Content available at: https://www.ipinnovative.com/open-access-journals

IP International Journal of Medical Paediatrics and Oncology

Journal homepage: https://www.ijmpo.com/

Original Research Article

Fecal Calprotectin as early predictor for screening and relapse in pediatric chronic diarrhea in India

Gujjarlapudi Deepika[1,*], Namburu Veeraiah[1], Syed Hassan Naveed[1], D. Nageshwar Reddy[2]

[1]*Dept. of Biochemistry, AIG Hospitals, Hyderabad, Telangana, India*
[2]*Dept. of Gastroenterology, AIG Hospitals, Hyderabad, Telangana, India*

ARTICLE INFO

Article history:
Received 28-10-2021
Accepted 20-11-2021
Available online 22-12-2021

Keywords:
Inflammatory bowel diseases (IBD) and Irritable bowel syndrome (IBS)
Crohn's disease (CD)
Ulcerative colitis (UC)
Disease monitoring.

ABSTRACT

Introduction: IBS and IBD are two abdomen ailments commonly seen in children. IBD is a life-long disorder that includes two major forms of chronic illness UC and CD, IBS may occur when the bowel is sensitive to specific foods or other triggers like stress.

Aims & Objective: The aims of the study is to investigate clinical usefulness of FC as early predictor for screening and differentiating IBD and IBS and to monitor the treatment for relapse and remission in pediatric Indian population.

Materials and Methods: This was hospital based observational cohort study, conducted over a period of twelve months from January 2019 to December 2019 Total 325 patients attending OPD were included in the study, in children between 1-18years in which FC was measured using commercially available CLIA kit. HB, ESR, Hscrp were also assessed, these patients were followed up.

Results: Patients were grouped as Group I: IBS: 115(50:65M/F), Group II: 185 IBD, had Subgroup I:116 CD(48:68M/F);Group A: 62.7% presented with relapse Group B: 37.3% had disease in remission Subgroup II: 69 patients had UC(31:38 M/F); Group A: 60.9% had relapse and Group B: 39.1% in remission after follow up. Subgroup III: Others were 25(7.7%). In Study I: Levels of FC were significantly lower in patients with group I when compared to group II. In Subgroup I & Subgroup II Group A had higher FC levels when compared to group B. In Study II: A significant difference (P<0.001) and lower values of the FC, ESR, Hs-crp, frequency of stools in IBS than in CD and UC patients were observed. In Study III: FC in IBD has positive correlation (p<0.01), with the activity of the inflammatory disorder, HB, ESR, Hs-CRP and with increased frequency of diarrhea. In Study IV**:** Fecal calprotectin value of ≥100 ug/g was diagnostic of IBD with sensitivity of 94.1%, specificity of 82.2%, PPV of 86.32%, NPV of 80.39%.

Conclusion: The present study showed that the determination of FC assists to differentiate between IBD and IBS also useful in monitoring of remission and in early prediction of relapse in pediatric IBD.

1. Introduction

Chronic abdominal pain or discomfort with diarrhoea or constipation, are common symptoms in children. These symptoms may be caused by an organic diseases (IBD) inflammatory bowel diseases, of which (UC) Ulcerative colitis and Crohn's disease (CD) are the most common or functional disease (IBS) irritable bowel syndrome. Differentiating may be difficult in clinical practice.

IBS is functional bowel disorder does not cause inflammation and rarely requires hospitalization can be treated symptomatic. The etiology of IBD is not yet understood but it seems to arise from interactions between genetic and environmental factors.[1] IBD is a

* *Corresponding author*.
E-mail address: dr.deepikapavan@gmail.com (G. Deepika).

https://doi.org/10.18231/j.ijmpo.2021.036

chronic condition can cause destructive inflammation and permanent damage to the gastrointestinal tract characterized by recurrent episodes of inflammation, diarrhea, abdominal pain, disrupted digestion, rectal bleeding, weight loss and a substantial personal burden.[2]

