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# Correlation between fecal (calprotectin and lactoferrin) results and colonoscopic findings in chronic diarrhea and recurrent abdominal pain in children and adolescents

**Raafat Abdel-Raouf Muhammad Khattab**
Pediatric department, Faculty of Medicine, Al-Azhar University, Egypt

**Hany Ali Hussien Samy**
Pediatric department, Faculty of Medicine, Al-Azhar University, Egypt

**Ahmed Helal El Sayed**
Pediatric department, Faculty of Medicine, Al-Azhar University, Egypt

**Ahmed Ali Ali Assem**
Clinical Pathology department, Faculty of Medicine, Al-Azhar University, Egypt

**Mohammed Sobhy Mohammed Mansour**
Pediatric department, Faculty of Medicine, Al-Azhar University, Egypt
Corresponding author email: mohammedmansour908@gmail.com

***Abstract*---**Background: Currently, endoscopy with biopsy is still considered the gold standard for the evaluation and diagnosis of mucosal inflammation and a number of scores exist to assess endoscopic activity in Crohn's disease (CD) and ulcerative colitis (UC). Aim and objectives: the aim of the study was to determine the benefit of using both of fecal markers (calprotectin and lactoferrin) in patients presenting with chronic diarrhea and recurrent abdominal pain for differentiation between organic diseases, particularly inflammatory bowel disease (IBD) from non-organic disease, making colonoscope unnecessary. Subjects and methods: This prospective, observational and analytic study was carried out on 44 children who fulfilling the designed inclusion criteria. The study was carried out from Outpatient Clinic of Pediatric gastroenterology unit and from the Inpatient Units of the Pediatric department Faculty of Medicine, Al-Azhar University Hospitals (Al-Hussein & Sayed Galal Hospitals), as well as referral from other hospitals complaining of recurrent abdominal pain and chronic diarrhea from March 2020 to March 2022. Results: there was statistically significant difference between IBD group and functional abdominal pain group as regard fecal

calprotectin with p-value≤ 0.001. There was statistically significant difference between IBD group and functional abdominal pain group as regard fecal lactoferrin with p-value≤ 0.001. Conclusion: Fecal calprotectin and lactoferrin is a useful screening tool for identifying children and adolescents with chronic diarrhea and recurrent abdominal pain, for differentiation between organic diseases, particularly inflammatory bowel disease (IBD) from non-organic disease

***Keywords*---**abdominal pain, chronic diarrhea, endoscopy, fecal calprotectin, lactoferrin inflammatory bowel disease.

## Introduction

The exact etiology of chronic diarrhea are many different causes, causes will vary depending on the socioeconomic status of the individual. Individuals in a lower socioeconomic status will be more likely to have chronic bacterial, and parasitic infections , while mid to high socioeconomic status individuals are more likely to have irritable bowel syndrome, inflammatory bowel disease, and malabsorption syndromes**.** [1]

Recurrent abdominal pain (RAP) in children is defined as episodes of pain occurring at least monthly for 3 consecutive months with a severity that interrupts routine functioning. RAP continues to be one of the most ubiquitous conditions faced by the healthcare team and has a significant emotional and economic impact. [2]

Chronic abdominal pain (CAP) in childhood accounts for 2% to 4% of office visits to primary care clinicians and 50% to pediatric gastroenterologists. Differentiation among organic gastrointestinal, organic non-gastrointestinal and functional gastrointestinal disorders can be difficult, but specific criteria are available [3]

Chronic abdominal pain is defined by the **American Academy of Pediatrics**' **(AAP)** [4] clinical report as "long-lasting intermittent or constant abdominal pain that is functional or organic.", Chronic abdominal pain in children makes significant anxiety in both patients and their families. In addition, the economic impact on health care is substantial.

