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Diagnostic Accuracy Of Fecal Calprotectin In Prediction Of Ulcerative Colitis In Patients Of Inflammatory Bowel Disease

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Abstract

Background : Ulcerative colitis is an idiopathic inflammatory condition of the colon which results in diffuse friability and superficial erosions on the colonic wall associated with bleeding. We will assess how faecal calprotectin can be used as a non-invasive tool to aid referral to GI services, and how this improves cost effectiveness of resource allocation through reduction of unnecessary colonoscopies.

Objective: To determine the diagnostic accuracy of fecal calprotectin in prediction of ulcerative colitis in patients of inflammatory bowel disease.

Study Design: A Cross Sectional Validation Study.

Setting: Department of Gastroenterology, ATH, Abbottabad.

Duration of Study: This study was conducted from 10th May 2021 to 10th November 2021.

Methods: A total of 313 patients of both gender with inflammatory bowel disease were included in the study. Ulcerative colitis was noted as per 2 operational definition from fecal calprotectin and histopathology as positive/negative on especially designed proforma.

Results: In this study age range was 18 to 50 years with mean age of 41.530±5.63 years and mean duration of complaints was 11.258±3.72 months. Fecal calprotectin diagnosed 54(17.3%) patients while histopathology diagnosed 40(12.8%) patients with ulcerative colitis.Fecal calprotectin has shown sensitivity of 70%, specificity 90.5% and diagnostic accuracy by 88%, PPV 51.9% and NPV 95.4% in diagnosisof ulcerative colitis.

Conclusion: fecal calprotectin is a highly reliable predictor of endoscopic activity in IBD patients. It performs better for ulcerativecolitis prediction.

Keywords: Inflammatory bowel disease, Ulcerative colitis prediction, Histopathology, Fecal calprotectin

Introduction

Ulcerative colitis is a form of chronic idiopathic inflammatory bowel disease characterised by inflammation of colon and rectum. It is cyclic, with episodes of relapse and remission, and is manifested by diarrhea, abdominal pain, rectal bleeding, and tenesmus, which may cause substantial decrease in the quality of life [1]. It is still not clear what causes UC, but it is thought that the disease may stem from an abnormal reaction by the immune system to the bacteria and other microbes naturally present in the gut, in vulnerable people who also have certain genetic markers [2]. Histo-pathological assessment of colonic biopsies has been considered the most reliable method of diagnosing UC; Though pulse biopsies is invasive, labour expensive and can be associated with complications in some patients [3]. Due to the high seriousness of the disease and the necessity of repeated testing, there is significant interest in noninvasive biomarkers that would provide an accurate representation of disease activity in order that management decisions might be made. Friably, fecal calprotectin (FC), a calcium and zinc-binding protein primarily contained in neutrophils is one of the most promising biomarkers for this purpose [4]. FC is liberated during inflammation and is not susceptible to degradation in the intestine thereby it serves as an antecedent of the gastrointestinal inflammation [4]. Faecal calprotectin has also been found to be significantly raised in IBD and has been reported to be in concordance to endoscopic and histologic activity; it may therefore be considered a biomarker for mucosal healing [6]. Fecal calprotectin has been assessed in many investigations for determination of the diagnostic reliability between IBD and IBS, and judging the level of inflammation in patients with IBD [7]. All the same, there is scarcity of information about the fecal calprotectin in determining presence of ulcerative colitis in patients with IBD. Fecal calprotectin is an easy, noninvasive method to distinguish between UC and other conditions, which could decrease the requirement of hi-tech colonoscopy for UC diagnosis and, thus, lower the pain and cost for patients [8]. The general objective of this study will be to evaluate the diagnostic performance of fecal calprotectin in risk assessment of ulcerative colitis in IBD patients with histopathological examination as gold standard. An objective of this study is therefore to evaluate the diagnostic accuracy of fecal calprotectin where we will compare the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall diagnostic accuracy of fecal calprotectin in the UC management plan.

Methods

A total of 313 patients with confirmed diagnosis of inflammatory bowel disease, aged between 18-50 years, were recruited in the study. Especially, those who had other diseases such as Crohn's disease were not included and patients who had undergone recent gastrointestinal surgery were excluded. These patients were chosen in a purposive manner consecutively as they sought treatment at the outpatient department of the study site.

Data Collection

Information was obtained by means of a specific proforma prepared for this research. Faecal calprotectin values were assayed using a commercially available enzyme-linked immunosorbent assay (ELISA) kit, and the outcomes were dichotomised as positive or negative according to the cut-off points. The diagnoses of ulcerative colitis in the official reports were based on histopathological examination of colonic biopsy specimens.