The initial blood tests Hemogram to exclude anaemia, markers of inflammation such as the erythrocyte sedimentation rate (ESR) and HsC-reactive protein (hsCRP), serological testing for celiac disease, cannot localize lesion in the gut, but are used to assist in deciding which patients should proceed to magnetic resonance imaging (MRI) and computed tomography (CT) as both are relatively expensive modalities, but they can help to identify prior to endoscopy, which remains the "gold standard" to take biopsy for the histological examination. CT has the disadvantage of exposure to ionizing radiation and MRI is the preferred, but it is not always available or well tolerated. Colonoscopy is an invasive expensive procedure that requires sedation of the patient. Thus, the reliable and non-invasive markers are suitable for paediatric patients are required.

Fecal Calprotectin (FC) is a 36 kilo Dalton calcium-binding protein, calgranulin and is a heterodimer of S100A8/A9, zinc-binding proteins with antimicrobial and anti proliferative properties, It was first discovered in 1980 and was found to contribute ~60% of the protein content of the cytosol in neutrophils.[3]FC in feces is more specific to gastrointestinal inflammation than FC found in other body fluids, it may vary with age, it has been found to be useful in screening and distinguishing inflammatory from non-inflammatory gastrointestinal conditions.[4–6] It is resistant to enzymatic degradation, preserved and easily measured in stools for periods of time sufficient to allow for collection, analysis for clinical utility[7] Elevated FC have been seen in cystic fibrosis, rheumatoid arthritis, and bacterial infection.[8] as well as (NSAID) induced enteropathy, neoplasia's,[9] polyps, diverticular disease[10].Celiac disease,microscopic and allergic colitis, are not uniformly characterized by significant neutrophil infiltrate, So FC can be detected but in lower than those in IBD[11] Jensen et al.[12] reported that FC is equally sensitive in CD, affecting both small bowel and colon. These correlations also make FC is a specific and sensitive but should not be thought to of organic disease rather marker in indicating neutrophil intestinal inflammation.[13,14]

FC also useful in determining whether clinical symptoms in patients with known IBD are caused by disease flares, non-inflammatory complications, or underlying IBD.[15,16] Because FC concentration has been shown to correlate with endoscopic and histological inflammation in IBD, it could be a useful marker to follow response to treatment.[17–19] For young infants, the concentration of FC may be falsely increase by 30% by the absorption of water in the diaper.[20] FC values also show large variation during bowel cleansing and after a lower bowel endoscopy.[21] It has been observed, that menstrual, nasal bleeding, anal fissures and haemorrhoids influence FC levels.[22]

The aim of this study is to evaluate the usefulness of the FC, as it is non-invasive, simple, easy to perform, rapid, and reproducible biomarker in differential diagnosis of IBS and paediatric IBD patients and in monitoring the effectiveness of therapy and relapses.

2. Materials and Methods

The present study was conducted observational cohort over a period of one year from January 2019-December 2019 and data was collected and analysed. The study was conducted in the Department of Biochemistry, Asian Institute of Gastroenterology Hospital; Hyderabad India. Institutional Ethics Committee (IEC) permission was obtained before starting the study, Reference Number: AIG/IEC 35/11.2018-19/ ER-049; 20DEC 2018). All participants gave informed written consent.

2.1. Study population: Inclusion criteria

Chronic abdominal pain or discomfort with diarrhoea for more than 2 weeks were included. All 325 patients were included in the study, After clinical, laboratorial evaluation IBD was diagnosed by esophago-gastroduodenoscopy, ileo-colonoscopy, and histopathologic examination according to the Porto criteria.[23] These patients were monitored for one year during the course of treatment for remission and relapse.

2.2. Exclusion criteria

Stool cultures were performed in all samples to exclude gastrointestinal infection. Those patients who suffered from infectious colitis within 1 month or had bacterial infection, other GI tract disorders such as gastroesophageal reflux, Helicobacter pylori infection, or colon polyps, antibiotics, probiotics, NSAIDs, or steroids, abdominal surgery or other congenital conditions were excluded.