Functional abdominal pain is not uncommon; however, a diligent evaluation is paramount, even if suspicion is high, to exclude organic conditions.[3] Inflammatory bowel disease (IBD) is a chronic disorder of intestinal inflammation characterized by a relapsing and remitting course. IBD encompasses the diagnoses which include Crohn's disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBD-U). [5]

Among children with IBD, 4% present before the age of 5 years and 18% before the age of 10 years, with the peak onset in adolescence. [6] Markers of inflammation detected in the stool play a significant role in the diagnosis of inflammatory bowel disease. The best known belong to calprotectin and lactoferrin, which are

produced by natural granulocytes. These markers are suitable for their usage in diagnosis, assessment of the treatment results, disease relapse and mucosal healing in both crohn's and ulcerative colitis. [7]

Fecal calprotectin has the most diagnostic value to symptoms of inflammatory bowel disease compared with blood markers. Fecal calprotectin is added to diagnostic workup of pediatric patients with symptoms suggestive with inflammatory bowel disease. [8]

Some previous studies indicated that fecal LF has the potential to act as the biomarker for IBD, both Crohn's disease (CD) and ulcerative colitis (UC), but its performance in diagnosing UC patients was better than that in CD patients. [9] Combination of both markers lactoferrin and calprotectin may accurately distinguish IBD from non-IBD conditions (such as irritable bowel syndrome). [10] The aim of this study was to determine the benefit of using both of fecal markers(calprotectin and lactoferrin ) in patients presenting with chronic diarrhea and recurrent abdominal pain for differentiation between organic diseases, particularly inflammatory bowel disease (IBD) from non-organic disease, making colonoscope unnecessary.

**Patients and Methods**

Prospective, observational and analytic study was carried out to find correlation between (fecal claprotectin and fecal lactoferrin) levels and colonscopic finding in children and adolescence complaining of chronic diarrhea and recurrent abdominal pain.

**Sampling and study setting**

The study was conducted on 44 children who fulfilling the designed inclusion criteria. The study was carried out from Outpatient Clinic of Pediatric gastroenterology unit and from the Inpatient Units of the Pediatric department Faculty of Medicine, Al-Azhar University Hospitals (Al-Hussein & Sayed Galal Hospitals), as well as referral from other hospitals complaining of recurrent abdominal pain and chronic diarrhea from March 2020 to March 2022. Inclusion criteria: Age: from 2 to 18 years, Sex: both sexes will be involved, Complaint: Chronic diarrhea more than 4 weeks and recurrent abdominal pain (defined as: episodes of abdominal pain occurring at least monthly for 3 consecutive months with a severity that interrupts routine functioning) as the chief complaint.

**Exclusion criteria:** Age less than 2 or more than 18 years, chronic use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), patient with acute diarrhea, past history of any malignant condition and chemotherapy, major gastrointestinal surgical procedures, liver cell failure, coagulopathy, and chronic renal failure, congestive heart failure, and endocrinal diseases (diabetes, thyroid disease), immune-compromised patients, smokers, drug or alcohol abuse, mentally disabled children and adolescents and patients with active inflammatory condition like acute otitis media, glomerulonephritis, cystic fibrosis, rheumatoid and psoriatic arthritis or Kawasaki disease.

For all patients the following were done: A written informed consent was taken from the parent prior to involvement any patient in this study. The study was approved by the local Ethics Committee, Faculty of Medicine, Al-Azhar University. Detailed medical history and physical examination: patient's details questionnaire regarding history taking with special emphasis on abdominal pain, weight loss, rectal bleeding, diarrhea, constipation, malaise, lethargy, anorexia, nausea, tenesmus, abdominal distension, passage of mucus.

**Laboratory investigations: CBC, CRP and ESR, liver function tests and kidney function tests and PT, PTT, INR, PC**

Stool sample for: Stool analysis, PH, reducing substances and stool culture, fecal calprotectin test by (quantitative) ELISA method All the eligible subjects were asked to provide a stool sample for measurement of calprotectin, and lactoferrin levels, within 2 days of endoscopic examination and before starting specific therapy. Specimen Collection: Collect fecal sample with a commercial stool sample collection device. The collected sample can be stored stable for 3 days at room temperature (15 °C - 30 °C), 4 days at( 2 °C - 8 °C )or up to 6 month at (-20 °C).

**Fecal lactoferrin test by (quantitative) ELISA method:** Specimen Collection: Collect fecal sample with a commercial stool sample collection device. The collected sample can be stored stable for 3 days at room temperature (15 °C - 30 °C), 4 days at( 2 °C - 8 °C )or up to 6 month at (-20 °C).

