

Analysis of the Relationship between Inflammatory Activity and Fecal Calprotectin Levels and Fecal Occult Blood as Biomarkers for Gastritis Sufferers

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ABSTRACT

Gastritis is a disease in the form of inflammation of the stomach. Inflammatory activity in gastritis sufferers can be detected through biomarker examinations such as fecal calprotectin and fecal occult blood tests (FOB). This study was to analyze the relationship between inflammatory activity and fecal calprotectin levels and occult blood as a biomarker in chronic gastritis sufferers. The research method uses a cross-sectional design, Chi-Square statistical test data analysis, with a confidence level of 95% (α 0.05). The research used secondary data with a sample size of 64 people suffering from chronic gastritis who experienced inflammation that developed gradually over a long period of time. Research variables were obtained from Local Information System (LIS) Laboratory data for inflammatory activity of non-active chronic gastritis and histologically active chronic gastritis, fecal calprotectin and occult blood from the measurement results of the fecal calprotectin reagent test kit insert and FOB oncoprobe. The results of the study showed that 30.4% of positive occult blood and 54.3% fecal calprotectin levels increased significantly in non-active chronic gastritis inflammatory activity. The results of the analysis showed that there was no significant relationship between inflammatory activity and fecal calprotectin levels with a p-value of 0.413 ($p > 0.05$) and there was no relationship between inflammatory activity and occult blood (FOB) p-value 1.000 ($p > 0.05$) in chronic gastritis sufferers. The conclusion is that there is no significant relationship between inflammatory activity and fecal calprotectin levels and occult blood as a biomarker in chronic gastritis sufferers.

KEYWORDS: Inflammatory Activity; Biomarkers; Fecal Calprotectin; Fecal Occult Blood (FOB); Chronic Gastritis.

ARTICLE DETAILS

Published On:
06 September 2024

Available on:
<https://ijpbms.com/>

I. INTRODUCTION

Gastritis or ulcers is one of the digestive disorders that is often found in clinics or internal medicine clinics and is one of the diseases that often occurs in society, suffered by teenagers and adults.

Gastritis is inflammation of the lower stomach lining, characterized by nausea, vomiting, heartburn, bloating, bleeding in advanced cases, weakness and decreased appetite.¹ This condition can manifest in various forms, ranging from mild cases with no symptoms to severe symptoms accompanied by significant morbidity. The classification of gastritis is based on the course of time, namely acute and chronic.²

According to the Ministry of Health of the Republic of Indonesia in 2018, gastritis was in seventh place, with 201,083 patients hospitalized.³ Gastritis is the disease with the highest prevalence in Indonesia, with 274,396 cases per 238,452,952 population, or 40.8%. The percentage of cases in big cities in Indonesia, such as Jakarta, Palembang, Bandung, Denpasar, Surabaya, Aceh and Pontianak, reached 31.2%, and in Medan it reached 91.6%.⁴

Fecal calprotectin is a calcium and zinc binding cytosolic protein found in neutrophils, migrating into the digestive tract due to mucosal inflammation which causes leukocyte infiltration.⁵ Elevated fecal calprotectin levels have been reported in peptic ulcer disease. In a study fecal calprotectin

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with a cutoff of 50 μ g/g predicted endoscopic findings in the upper gastrointestinal tract with a sensitivity of 59% and a specificity of 82%.⁶ Fecal calprotectin values also increase with the severity of the disease. Fecal calprotectin provides added value to clinical decision making in patients experiencing abdominal discomfort, to decide on endoscopy, as it predicts the presence of esophageal and gastric mucosal lesions.⁷ However, its ability to predict positive endoscopic findings in the upper intestinal tract was not as good as findings in the colon (sensitivity 84% and specificity 92% in the colon). Fecal calprotectin is not useful as a screening test in asymptomatic patients.⁶ Fecal occult blood (FOB) examination is a diagnostic method used to see the presence of blood in feces that is not detected by the eye. This examination is carried out to detect digestive problems, such as hemorrhoids, colon cancer, inflammatory bowel disease (IBD), and other diseases that can cause bleeding in the upper or lower digestive tract.⁸