Blood sample collection During the inclusion in the study, 3 ml blood was collected in a vial containing dipotassium EDTA for Hb%, ESR and 5 ml of venous blood was collected in an iron free plastic tube. Serum was separated for haematological HB%, ESR and clinical chemistry for Hs-crp were obtained. The serum was then used for estimation of Hs-crp by turbidmetric immunoassay using Beckman Coulter AU 480 auto analyser Complete blood count, ESR was done using Beckman Coulter Autoanalyser

Stool samples for fecal Calprotectin were collected and were stored at −20°C and analyzed by a commercially available quantitative CLIA (Diasorin Ltd). Optimal cut-off level of 50 μg/g appears to be the most proper cut-off point for the FC test in children according to manufactures

instruction.

2.3. Statistical analysis

Statistical analysis was conducted using the SPSS version 19.0 with 95% confidence intervals, all the data was represented as mean±Standard Deviation (SD). Continuous variables were compared between the two groups using Student's t-test, Pearson correlation coefficient regression analysis were applied. P values < 0.05 were considered statistically significant.

3. Results

The study recruited a total of 325 children Cases were divided into the Group I: IBS group:115 patients (65 Females / 50 Males). Group II: IBD group:185 patients were followed Subgroup I:116(CD) (68 F; 48 M); Group A 62.9% presented with relapse after follow up, and Group B 37.1% had disease in remission Subgroup II: 69 (UC)Patients (38 F;31 M; Group A 60.8% classified with relapse and Group B 39.2% in remission Subgroup III: Others 25 patients (3 mesenteric angina, 12 celiac disease, 3lymphoma, 4 diverticular disease,& 3 acute intestinal infections which were excluded from the study.

In Study I (Table 1 /Figure 1) Shows the FC Values IBS with IBD(UC&CD) in Relapse and Remission: In this study we could see female predominance of 56.5% in than male 43.5% IBS against 58.6 % in CD and 55.1% in UC female predominance against male 41.4% in CD and 44.9% in UC. We could observe Levels of FC were significantly higher in patients in group II (322.5 ± 493.3) CD and (351 ±409) UC when compared to group I (52.3±81.8) IBS.

In CD relapse cases we could see male predominance 53.4% than female of 46.6%. In UC active relapse also male predominance is 57.1% than female 42.9%.

We observed FC values of CD relapse were more than the UC relapse.

In CD remission we could see male predominance 53.5% than female of 46.5%. In UC active relapse also male predominance is 63.0% than female 37.0%.

When compared Levels of FC were significantly lower in patients with Group B (CD and UC) in remission when compared with Group A(CD and UC) active relapse disease.

In Study II (Table 2): shows the different biochemical parameters of the study population between IBD and IBS: Among the parameters compared between group I and II, with HB%, ESR, Hs-crp and FC. The mean age of the IBS was 7.2±9.94 years in IBD was 4.5±9.49 years shows a stastical significant difference (P<0.001) was observed with less FC, hs-crp and ESR value in IBS than the CD patients and in UC patients. No much difference was observed between the values found in the patients with CD and UC.

In Study III (Figure 1 & Table 3). Shows the correlation & Regression analysis between FC Values in IBD with other biochemical parameters: It also shows the levels of FC in patients with IBD and also the positive correlation (p<0.01), concerning the activity of the inflammatory disorder, chronicity of the disease, HB level, ESR, Hs-CRP and with increased frequency of diarrhea. On the other hand, there was a negative correlation between FC level and age& gender of the patients (p<0.03). (Table 3) demonstrates the linear regression analysis of FC to other parameters. High level of FC predicts stastical significance coefficient p value (p<0.001) with low level of HB, high ESR and high Hs-CRP, increased frequency of diarrhea, and more active disease p<0.001 with no stastiscal significance for age p-value (0.03) and sex p-value (0.725).