**Colonoscopy and biopsy**: for all patients with chronic diarrhea, bleeding per rectum,and recurrent lower abdominal pain ,the macroscopic endoscopic features of mucosa was evaluated and multiple biopsies were taken (from both diseased and healthy areas) for histopathological examination.

**upper GIT endoscope and biopsy for selected cases with:** recurrent upper abdominal pain and chronic diarrhea , the macroscopic endoscopic features of mucosa was evaluated and multiple biopsies were taken (from both diseased and healthy areas) for histopathological examination.

**Histopathological examination of biopsy specimens**

**Statistical Analysis:** Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 **(**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. The Shapiro-Wilk test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The used tests were: Chi-square test, Fisher's Exact or Monte Carlo correction, Mann Whitney test, Student t-test and Spearman coefficient

Receiver operating characteristic (ROC curve) analysis was used to find out the over all predictivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value.

- Sensitivity = (true +ve)/ [(true +ve) + (false –ve)].
- Specificity = (true –ve) / [(true –ve) + (false +ve)].
- PPV = (true +ve) / [(true +ve) + (false +ve)].

•NPV = (true –ve)/ [(true –ve) + (false –ve)].
•Accuracy = (TP+TN)/[TP+FP+TN+FN]
The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value <0.05was considered significant, P-value <0.001 was considered as highly significant, P-value>0.05wasconsidered insignificant.

**Results**

Table (1)
Different complain of the studied cases: (n = 44)

| Complain | No. | % |
|---|---|---|
| Chronic Abdominal pain | 44 | 100.0 |
| Chronic diarrhea | 31 | 70.5 |
| Bleeding per rectum | 25 | 56.8 |
| Extra intestinal manifestation | | |
| Ankylosing spondylitis | 1 | 2.3 |
| Sacroilitis | 1 | 2.3 |

There was (100%) of patient were complaining of chronic abdominal pain, (31patient) 70.5% of patient were complaining of chronic diarrhea, (25patient) (56.8%) of patient were complaining of bleeding per rectum, and 2 patient (4.5%) were complaining of Extra intestinal manifestation.

Table (2)
Fecal calprotectin and Fecal lactoferrin results of the studied cases (n = 44)

| | No. | % |
|---|---|---|
| Fecal calprotectin(ug/gm) | | |
| Normal <50 | 19 | 43.2 |
| Abnormal ≥50 | 25 | 56.8 |
| Min. – Max. | 13.0 –1500.0 | |
| Mean ± SD. | 310.4 ±378.8 | |
| Median (IQR) | 112.5 (32.50 –515.5) | |
| Fecal lactoferrin (ng/dl) | | |
| Normal <25 | 25 | 56.8 |
| Abnormal ≥25 | 19 | 43.2 |
| Min. – Max. | 4.50 –820.0 | |
| Mean ± SD. | 63.81 ±126.8 | |
| Median (IQR) | 19.0 (11.50 –80.0) | |

IQR: Inter quartile range SD: Standard deviation

Fecal calprotectin and Fecal lactoferrin results of the studied cases,as regard fecal calprotectin was postive (abnormal) in(56.8%)of patients, while fecal lactoferrin was postive (abnormal) in(43.2%)of patients.

Table (3)
Correlation between Fecal calprotectin and different laboratory parameters (n= 44)

| | Fecal calprotectin | |
|---|---|---|
| | $r_s$ | p |
| HB (g/dl) | 0.024 | 0.875 |
| TLC(1000/mm3) | 0.153 | 0.321 |
| Eosinophil (%) | 0.048 | 0.755 |
| PLT (1000/mm3) | 0.562 | <0.001* |
| ESR mm/h (1sthr) | 0.090 | 0.562 |
| ESR mm/h (2ndhr) | 0.161 | 0.295 |
| PT (sec) | 0.003 | 0.983 |
| PTT (sec) | -0.295 | 0.052 |
| INR | 0.069 | 0.658 |
| ALT (u/l) | 0.087 | 0.576 |
| AST (u/l) | 0.377 | 0.012* |
| Creatinin (mg/d) | -0.115 | 0.457 |

