the levels never fall to those found in unaffected patients. However, lactoferrin levels increase in the feces of IBD patients about 2 weeks prior to overt expression of IBD symptoms. Monitoring these proteins can be helpful in evaluating the efficacy of anti-inflammatory therapies. For example, when elevated lactoferrin or calprotectin is identified, it is recommended that the same test be repeated after about 4 to 6 weeks. If the repeat test results remain abnormally elevated, it is recommended that the patient see a specialist for endoscopy and perhaps biopsy.

Monoclonal vs. Polyclonal Assays

Some laboratories use a polyclonal assay for lactoferrin that provides only a positive or negative result. These less-sensitive, quantitative, antibody-based immunoassays for lactoferrin and calprotectin can be valuable for noninvasive distinction between IBD and IBS, but not for identifying the changes in protein levels that can predict relapse or identify therapy issues.

Fortunately, a monoclonal antibody-based immunoassay for calprotectin has been developed that is superior to the older calprotectin ELISA polyclonal assay.

With the new monoclonal assay, fecal calprotectin levels below 50 μg/gm are considered to be normal and no further testing is recommended. At moderately elevated calprotectin levels between 50 and 100 μg/gm, mild organic disease such as inflammation caused by NSAID drugs, mild diverticulitis, or IBD in remission should be considered. That mild inflammatory response may suggest value in repeat testing after 4 to 6 weeks as well as further investigation including a thorough patient history with respect to NSAID use. Fecal calprotectin levels greater than 100 μg/gm are consistent with active IBD and further investigation is strongly recommended.

Ultimately, the monoclonal antibody test for calprotectin provides tremendous value for clinicians by offering greater discrimination for the noninvasive evaluation of IBD as well as gauging the extent of GI inflammation.

Tests Offered by Doctor’s Data

Doctor’s Data is constantly updating our test offering to provide clinicians with the latest advances in comprehensive stool analysis, blood testing, and more. Even though the monoclonal calprotectin test has demonstrated greater sensitivity compared to the lactoferrin assay, some studies have indicated that lactoferrin has greater specificity for ulcerative colitis verses Crohn's disease. As a result, we prefer to view the 2 biomarkers together because we believe that maximizes our ability to aid in the proper identification of these diseases.

In addition, we offer lysozyme testing, because an isolated abnormal result for lysozyme indicates inflammation not associated with IBD and is typically associated with enteropathogens such as dysbiotic yeast, bacteria, or parasites. If such enteropathogens are not reported, the elevated lysozyme result may be associated with a GI virus, toxicant-induced GI inflammation, or possibly celiac disease. However, when celiac is suspected, there are more appropriate tests, such as the Doctor’s Data Celiac, Gluten Sensitivity, and Wheat Allergy Profile, based on serology testing set forth by the American College of Gastroenterology.

For more information about Doctor’s Data tests and to place an order, please visit www.doctorsdata.com.
**Calprotectin, Stool**

<table>
<thead>
<tr>
<th>Result</th>
<th>Reference Interval</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>24</td>
<td>&lt; 50</td>
<td>Normal</td>
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Calprotectin is a relative noninvasive marker for differentiating gastrointestinal inflammation associated with inflammatory bowel disease (IBD) from inflammation that may be associated with irritable bowel syndrome (IBS). Such differentiation is very important in determining the effectiveness of clinical intervention, and it is a good predictor of IBD remission and relapse. Calprotectin provides clinicians with a valuable tool, not only for differentiating IBD from IBS, but also allowing them to monitor and predict treatment outcomes and enabling better management of IBD flare-ups.

**Reference Intervals**

- **<50 μg/g**: Fecal calprotectin values <50 μg/g are not indicative of inflammation in the gastrointestinal tract. Subjects with low fecal calprotectin levels normally do not need to be further investigated by invasive procedures.
- **50 - 200 μg/g**: Fecal calprotectin values between 50 and 200 μg/g can represent mild organic disease such as inflammation caused by NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), mild diverticulitis and IBD in remission phase. The inflammatory response shown within this range may suggest repeating the measurement and performing further investigations.
- **>200 μg/g**: Fecal calprotectin values >200 μg/g are indicative of active organic disease with inflammation in the gastrointestinal tract. Appropriate further investigative and curative procedures by specialists are suggested.  

**IBD Management**

In patients with IBD, calprotectin levels of <150 μg/g have been shown to predict remission with a low risk of relapse. Elevated calprotectin levels of <200 μg/g in patients after treatment indicate endoscopic mucosal healing and can help optimize IBD treatment.

**References**


**Comments**

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**For research use only. Not for use in diagnostic procedures.**