In Study IV (Table 4): Accuracy of FC measurement in diagnosis of IBD: FCvalue of ≥100μg /g had better sensitivity of 94.1%, specificity of 93 % than > 50 μg/g which has 99% of sensitivity and 84% specificity

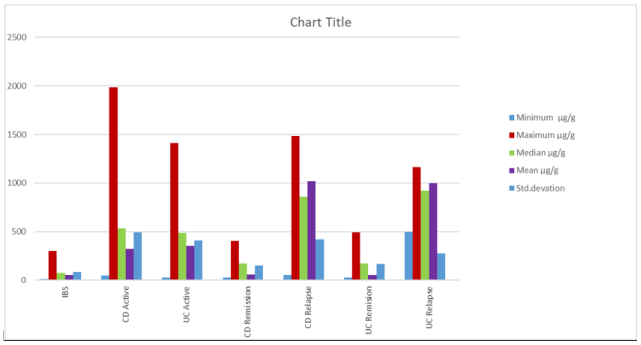

Fig. 1: Fecal calprotectin levels in studied group IBS; Irritable bowel disease, UC Ulcerative Colitis, Crohn's Disease

4. Discussion

The differential diagnosis of IBD and IBS can be challenging. At present, growing clinical experience shows an expanded role for FC in diagnosis, the monitoring of remission and, and in the prediction of relapse in pediatric IBD. There are no simple diagnostic tests for monitoring intestinal inflammation. Currently available laboratory parameters correlate poorly with intestinal disease activity, and they have no predictive value to confirm remission or to detect early relapses. Kaiser T et al shows colonoscopy is considered for evaluating the inflammation, location, extent and severity of IBD, although it is an invasive method and carries the risk of complications.[24]

Present study shows below < 50 μg/g can be considered as IBS and values between 50-100 μg/g should be re-evaluated for other colitis cases and rechecked after 2-3 weeks along with the other inflammatory markers. A recently published meta-analysis by Von roon AC et al. concludes that faecal calprotectin gives a diagnostic precision in distinguishing IBD from non-IBD diagnosis, with higher precision at a cut-off of 100μg/g versus

Table 1: Fecal calprotectin levels in studied group (IBS VS UC& CD active, UC & CD) remission

	IBS N=115	CD N=116	UC N=69	CD Remission N=43	CD active (Relapse) N=73	UC Remission N=27	UC active (Relapse) N=42
Male	50(43.5)	48(41.4)	31(44.9)	23(53.5)	39(53.4)	17(63.0)	24(57.1)
Female	65(56.5)	68(58.6)	38(55.1)	20(46.5)	34(46.6)	10(37.0)	18(42.9)
Minimum μg/g	10	46.4	25.1	28.2	52	26.2	497.9
Maximum μg/g	302.7	1986.2	1413.4	402.7	1484.3	490	1164
Median μg/g	73.7	534.2	489.7	169.6	858.7	171.6	922.6
Mean μg/g	52.3	322.5	351.0	60.6	1020	52.2	1000
Std.devation	81.8	493.3	409.9	150.7	420.6	166.5	273.3
Lower 95% Cl of mean	58.75	447	329.9	124.5	762.6	108.8	580.8
Upper 95% Cl of mean	88.65	624.3	586.4	214.6	955.2	234.4	994.4

UC & CD relapse.; IBD; Inflammatory Bowel Disease, IBS; Irritable bowel disease, UC Ulcerative Colitis, Crohn's Disease.

Table 2: Patient's characteristics of IBS versus IBDp< 0.05 stastically significant;IBD; Inflammatory Bowel Disease, IBS; Irritable bowel disease

	IBS N=115	IBD N=185	P value
Age (years)	7.21±9.94	4.54±9.49	0.322
HB (g/dl)	11.60±0.58	9.47±2.28	< 0.001
ESR (ml/h)	12.11±2.18	39.2±3.39	< 0.001
hsCRP (mg/dl)	16.5±5.6	27.19±15.617	< 0.001
Frequency of diarrhea	-	-	-
Mild (< 4/day)	5	9	0.442
Moderate (4-6/day)	8	12	-
Severe (> 6/day)	6	20	-
Fecal calprotectin (ug/gm)	52.3	322.134±128.18	< 0.001

Table 3: Correlation between fecal calprotectin and other parameters in IBD p< 0.05 stastically siginificant ;IBD; Inflammatory Bowel Disease