$r_s$: Spearman coefficient *: Statistically significant at $p \leq 0.05$

There was a highly statistically significant difference between fecal calprotectin level and CBC as regard PLT count with p-value ≤ 0.001 But no statistically significant difference with HB ,TLC ,Eosinphilic count , with p-value >0.05. There was a statistically significant difference between fecal calprotectin level and liver function s as regard AST, with p-value ≤ 0.05, But no statistically significant difference with ALT , with p-value >0.05. There was a no statistically significant difference between fecal calprotectin level and (ESR, coagulation profil and serum creatinin) with p-value >0.05

Table (4)
Correlation between Fecal lactoferrin and different laboratory parameters (n= 44)

| | Fecal lactoferrin | |
|---|---|---|
| | $r_s$ | p |
| HB (g/dl) | -0.106 | 0.495 |
| TLC(1000/mm3) | 0.230 | 0.133 |
| Eosinophil (%) | -0.002 | 0.989 |
| PLT (1000/mm3) | 0.450 | 0.002* |
| ESR mm/h (1sthr) | 0.252 | 0.099 |
| ESR mm/h (2ndhr) | 0.277 | 0.069 |
| PT (sec) | 0.191 | 0.215 |
| PTT (sec) | -0.252 | 0.099 |
| INR | 0.212 | 0.168 |
| ALT (u/l) | -0.015 | 0.922 |
| AST (u/l) | 0.382 | 0.010* |
| Creatinin (mg/d) | -0.093 | 0.548 |

$r_s$: Spearman coefficient *: Statistically significant at $p \leq 0.05$

There was a statistically significant difference between fecal lactoferrin level and CBC as regard PLT count with p-value ≤ 0.05, But no statistically significant difference with (HB ,TLC ,Eosinphilic count) with p-value >0.05. There was a statistically significant difference between fecal lactoferrin level and liver function s as regard ALT , with p-value ≤ 0.05 ,But no statistically significant difference with AST , with p-value >0.05. There was a no statistically significant difference between fecal lactoferrin level and (ESR, coagulation profil and serum creatinin), with p-value >0.05

Table (5)
Comparison between IBD and non IBD as regard Fecal calprotectin (ug/g)

| Fecal calprotectin (ug/g) | IBD (n = 14) | | Non IBD (n = 30) | | p |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Normal <50 | 0 | 0.0 | 19 | 63.3 | <0.001* |
| Abnormal ≥50 | 14 | 100.0 | 11 | 36.7 | |
| Mean ± SD. | 758.3 ± 349.5 | | 101.4 ± 126.2 | | <0.001* |
| Median (Min. – Max.) | 710.0 (207.0 – 1500) | | 41.0 (13.0 – 447.0) | | |

$\chi^2$: Chi square test U: Mann Whitney test
p: p value for comparing between **IBD** and **Non IBD**
*: Statistically significant at p ≤ 0.05

There was a highly statistically significant difference between IBD group and non IBD group as regard fecal calprotectin using Chi square test with p-value≤ 0.001

Table (6)
Comparison between IBD and non IBD as regard fecal lactoferrin

| Fecal lactoferrin (ng/dl) | IBD (n = 14) | | Non IBD (n = 30) | | p |
|---|---|---|---|---|---|
| | No. | % | | | |
| Normal <25 | 0 | 0.0 | 25 | 83.3 | <0.001* |
| Abnormal ≥25 | 14 | 100.0 | 5 | 16.7 | |
| Mean ± SD. | 143.9 ± 197.5 | | 26.42 ± 42.42 | | <0.001* |
| Median (Min. – Max.) | 97.0 (39.0 – 820.0) | | 12.50 (4.50 – 186.0) | | |

$\chi^2$: Chi square test U: Mann Whitney test
p: p value for comparing between IBD and Non IBD
*: Statistically significant at p ≤ 0.05

There was a highly statistically significant difference between IBD group and non IBD group as regard fecal lactoferrin using Chi square test with p-value≤ 0.001