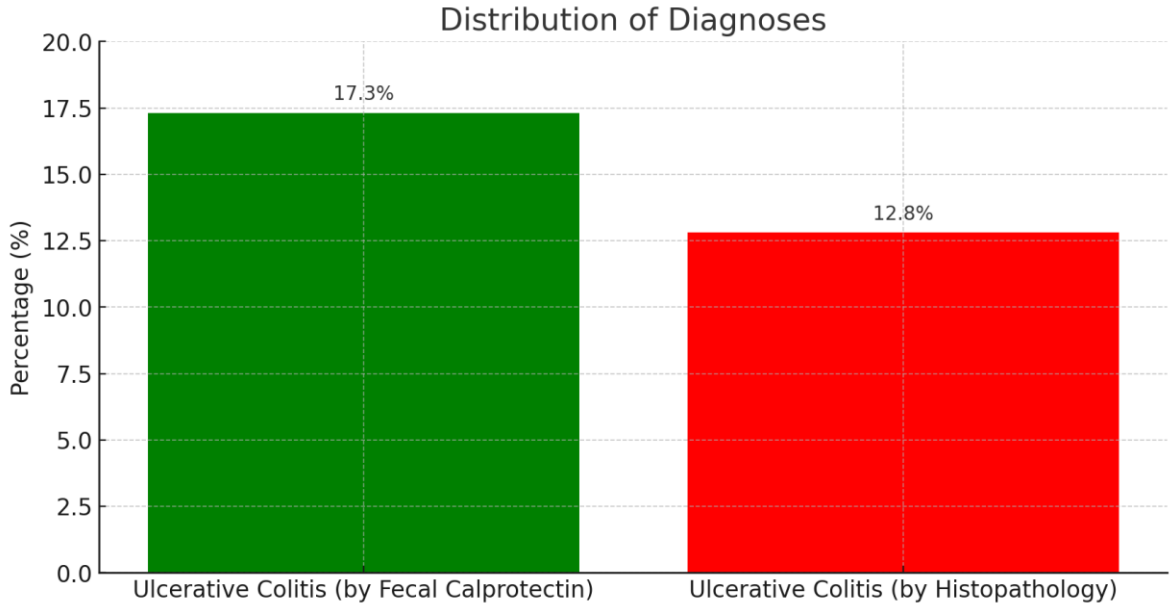
Statistical Analysis

Data was analyzed using the statistical package of Social Science System (SPSS) version 24. The overall diagnostic yield, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of fecal calprotectin were determined by using histopathological outcome as the reference

standard. In the case of continuous data, results are presented using mean ± standard deviation (SD) and in case of categorical data using absolute number and percentage.

Results

The study involved 313 patients of the mean age 41. 53 ± 5. 63 and the mean complaints' duration, 11. 26 ± 3. 72 months. Of these, fecal calprotectin identified ulcerative colitis in 54 (17. 3%) patients, and histopathology in 40 (12. 8%) patients. The compiled prevalence of fecal calprotectin in this condition was observed to have sensitivity of 70% for ulcerative colitics, specificity of 90. 5%,PPV of 51. 9% and NPV of 95. 4%. Diagnostic accuracy for all numbers was 88%. Altogether, the presented findings indicate that fecal calprotectin is accurate in the diagnosis of ulcerative colitis in patients with IBD since it helps avoid many colonoscopies.



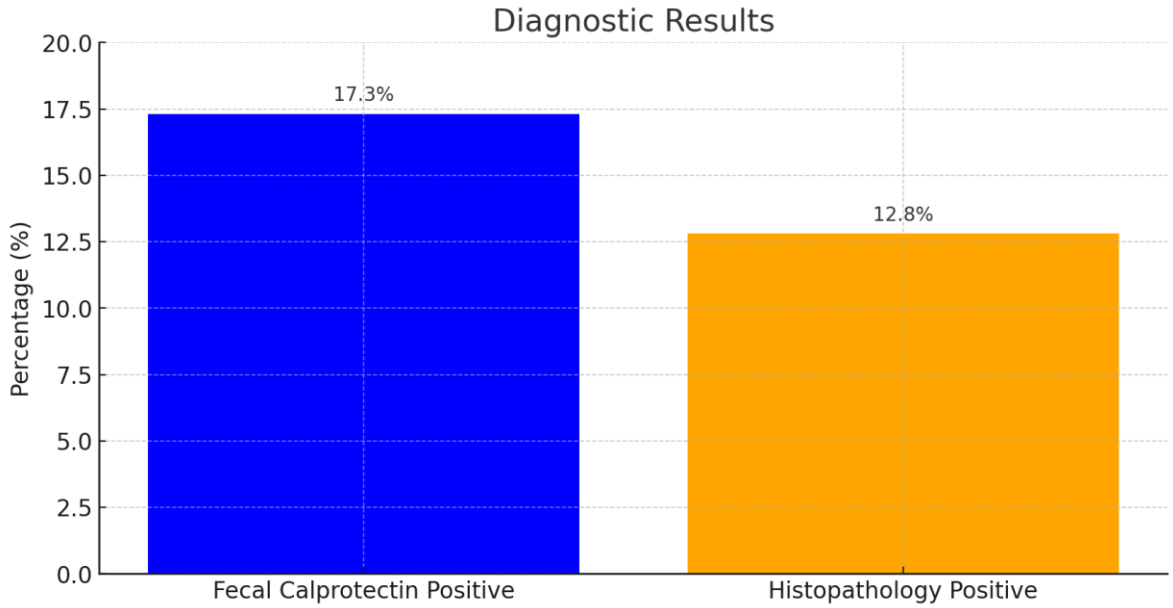


Table 01: Demographic Characteristics

Characteristic	**Mean ± SD**	**Range**
Age (years)	41.53 ± 5.63	18-50
Duration of Complaints (months)	11.26 ± 3.72	1-36