Parameter	Correlation Coefficient	p Value	95% Confidence Interval	
Age (year)	-0.83	0.03	- 2.68	8.028
Sex	0.43	0.007		
HB (g/dl)	-0.51	0.001	1.059	3.194
ESR (ml/h)	0.91	0.001	-37.83	-16.20
hsCRP (mg/dl)	0.89	0.001	-28.40	-13.99
Increased frequency of diarrhea	0.65	0.001		

Table 4: Regression analysis betweenfecal calprotectin and parameters in IBD group p< 0.05 stastically siginificant; IBD; Inflammatory Bowel Disease

Parameter	IBD	p value
Age (year)	7.7	0.03
Sex	1.49	0.725
HB (g/dl)	9.37	< 0.001
ESR (ml/h)	14.6	< 0.001
hsCRP (mg/dl)	15.9	< 0.001
Increased frequency of diarrhea	5.18	< 0.001

Table 5: Accuracy of fecal calprotectin measurement in diagnosis of IBD ;IBD; Inflammatory Bowel Disease

Test Characteristic	Fecal calprotectin cutoff		
	>50 μg/g	>100 μg/g	>200 μg/g
Sensitivity (95% Cl)	0.99 (0.89-1.00)	0.94 (0.62-0.96)	0.81 (0.58-0.93)
Specificity (95% Cl)	0.84 (0.74-0.91)	0.93 (0.84-0.97)	0.98 (0.92-0.99)

50μg/g.[25] Therefore, a negative Fecal result may safely rule out IBD and thereby reduce the number for evaluation of IBD in children. According to Pavlidis et al. fecal calprotectin is increased in gastroenteritis associated with viral or bacterial infection a value between 50μg/g and 150 μg/g should always be repeated 2–3 weeks later.[26] According to Henderson et al.[27] FC is characterized by high sensitivity but low specificity in children with suspected IBD. Van de Vijver et al.[28] propose that a calprotectin cut-off point of 50 μg/g helps avoid endoscopy in 20% of children with gastrointestinal symptoms suggesting IBD, whereas with the increase in the cut-off 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% were obtained by Sipponen and Kolho.[29]

Present study reveals Levels of FC were significantly higher in patients in (322.5 ± 493.3) CD and (351 ±409) UC. Calprotectin reflects disease activity better in the course of UC in comparison to CD[27]. According Van de Vijver et al Calprotectin constitutes a diagnostic tool not only in IBD diagnosis but can also serve to monitor inflammatory lesions in the course of treatment. In the case of increased activity of the disease, relevant higher value of calprotectin is observed than patients with the disease in remission.[29]

FC showed high sensitivity at > 100 μg/g (0.93; 95% CI, 0.86–0.97) in our study. The specificity of 0.93 that we identified in our study is higher than that reported in studies performed in specialist care, where the pooled specificity ranged between 0.68 and 0.76.[30] According to Olender et al.[31] Van de-vijer et al in patients a cut-off point of 100 μg/g, instead of 50 μg/g, has higher specificity in the diagnosis of IBD in the pediatric group[28] Nielsen et al evaluated a financial model in 100 adults and 100 children screened with calprotectin prior to colonoscopy using 50 μg/g and 100 μg/g cut-offs. Additionally, the test appears to have better diagnostic precision for IBD at a cut-off of 100μg/g than at 50μg/g.[32]

In present study FC levels were significantly lower in patients with CD (60.6 ± 150.7) and UC (52.2 ± 166.5) in remission. We also observed FC levels were significantly higher in patients with CD (1020 ± 420.6) and UC (1000 ± 273.3) in relapse while According to Paul et al.[33] in patients with CD, the value of FC <250 μg/g confirms remission of mucosal inflammation. Naismith et al[34,35] using the largest prospective data set in the literature, provide evidence that adults with quiescent CD with an FC level below 256 μg/g are unlikely to relapse within 6 months. Thus, this level could become a therapeutic target for physicians treating CD patients who are in clinical remission when attending the outpatient clinic.[35]