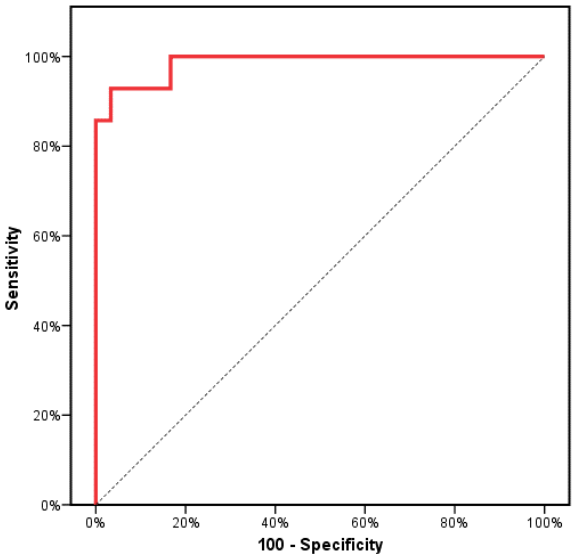


Figure (1): ROC curve for Fecal calprotectin to discriminate IBD patients (n = 14) from Non IBD (n = 30)

There was a highly statistically significant difference between IBD group and non IBD group as regard fecal calprotectin with p-value≤ 0.001,with cut off level >340, Sensitivity 92.86%, Specificity 90.0%, PPV81.2, and NPV96.4.

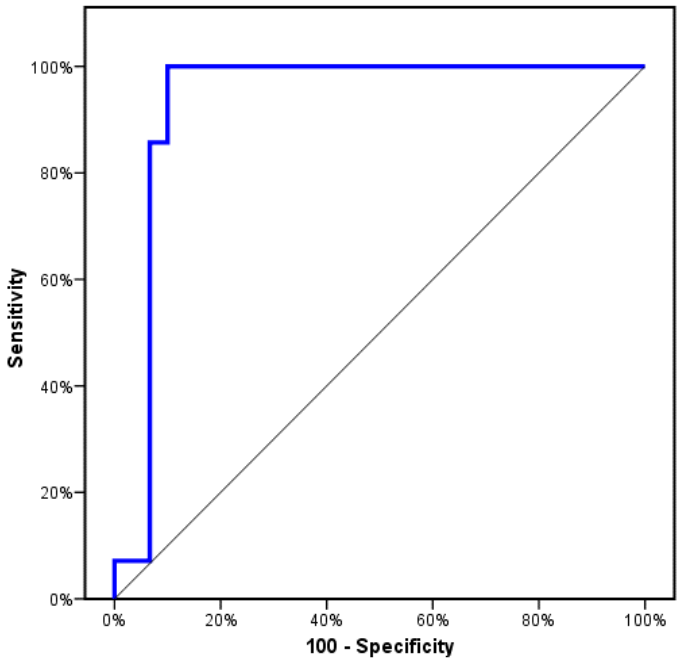


Figure (2): ROC curve for Fecal lactoferrin to discriminate IBD patients (n = 14) from Non IBD (n = 30)

There was a highly statistically significant difference between IBD group and non IBD group as regard fecal lactoferrin with p-value≤ 0.001,with cut off level >45, Sensitivity 85.71%, Specificity 90.0%. PPV80.0 and NPV93.1

Table (7)
Comparison between IBD and Functional abdominal pain- not otherwise specified as regard Fecal calprotectin (ug/g)

| Fecal calprotectin (ug/g) | IBD (n = 14) | | Functional abdominal pain- not otherwise specified (n = 7) | | P |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Normal <50 | 0 | 0.0 | 7 | 100.0 | $^{FE}p$ <0.001* |
| Abnormal ≥50 | 14 | 100.0 | 0 | 0.0 | |
| Mean ± SD. | 758.3 ± 349.5 | | 27.43 ± 14.12 | | <0.001* |
| Median (Min. – Max.) | 710.0 (207.0 – 1500) | | 18.0(15.0 – 46.0) | | |

$\chi^2$: Chi square test U: Mann Whitney test
p: p value for comparing between IBD and Functional abdominal pain- not otherwise specified
*: Statistically significant at p ≤ 0.05

This table shows highly statistically significant difference between IBD group and functional abd pain- not otherwise specified as regard fecal calprotectin with p-value≤ 0.001