Fecal calprotectin represents or reflects the presence of neutrophilic inflammation in the stomach.^{4,5} Furthermore, fecal calprotectin was best at detecting active inflammation in colitis, while occult blood was better at detecting mucosal healing, and both were able to predict recurrence in colitis. Thus, a plan is needed to utilize both evaluations according to the patient's condition. If active inflammation is detected in a patient, a fecal calprotectin check is needed to monitor active inflammation of the disease. When the patient is in clinical recovery, occult blood is necessary to monitor mucosal healing and predict the risk of recurrence.^{3,8}

Fecal calprotectin levels were higher in patients with active chronic gastritis than in patients with inactive chronic gastritis in pediatric patients. In addition, fecal calprotectin levels were higher in patients with chronic gastritis than in the healthy group and lower than in the inflammatory bowel disease (IBD) group. In chronic gastritis patients, inflammation of the gastric mucosa causes a significant increase in fecal calprotectin levels, compared with healthy controls. However, the increase in fecal calprotectin levels in chronic gastritis patients was lower compared with fecal calprotectin (FC) levels in the IBD group, due to the lack of widespread involvement of gastrointestinal inflammation in chronic gastritis.^{2,1}

Difficulty determining the level of inflammation and damage to the stomach is one of the problems in the diagnosis and treatment of gastritis. Gastritis is often difficult to diagnose based on clinical symptoms alone, histological or endoscopic examination is required, it may not correlate with the severity of symptoms. Acute gastritis occurs with sudden pain in the upper stomach area, flatulence, nausea, and vomiting (dyspepsia), and generally disappears on its own. Diagnosis of gastritis is currently usually made through endoscopy and biopsy which is the gold standard for confirming the diagnosis. The results of endoscopy and

biopsy can show inflammatory activity from gastritis or ulcers, but these techniques are invasive and expensive.⁹

Examination of fecal calprotectin levels and occult blood can help identify inflammatory activity, mucosal conditions, and predict recurrence in patients with gastritis. The fecal calprotectin biomarker can be a simple, cheap and non-invasive test for detecting inflammation in digestive disorders. Fecal calprotectin examination has also been recommended by the Food and Drug Administration (FDA) and recommended by global gastroenterology organizations.^{10,11}

Many research results show that gastritis sufferers can cause increased levels of fecal calprotectin and occult blood, so researchers are interested in conducting this research. Hopefully this can provide useful information for the diagnosis and monitoring of this condition. This study analyzes inflammatory activity in chronic gastritis sufferers in the adult population at a private hospital in Jakarta for the period 2023.

II. MATERIAL AND METHODS

A. Research Ethics Clearance

Ethical clearance is submitted to the Ethics Commission of the Muhammadiyah University of Purwokerto with Ethics Review Number: KEPK/UMP/36/V/2024. Request a research permit from the agency where the research was conducted. Furthermore, researchers carry out research activities by emphasizing research ethics with an emphasis on health, welfare, maintenance, confidentiality, personal comfort and human dignity.

B. Design, subjects, and research variables

The research method used is analytical research, cross sectional design. The research subjects were secondary data from 2023 of chronic gastritis sufferers with active and non-active inflammatory activity who had fecal calprotectin and occult blood levels checked.

C. Data collection and Measurement

Data was taken from LIS in 2023 of adult patients suffering from chronic gastritis, both active and non-active based on histology and endoscopy results. The sample size used a total sample from a population of 64 sufferers.

D. Statistical analysis

Statistical analysis used the Chi-Square test to determine the correlation between inflammatory activity and fecal calprotectin levels and occult blood, with a confidence level (CI) of 95% or a value of α 0.05.

If the p value (Sig. 2-tailed) $< \alpha$ (0.05) then there is a significant relationship between inflammatory activity and fecal calprotectin levels and occult blood.