FC determination can also be used to predict flares of IBD.[36,37] The results of the present study suggest that the test be used as a guide to evaluate the efficacy of the treatment in each case, and monitor tightly the disease course, as referred by Kopylov et al.[38] Monitoring this intestinal marker in IBD as early as in the initial phase of therapy (e.g., after steroid administration) may objectively indicate a chance for clinical improvement.[39] Molander et al.[40] confirmed that FC <100 μg/g in patients with IBD after the induction phase of infliximab treatment is a good prognostic factor for clinical remission. Many studies show that changes in calprotectin levels may precede both clinical symptoms and endoscopic changes. This was confirmed by Shentova R et al. that in pediatric patients with UC; cut-off point 285 μg/g of FC correlated with exacerbation of the disease in endoscopic studies, despite no clinical progression.[41]

5. Limitation

Larger prospective analyses are required to confirm these findings and to assess better therapy strategies and long-term outcome based on non-invasive measurements of FC. Limitations to the interpretation of faecal calprotectin results include variability in extraction methodology, performance of test kits, and the need to establish local reference ranges.

6. Conclusion

The present study determines FC is less invasive and more cost-effective than colonoscopy and can help in management and assists to differentiate between IBD and IBS. We showed that continous monitoring of FC values will be helpful as diagnostic adjunct along with Hs CRP, ESR in detecting active disease, monitoring of remission and in early prediction of relapse in pediatric IBD to reconsider for any change of management. Future studies might show whether changes in FC levels can be of prognostic significance for hospital stay, the need for surgery, and impact on the quality of life in children.

7. Conflict of Interest

The author declares no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

8. Source of Funding

None.

References

1. Cho JH, Brant SR. Recent insights into the genetics of inflammatory bowel disease. *Gastroenterology*;2011(6):1704–12.
2. Aomatsu T, Yoden A, Matsumoto K. Fecal calprotectin is a useful marker for disease activity in pediatric patients with inflammatory bowel disease. *Dig Dis Sci*;2011(8):2372–7. doi:10.1007/s10620-011-1633-y.
3. Fagerhol M, Dale I, Andersson T. A radioimmunoassay for a granulocyte protein as a marker in studies on the turnover of such cells.