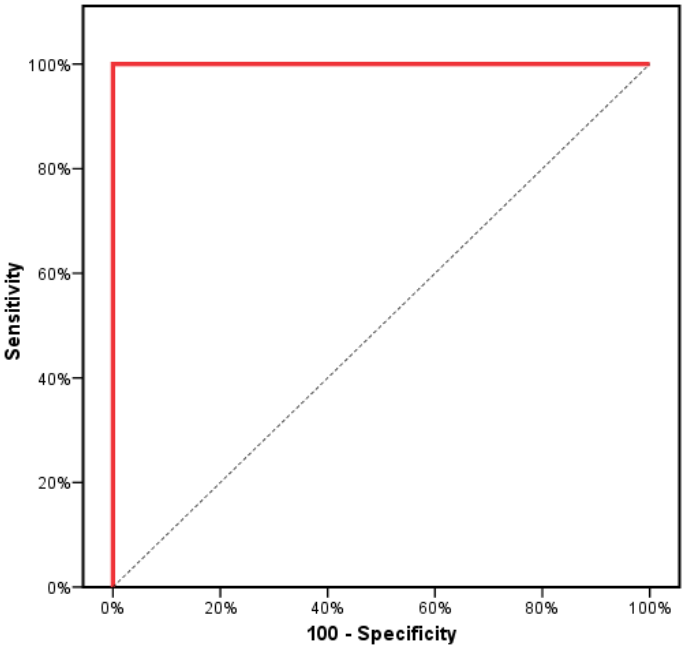


Figure (3): ROC curve for Fecal calprotectin to discriminate IBD patients (n = 14) from Functional abdominal pain- not otherwise specified (n= 7)

There was a highly statistically significant difference between IBD group and Functional abdominal pain- not otherwise specified group as regard fecal calprotectin with p-value≤ 0.001,with cut off level >46, Sensitivity 100%,and Specificity 100%.

Table (8)
Comparison between IBD and Functional abdominal pain- not otherwise specified as regard fecal lactoferrin

| Fecal lactoferrin (ng/dl) | IBD (n = 14) | | Functional abdominal pain- not otherwise specified (n = 7) | | P |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Normal <25 | 0 | 0.0 | 7 | 100.0 | $^{FE}p$ <0.001* |
| Abnormal ≥25 | 14 | 100.0 | 0 | 0.0 | |
| Mean ± SD. | 143.9 ± 197.5 | | 12.43 ± 4.50 | | <0.001* |
| Median (Min. – Max.) | 97.0 (39.0 – 820.0) | | 11.0(8.0 – 19.0) | | |

$\chi^2$: Chi square test U: Mann Whitney test
p: p value for comparing between IBD and Functional abdominal pain- not otherwise specified
*: Statistically significant at p ≤ 0.05

This table shows highly statistically significant difference between IBD group and functional abd pain- not otherwise specified group as regard fecal lactoferrin with p-value≤ 0.001

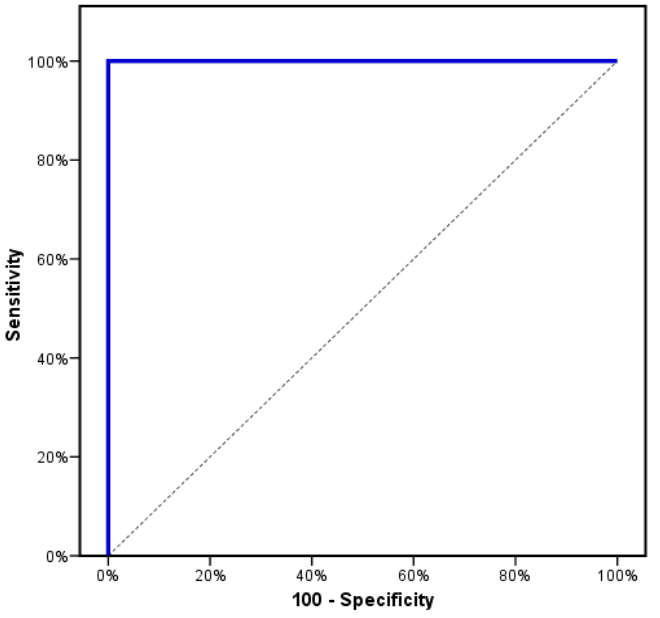


Figure (4 ) ROC curve for Fecal lactoferrin to discriminate IBD patients (n = 14) from Functional abdominal pain- not otherwise specified (n= 7)

There was a highly statistically significant difference between IBD group and Functional abdominal pain- not otherwise specified group as regard fecal lactoferrin with p-value≤ 0.001,with cut off level >19, Sensitivity 100%,and Specificity 100.0%.