If the p value (Sig. 2-tailed) $> \alpha$ (0.05) means there is no significant relationship between inflammatory activity and fecal calprotectin levels and occult blood.

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III. RESULTS

A. Frequency Distribution Of Inflammatory Activity Gastritis Sufferers Based On Fecal Occult Blood (FOB) Examination Results

Table 1. Frequency Distribution of Inflammatory Activity in Gastritis Sufferers Based on Fecal Occult Blood (FOB) Results

Inflammatory Activity	Fecal Occult Blood / FOB		
	Negatif	Positif	Total
Active Chronic Gastritis	12 (66.7%)	6 (33.3%)	18 (100%)
Inactive Chronic Gastritis	32 (69.6%)	14 (30.4%)	46 (100%)
Total	44 (68.8%)	20 (31.2%)	64 (100%)

In table 1, occult blood results were found to be 68.8% negative in gastritis sufferers from both active and non-active chronic inflammatory activity. These results show that chronic gastritis sufferers have more negative occult blood test results.

B. Frequency Distribution of Inflammatory Activity in Gastritis Sufferers Based on Examination Results of Fecal Calprotectin Levels

Table 2. Frequency Distribution of Inflammatory Activity in Gastritis Sufferers Based on the results of the fecal calprotectin examination

Inflammatory Activity	Fecal Calprotectin		Total
	Normal Slightly Increased	Increased Significantly	
Active Chronic Gastritis	6 (33.3%)	12 (66.7%)	18 (100%)
Inactive Chronic Gastritis	21 (45.7%)	25 (54.3%)	46 (100%)
Total	27 (42.2%)	37 (57.8%)	64 (100%)

In table 2, it was found that fecal calprotectin levels increased significantly by 57.8% in patients with active and non-active chronic gastritis. The results of the analysis in table 2 show that fecal calprotectin levels increased significantly in patients with non-active chronic gastritis inflammatory activity of 25%.

C. Correlation Between Inflammatory Activity in Chronic Gastritis Patients and Fecal Occult Blood (FOB)

Table 3. Correlation Between Inflammatory Activities in Chronic Gastritis Patients With Fecal Occult Blood (FOB)

Inflammatory Activity	Fecal Occult Blood / FOB		Total	OR 95 % CI	P Value
	Negatif	Positif			
Active Chronic Gastritis	12 (66.7%)	6 (33.3%)	18 (100%)	0.3-3.6 1.143	1.000
Inactive Chronic Gastritis	32 (69.6%)	14 (30.4%)	46 (100%)		
Total	44 (68.8%)	20 (31.2%)	64 (100%)		

In table 3, the results of statistical tests on the relationship between the inflammatory activity of chronic gastritis sufferers and fecal occult blood show a p-value = 1,000, meaning that it is proven that there is no relationship between the inflammatory activity of chronic gastritis sufferers, both active and inactive, and the patient's fecal occult blood. The OR value = 1.143 indicates that the inflammatory activity of chronic gastritis sufferers, both active and non-active, has a 1.143 times chance of being found positive for fecal occult blood.

D. Correlation Between Inflammatory Activity in Chronic Gastritis Patients and Fecal Calprotectin Levels

The results of statistical tests on the relationship between inflammatory activity in chronic gastritis sufferers and fecal calprotectin levels showed p-value = 0.413. This means that it is proven that there is no relationship between the inflammatory activity of chronic gastritis sufferers, both active and non-active, with fecal calprotectin levels. The OR value = 1,680, indicating that the inflammatory activity of chronic gastritis sufferers, both active and non-active, has a 1,680 times chance of increasing fecal protectin levels. The results can be seen in table 4 below :

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Table 4. Correlation between Inflammatory Activities in Chronic Gastritis Patients with Fecal Calprotectin Levels