Bull Eur Physiopathol Respir. 1980;16:273–82. doi:10.1016/b978-0-08-027379-2.50028-4.
4. Aadland E, Fagerhol MK. Faecal calprotectin: A marker of inflammation throughout the intestinal tract. *Eur J Gastroenterol Hepatol*. 2002;14(8):823–5. doi:10.1097/00042737-200208000-00002.
5. Pathirana W, Chubb SP, Gillett MJ, Vasikaran SD. Faecal calprotectin. *Clin Biochem Rev*. 2018;39(3):77–90.
6. Ricciuto A, Griffiths AM. Clinical value of fecal calprotectin. *Crit Rev Clin Lab Sci*. 2019;56(5):307–20. doi:10.1080/10408363.2019.1619159.
7. Haisma SM, Van Rheenen PF, Wagenmakers L. Calprotectin instability may lead to undertreatment in children with IBD. *Arch Dis Child*. 2019;105(10):996–8. doi:10.1136/archdischild-2018-316584.
8. Røseth A, Kristinsson J, Fagerhol M. Faecal calprotectin: a novel test for the diagnosis of colorectal cancer? *Scand J Gastroenterol*. 1993;28(12):1073–6. doi:10.3109/00365529309098312.
9. Poullis A, Foster R, Shetty A, Fagerhol MK, Mendall MA. Bowel inflammation as measured by fecal calprotectin: a link between life style factors and colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*. 2004;13(2):279–84.
10. Tursi A. Biomarkers in diverticular disease of the colon. *Dig Dis*. 2012;30(1):12–8. doi:10.1159/000335695.
11. Sutherland A, Gearry RB, Frizelle FA. Review of fecal biomarkers in inflammatory bowel disease. *Dis Colon Rectum*. 2008;51(8):1283–91.
12. Jensen MD, Kjeldsen J, Nathan T. Fecal calprotectin is equally sensitive in Crohn's disease affecting the small bowel and colon. *Scand J Gastroenterol*. 2011;46(6):694–700.
13. Thjodleifsson B, Sigthorsson G, Cariglia N, Reynisdottir I, Gudbjartsson DF, Kristjansson K, et al. Subclinical intestinal inflammation: an inherited abnormality in Corhn's disease relatives? *Gastroenterology*. 2003;124(7):1728–37.
14. Chen CC, Huang JL, Chuang CJ, Kong MS. Fecal calprotectin as a correlative marker in clinical severity of infectious diarrhea and usefulness in evaluating bacterial or viral pathogens in children. *J Pediatr Gastroenterol Nutr*. 2012;55(5):541–7.
15. Berrill JW, Green JT, Hood K, Campbell AK. Symptoms of irritable bowel syndrome in patients with inflammatory bowel disease: examining the role of sub-clinical inflammation and the impact on clinical assessment of disease activity. *Aliment Pharmacol Ther*. 2013;38(1):44–51.
16. Konikoff MR, Denson LA. Role of fecal calprotectin as a biomarker of intestinal inflammation in inflammatory bowel disease. *Inflamm Bowel Dis*. 2006;12(6):524–34. doi:10.1097/00054725-200606000-00013.
17. Lewis JD. The utility of biomarkers in the diagnosis and therapy of inflammatory bowel disease. *Gastroenterology*. 2011;140(6):1817–26. doi:10.1053/j.gastro.2010.11.058.
18. Roseth AG, Aadland E, Jahnsen J, Raknerud N. Assessment of disease activity in ulcerative colitis by fecal calprotectin, a novel granulocyte marker protein. *Digestion*. 1997;58(2):176–80.
19. Wang S, Wang Z, Shi H, Heng L, Juan W, Yuan B, et al. Faecal calprotectin concentration in gastrointestinal diseases. *J Int Med Res*. 2013;41(4):1357–61.
20. Olafsdottir E, Aksnes L, Fluge G. Faecal calprotectin levels in infants with infantile colic, healthy infants, children with inflammatory bowel disease, children with recurrent abdominal pain and healthy children. *Acta Paediatr*. 2002;91(1):45–50. doi:10.1080/080352502753457932.
21. Kolho KL, Alfthan H, Hamalainen E. Effect of bowel cleansing for colonoscopy on fecal calprotectin levels in pediatric patients. *J Pediatr Gastroenterol Nutr*. 2012;55(6):751–3. doi:10.1097/MPG.0b013e31825f4c77.
22. Fagerberg UL, o¨f LL, Merzoug RD. Fecal calprotectin levels in healthy children studied with an improved assay. *J Pediatr Gastroenterol Nutr*. 2003;37(4):468–72. doi:10.1097/00005176-200310000-00013.
23. Levine A, Koletzko S, Turner D, Escher JC, Cucchiara S, de Ridder L, et al. ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. *J Pediatr Gastroenterol Nutr*. 2014;58(6):795–806. doi:10.1097/MPG.0000000000000239.