**Discussion**

Chronic abdominal pain (CAP) is very common in children and adolescent and results in high personal and social costs. It is associated with reduced health-related quality of life comparable to organic gastrointestinal diseases. The worldwide prevalence has been estimated at 13.5% with comparable rates across continents. It is more common in females with peak prevalence in the early teens. [11]

There are many functional and organic gastrointestinal (GI) conditions that can lead to CAP, The presence of alarm signs and symptoms, notably anemia, hematochezia, and weight loss help identify patients with CAP who require further work-up and referral to a pediatric gastroenterologist. [12]

The final diagnosis of patients of this study total number (n = 44): (14 patient) (31.8%) IBD, (7 patient) (15.9%) Functional abdominal pain- not otherwise specified, (12patient) (27.3%) Infectious colitis, (2patient) (4.5%) Eosinophilic colitis, (1patient) (2.3%) Eosinophilic enterocolitis, (2) patients (4.5%) Familial adenomatous polyposis coli (FAP), (2patient) (4.5%) Tufting enteropathy, (1patient) (2.3%) Solitary rectal ulcer syndrome (SRUS), (1patient) (2.3%) Abeta lipoprotinemia, (1patient) (2.3%) Un diagnosed Chronic diarrhea, (1patient) (2.3%) Hemangioma colon.

There was no statistically significant difference between IBD group and non IBD as regard age, sex, residence, and consanguinity. in IBD group(14 patient ) mean age 6.36 year and male to femal ratio 1:1 .
Our results were supported by study of Gearry et al., [13] as they reported that study was carried out in Canterbury, New Zealand. Participants comprised 638 prevalent Crohn's disease (CD) cases, 653 prevalent ulcerative colitis (UC) cases and 600 randomly selected sex and age matched controls. There was no statistically significant difference between IBD group and non IBD group as regard age and sex.

The present study showed that there was statistically significant difference between IBD group and non IBD group as regard fecal calprotectin with p-value≤ 0.001. Using ROC curve for Fecal calprotectin to discriminate IBD patients (n = 14) from Non IBD (n = 30); AUC was 0.986, cutoff point was >340, sensitivity was 92.86%, specificity was 90.0%, PPV was 81.2% and NPV was 96.4%.

Our results were supported by study of Khalil, A. et al., [14] as they reported that observed significant elevation of faecal calprotectin in IBD cases compared to other non-IBD causes. Also found that a cut-off level of 744µg/g for faecal calprotectin may differentiate IBD from non-IBD cases with 86.8% specificity and 66.7% sensitivity. A cut-off level to distinguish between IBD and non-IBD is still lacking in the literature.

Also Degraeuwe PL, et al., [15] demonstrated that faecal calprotectin has a high overall sensitivity of 0.97 (95% confidence interval: 0.92–0.99) and a specificity of 0.70 (0.59–0.79) for diagnosing IBD. Increased concentrations of FC indicate an inflammatory process in the gastrointestinal tract. A high calprotectin value cannot be used for differential diagnosis in Crohn's disease (CD) and ulcerative colitis (UC). According to Henderson et al., [16] FC is characterized by high sensitivity but low specificity in children with suspected IBD. Being a first-degree relative of an IBD patient increases the likelihood of having elevated calprotectin value, despite the absence of evident gastrointestinal tract disease.

Our results showed that there was statistically significant difference between IBD group and non IBD group as regard fecal lactoferrin with p-value≤ 0.001 with cut off level >45, Sensitivity 85.71%,and Specificity 90.0%. Our results were in agreement with study of Nasser Abd Allah et al., [17] they reported that the fecal lactoferrin was significantly higher in patients with ulcerative colitis with positive correlation with the degree of activity of inflammation. While Using ROC cure, the sensitivity of FL was 83.1%, cut off point was >75.5 ng/gm and specificity was 71%.