Inflammatory Activity	Fecal Calprotectin		Total	OR 95% CI (0.5- 5.2) 1.680	P Val ue 0.4 13
	Normal	Increased			
Active Chronic Gastritis	6 (33.3%)	12 (66.7%)	18 (100%)		
Inactive Chronic Gastritis	21 (45.7%)	25 (54.3%)	46 (100%)		
Total	27 (42.2%)	37 (57.8%)	64 (100%)		

IV. DISCUSSION

Gastritis is an inflammatory condition of the stomach wall caused by various factors, including *Helicobacter pylori* bacterial infection, use of non-steroidal anti-inflammatory drugs (NSAIDs), alcohol, and stress.¹³ Chronic gastritis is a chronic inflammatory process of the gastric mucosa and is one of the most common findings of endoscopic and histopathological examination.¹⁴ Chronic non-active gastritis is a type of chronic gastritis in which inflammation of the stomach lining occurs, but this inflammation is not accompanied by significant activity of inflammatory cells. In non-active gastritis, there is damage to the acid-forming cells in the stomach without any signs of bleeding or signs of significant changes in the stomach tissue. Chronic active gastritis, is a type of chronic gastritis in which inflammation of the stomach lining is accompanied by increased activity of inflammatory cells. This can cause more obvious symptoms, such as abdominal pain, nausea, vomiting, or gastrointestinal bleeding.¹⁵

Inactive chronic gastritis patients in this study found 69.6% of negative occult blood results compared to 30.4% of positive occult blood results. This is possible because in cases of non-active chronic gastritis there is a gastric mucosal defense mechanism that is still functioning well, so the level of bleeding is low, and the results of occult blood tests tend to be negative. In non-active chronic gastritis, the gastric mucosa experiences chronic inflammation without significant ulceration or active bleeding. Gastric mucosal defense mechanisms, such as mucus secretion, bicarbonate, and prostaglandins, still function well to protect the mucosa from irritation and damage, resulting in the absence of active bleeding sufficient to produce positive results on occult blood

tests. On the other hand, in cases of active gastritis or peptic ulcers, more severe mucosal damage can cause bleeding that is detected by fecal occult blood examination.¹⁶ This is supported by the results of research by Yi-Chia Lee, et al, 2013 which suggested the use of the *Helicobacter pylori* fecal antigen test as a more accurate screening compared to guaiac-based tests for upper gastrointestinal lesions.¹⁷

Fecal calprotectin examination is a biochemical examination where Calprotectin is a protein with antibacterial properties mainly found in the cytoplasm of neutrophil granulocytes and has been used as a diagnostic tool to detect inflammation. When inflammatory processes occur, calprotectin is released due to degranulation of neutrophil granulocytes.^{5,18} Increased fecal calprotectin concentrations are a direct consequence of neutrophil degranulation resulting from mucosal injury.¹⁰ Table 2 shows the distribution of fecal calprotectin levels in chronic gastritis sufferers which are categorized as normal, slightly increased and significantly increased. For fecal calprotectin levels in active chronic gastritis, fecal calprotectin levels were found to be 12 (66.7%) in the significantly increased category and slightly increased by 6 (33.3%), while the distribution of fecal calprotectin levels in non-active chronic gastritis was found to be in the normal category slightly increased by 21 (45.7%) and categories increased significantly by 25 (54.3%).

Fecal biomarkers show good performance characteristics in identifying active inflammation endoscopically in IBD patients. This study also shows that the combination of an elevated fecal calprotectin test and occult blood is highly specific for endoscopically active disease.¹⁹ Fecal calprotectin levels were higher in patients with active chronic gastritis than in patients with inactive chronic gastritis.²¹ This research is not in line with the results of research conducted where fecal calprotectin levels in this study were found to increase significantly in non-active chronic gastritis sufferers. Fecal calprotectin is a biomarker that can detect inflammation in the digestive tract, including in cases of non-active chronic gastritis. Fecal calprotectin is a cytoplasmic protein released from neutrophils, monocytes, and macrophages in response to inflammation in the digestive tract mucosa. In cases of non-active chronic gastritis, even though there is no ulceration or active bleeding, there is still chronic inflammation of the gastric mucosa. This chronic inflammation causes increased infiltration of inflammatory cells, such as neutrophils, into the gastric mucosa. This increase in the number of inflammatory cells causes increased levels of fecal calprotectin found in fecal samples. Therefore, fecal calprotectin examination can be a sensitive biomarker for detecting inflammation in cases of non-active chronic gastritis, even though there are no signs of active bleeding. So, it can be concluded that the increase in fecal calprotectin levels in non-active chronic gastritis sufferers is caused by chronic inflammation of the gastric mucosa which persists even though there is no active ulceration or bleeding.¹⁹