24. Kaiser T, Langhorst J, Wittkowski H, Langhorst J, Wittkowski H, Becker K, et al. Faecal S100A12 as a non-invasive marker distinguishing inflammatory bowel disease from irritable bowel syndrome. *Gut*. 2007;56(12):1706–13. doi:10.1136/gut.2006.113431.
25. Roon ACV, Karamountzos L, Purkayastha S, Reese GE, Darzi AW, Teare JP, et al. Diagnostic precision of fecal calprotectin for inflammatory bowel disease and colorectal malignancy. *Am J Gastroenterol*. 2007;102(4):803–13.
26. Pavlidis P, Chedgy FJ, Tibble JA. Diagnostic accuracy and clinical application of faecal calprotectin in adult patients presenting with gastrointestinal symptoms in primary care. *Scand J Gastroenterol*. 2013;48(9):1048–54.
27. Henderson P, Anderson NH, Wilson DC. The diagnostic accuracy of fecal calprotectin during the investigation of suspected pediatric inflammatory bowel disease: a systematic review and meta-analysis. *Am J Gastroenterol*. 2014;109(5):637–45.
28. Van De Vijver E, Schreuder AB, Cnossen WR, Kobold ACM, Van Rheenen PF. Safely ruling out inflammatory bowel disease in children and teenagers without referral for endoscopy. *Arch Dis Child*. 2012;97(12):1014–8.
29. Sipponen T, Kolho K. Fecal calprotectin in diagnosis and clinical assessment of inflammatory bowel disease. *Scand J Gastroenterol*. 2015;50(1):74–80.
30. Degraeuwe PL, Beld MP, Ashorn M. Faecal calprotectin in suspected paediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2015;60(3):339–46.
31. Olender K, Bergmann K, z-Sypniewska GO. Fecal calprotectin as an inflammatory marker in inflammatory bowel disease. *Diagn Lab*. 2012;48:433–9.
32. Nielsen HL, Engberg J, Ejlertsen T, Nielsen H. Evaluation of fecal calprotectin in Campylobacter concisus and Camplylobacter jejuni/coli gastroenteritis. *Scand J Gastroenterol*. 2013;48(5):633–5.
33. Paul S, Tedesco ED, Marotte H, Rinaudo-Gaujous M, Moreau A, Phelip JM, et al. Therapeutic drug monitoring of infliximab and mucosal healing in inflammatory bowel disease: a prospective study. *Inflamm Bowel Dis*. 2013;19(12):2568–76. doi:10.1097/MIB.0b013e3182a77b41.
34. Naismith GD, Smith LA, Barry S, Munro JI, Laird S, Rankin K, et al. A prospective evaluation of the predictive value of faecal calprotectin in quiescent Crohn's disease. *J Crohns Colitis*. 2014;8(9):1022–9.
35. Turner D, Griffiths AM, Veerman G, Johanns J, Damaraju L, Blank M, et al. Endoscopic and clinical variables that predict sustained remission in children with ulcerative colitis treated with infliximab. *Clin Gastroenterol Hepatol*. 2013;11(11):1460–5.
36. D'inca R, Pont ED, Lamboglia F, Leo VD, Benazzato L, Martinato M, et al. Can calprotectin predict relapse risk in inflammatory bowel disease? *Am J Gastroenterol*. 2008;103(8):2007–14.
37. Ho GT, Lee HM, Brydon G, Ting T, Hare N, Drummond H, et al. Fecal calprotectin predicts the clinical course of acute severe ulcerative colitis. *Am J Gastroenterol*. 2009;104(3):673–8.
38. Kopylov U, Rosenfeld G, Bressler B, Seidman E. Clinical utility of fecal biomarkers for the diagnosis and management of inflammatory bowel disease. *Inflamm Bowel Dis*. 2014;20(4):742–56.
39. Pathirana WGW, Chubb SP, Gillett MJ, Vasikaran SD. Faecal calprotectin. *Clin Biochem Rev*. 2018;39(3):77–90.
40. Molander P, Björkesten CG, Mustonen H, Haapamäki J, Vauhkonen M, Kolho KL, et al. Fecal calprotectin concentration predicts outcome in inflammatory bowel disease after induction therapy with TNFα blocking agents. *Inflamm Bowel Dis*. 2012;18(11):2011–7.
41. Shentova R, Baycheva M, Hadjiiski P, Kofinova D, Yaneva P. Role of faecal calprotectin as a predictor of endoscopic activity in paediatric patients with ulcerative colitis. *Gastroenterol Hepatol*. 2020;43(1):57–61.

Author biography

Gujjarlapudi Deepika, Director and HOD

Namburu Veeraiah, Lab Manager

Syed Hassan Naveed, Technical Manager

D. Nageshwar Reddy, Chairman and Chief

Cite this article: Deepika G, Veeraiah N, Naveed SH, Reddy DN. Fecal Calprotectin as early predictor for screening and relapse in pediatric chronic diarrhea in India. *IP Int J Med Paediatr Oncol* 2021;7(4):178-184.