Also in the study of Lamb et al., [18] who revealed that lactoferrin levels were significantly higher in patients with active IBD compared with inactive IBD. This suggests that lactoferrin could be used in conjunction with other parameters (clinical and blood inflammatory markers) to determine the subset of patients who have active disease or who may require a step up of therapy. Our results showed that there was highly statistically significant difference between IBD group and Functional abdominal pain- not otherwise specified group as regard fecal calprotectin with p-value≤ 0.001,with cut off level >46, Sensitivity 100%,and Specificity 100%.

Our results were supported by study of Pieczarkowski et al., [19] as they found that sensitivity and specificity of FCC levels >45 µg/g for the diagnosis of nonfunctional gastrointestinal disorders were 83.8% and 85.9%, respectively (positive predictive value [PPV] 0.75; negative predictive value [NPV] 0.91). Assuming higher FCC (>100 µg/g) as a cutoff point resulted in increased specificity of the test (90%) but it reduced its sensitivity (78%) (PPV 0.80; NPV 0.88) While in the study of Tavabie et al., [20] calprotectin levels <8 µg/g allow for being excluded from the IBD risk group. In the literature, the most frequent cutoff point suggesting the presence of organic intestinal disease is >50 µg/g. However, when examining patients with symptoms suggesting the presence of irritable bowel syndrome (IBS), it was stated that in 1/3 of patients, the value of calprotectin was >50 µg/g; eventually, 28% of them were diagnosed with organic intestinal disease, whereas in the group of patients with a calprotectin level <50 µg/g, organic intestinal disease was diagnosed in only 3% of patients.

Also Van de Vijver et al., [21] propose that a calprotectin cutoff point of 50 µg/g helps avoid endoscopy in 20% of children with gastrointestinal symptoms suggesting IBD, whereas with the increase in the cutoff point value to >150 µg/g, the number of patients referred for endoscopic examination in the group of people with IBD symptoms would decrease by an additional 7%.

On other hand Sipponen and Kolho, [22] found that patients diagnosed with organic diseases, including IBD, calprotectin levels were reported to surpass 100µg/g. On the basis of this test, high specificity was stated when normal levels were assumed as being <100 µg/g. A meta-analysis held by Degraeuwe et al., [15] suggested that assuming a calprotectin cutoff as 212µg/g should increase the accuracy of referral for endoscopy.

According to Holtman et al. [8] the addition of FC to an evaluation of alarm symptoms can be an optimal strategy for stratifying children identified by their general practitioner as being at risk for IBD. As regarf fecal lactoferrin ,Our results showed that there was highly statistically significant difference between IBD group and Functional abdominal pain- not otherwise specified group as regard fecal lactoferrin with p-value≤ 0.001,with cut off level >19 Sensitivity 100%,and Specificity 100.0%.

Our results were supported by study of Nasser Abd Allah et al., [17] they reported that the fecal lactoferrin was significantly higher in patients with ulcerative colitis with positive correlation with the degree of activity of inflammation. While Using ROC curve, the sensitivity of FL was 83.1%, cut off point was >75.5 ng/gm and specificity was 71%.

Furthermore, Sipponen et al., [22] stated that both fecal calprotectin and lactoferrin correlated significantly with CDEIS (Crohn's disease index of severity) (Spearman's r 0.729 and 0.773, P < 0.001). With a cutoff level of 200 µg/g for a raised fecal calprotectin concentration, sensitivity was 70%, specificity 92%, positive predictive value (PPV) 94%, and negative predictive value (NPV) 61% in predicting endoscopically active disease (CDEIS ≥ 3). A fecal lactoferrin concentration of 10µg/g as the cutoff value gave a sensitivity, specificity, PPV, and NPV of 66%, 92%, 94%, and 59%.

**Conclusion**

Fecal calprotectin and lactoferrin is a useful screening tool in children and adolescents with chronic diarrhea and recurrent abdominal pain, for differentiation between organic diseases, particularly inflammatory bowel disease (IBD) from non-organic disease, making colonoscope unnecessary.

**Recommendation**

Further prospective and large-scale research are required to support these findings.

**Ethics**

Ethics Committee Approval and Informed Consent: Ethical review board of AlAzhar University approved the study protocol.

**Source of Finance**

During this study, there is no donor for any financial or moral support that affects the results of this research or negatively affects it.

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