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The results of statistical tests on the relationship between gastritis inflammatory activity and occult blood showed p value = 1,000, meaning it was proven that there was no relationship between non-active and active chronic gastritis inflammatory activity and the patient's fecal occult blood. For the statistical test results regarding the relationship between gastritis inflammation activity and fecal calprotectin, it was found that p value = 0.413, meaning that it was proven that there was no relationship between chronic gastritis inflammation activity, both inactive and active, and fecal calprotectin. Answering the researcher's hypothesis, namely that there is a relationship between inflammatory activity and fecal calprotectin levels and occult blood in chronic gastritis sufferers at Mitra Kemayoran Hospital, the hypothesis was rejected because this study did not find a significant relationship between inflammatory activity and fecal calprotectin levels and occult blood in chronic gastritis sufferers. at Mitra Kemayoran Hospital.

This is contrary to research by Demirbas F, et al,²⁰ found an association with higher fecal calprotectin levels in patients with active chronic gastritis compared to patients with inactive chronic gastritis. Likewise in the research of Aksoy ÖY, et al,²¹ where the results of the research showed that fecal calprotectin levels correlated with the level of neutrophil activity in the stomach. Fecal calprotectin represents or reflects the presence of neutrophilic inflammation in the stomach. The results showed no significant relationship between inflammatory activity and fecal calprotectin levels and occult blood. Researchers tried to find out what factors occurred that could explain the findings. Inflammatory activity in gastritis may not be severe enough to cause significant changes in the levels of fecal calprotectin and occult blood biomarkers. There are factors other than inflammatory activity that can influence fecal calprotectin and occult blood levels. Biomarker measurement methods may be less sensitive to detect significant changes small.

V. CONCLUSION

1. Characteristics of gastritis inflammatory activity: 18 patients (28.1%) had active chronic gastritis inflammatory activity and 46 patients (71.9%) had non-active chronic gastritis inflammatory activity.
2. It was found that fecal calprotectin levels in patients with chronic gastritis with non-active inflammatory activity in the normal category increased slightly in 21 (45.7%) people and increased significantly in 25 (54.3%). Meanwhile, for active inflammatory activity, the normal category increased slightly in 6 (33.3%) and the significantly increased category was found in 12 (66.7%) people.
3. There were 12 (66.7%) negative gastritis patients with active inflammatory activity, 6 (33.3%) positive occult blood results, while 32 (69.6%) occult blood

results were negative for chronic gastritis patients with inactive inflammatory activity, and 14 (30.4%) had negative occult blood results. %) positive occult blood.

4. There is no significant relationship between inflammatory activity and occult blood at p value $1,000 > 0.05$ and there is no significant relationship between inflammatory activity and fecal calprotectin levels with p value $0.413 > 0.05$.

VI. CONFLICT OF INTEREST

There are no conflict of interest.

VII. AUTHORS CONTRIBUTION

All authors contributed to the data writing process up to publication

VIII. FUNDING

There was no funding in this study and the authors used independent funding

ACKNOWLEDGMENT

The authors would like to thank Department of Medical Laboratory Technology, Health Polytechnic Ministry of Health Jakarta III, Indonesia;, and Mitra Kemayoran Hospital, Centre of Jakarta, Indonesia

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