Table 02: Diagnostic Results

Test	Number of Patients	Percentage (%)
Fecal Calprotectin Positive	54	17.3
Histopathology Positive	40	12.8

Table 03: Diagnostic Accuracy of Fecal Calprotectin

Parameter	**Value (%)**
Sensitivity	70.0
Specificity	90.5
Positive Predictive Value (PPV)	51.9
Negative Predictive Value (NPV)	95.4
Diagnostic Accuracy	88.0

Tale 4: Distribution of Diagnoses

Diagnosis	**Number of Patients**	**Percentage (%)**
Ulcerative Colitis (by Fecal Calprotectin)	54	17.3
Ulcerative Colitis (by Histopathology)	40	12.8

Discussion

Fecal calprotectin as a non invasive biomarker for UC in patients with IBD has been a topic of much investigation with regards to diagnostic accuracy. In a cross sectional study in our centre, we showed that FC has a sensitivity of 70% and a specificity of 90. 5% in diagnosing UC, with an overall diagnostic accuracy of 88%. Such findings relate with other studies on the applicability of FC in IBD especially in distinguishing UC from conditions like IBS and CD. The sensitivity of 70% is not far off from the results of other studies by Burri et al, for whom the sensitivity of FC ranged between 66% and 83% when predicting endoscopic activity in UC patients [7]. This moderate sensitivity means that FC is a valid test for the detection of patients with active UC, but does not necessarily include those with inactive or very mild UC. This limitation explains why FC should be utilized in combination with other modalities in patient with ambiguous symptoms. Our specificity of 90. 5% is similar to the observation made by Røseth et al where FC had a specificity of 88-93% in differentiating IBD from non-inflammatory conditions such as IBS. This high specificity means that FC is a good negative criterion for UC in patients who test negative implying low probability of UC and thus the need to avoid invasive exams such as colonoscopy in such patients.

Specificity of FC in our study is also acceptable, if we compare it with the other non invasive tests, like fecal lactoferrin, whose specificity in UC patients was reported to be lower [9]. Hence, the figure of 88% that we found in the present study for the overall diagnostic accuracy of FC is acknowledging with other meta-analysis with regard to the application of FC in IBD. For example, van Rheenen et al assigned a pooled diagnostic accuracy of 85% in a systematic review of the utility of FC in diagnosing mucosal inflammation in IBD patients [10]. What this implies is that FC is not only useful in confirming active inflammation but also a sensitive marker for quantifying the severity of UC over a period of time as long term management of the disease is considered. The study has demonstrated a PPV of 51. 9% which suggests that although FC is highly specific for UC if positive, there is still considerable number of ‘‘false-positive’’ results. This is in line with Laharie et al. , who observed that FC can be sometimes elevated in patients with non-IBD disorders for instance infection or inflammation [11]. Hence, although the presence of a positive FC test raises the probability of UC, it can by no measure be relied on to provide a conclusive diagnosis. On the other hand, Cage et al also indicated a negative predictive value of 95. 4% in the same study this shows that FC is very efficient in excluding UC in patients where the test is negative. As Jason Schoepfer and other researchers pointed out, FC levels below a specific level are well correlated with the lack of inflammation, which means that there is a low likelihood of ND will be required in these patients [12]. Surprisingly enough our results pinpoint certain parameters of FC diagnostic performance to be even higher than in some of the prior studies, for instance, those by Konikoff et al reporting about 80% diagnostic accuracy of FC in UC [13]. This could be due to differences in the kind of patients taking part in different studies, the degree of disease that the participants had or the different cut off values used for the determination of FC. Consequently, the present study re-asserts the use of fecal calprotectin as a biomarker that can be used in determining patients with ulcerative colitis based on the IBD patients selected from the private health centres in Hong Kong. Despite high specificity and a high NPV, FC tested moderately in sensitivity and PPV, and as such should be employed in conjunction with other diagnostic analyses, instead of being a stand-alone detection method[14]. As per the previous research studies, these results support and demonstrate the role of FC as an effective methodology in enhancing the cost efficiency of IBD management by minimizing the unneeded colonoscopies.

Conclusion

Fecal calprotectin is an accurate and very sensitive inflammatory bowel disease, and ulcerative colitis biomarker. Our study shows that utilising fecal calprotectin with its high specificity and negative predictive value can help in avoiding unnecessary invasive investigations such as colonoscopies in patients who are less likely to have a high activity of the disease. As suggested by moderate sensitivity, it may not identify all cases, especially those with less severe form of the disease, but it is nonetheless useful in the clinical management of ulcerative colitis. These results are in line with previous studies, despite some limitations, and have strong evidence of the impact of fecal calprotectin in enhancing the cost and work-related productivity of IBD. There is a need for further studies that will establish the best approach in utilising Fecal calprotectin along with other diagnostic tools to improve its diagnostic role in different contexts.

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