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Fecal Calprotectin as a Screening Marker for Inflammatory Bowel Disease

We compared fecal calprotectin and endoscopic findings of 53 children with possible inflammatory bowel disease and found an optimal cut-off of 68 µg/g in Receiver operative curve [AUC 0.88 (95% CI 0.79, 0.97)] to discriminate inflammatory bowel disease with other inflammatory gastrointestinal conditions.

Keywords: *Crohn's disease, Diagnosis, Ulcerative colitis*.

Diagnosis of Inflammatory bowel disease (IBD) is confirmed by clinical evaluation and a combination of endoscopic, radiological, histological investigations. Non-invasive biomarker such as fecal calprotectin, which is released during times of cell stress/damage, it is a highly sensitive marker of intestinal inflammation, and represents a novel and under-utilized modality to aid in diagnosis of IBD. Growing body of literature has identified fecal calprotectin (FCP) as a non-invasive predictive test with high sensitivity for inflammatory bowel disease.

This cross-sectional study was done over a period of one year in Apollo Children's Hospital, Chennai, a tertiary referral center in Southern India. Ethics approval was obtained from Institute Ethics Committee, and informed consent of participants was obtained. We tested 53 consecutive patients (mean (SD) age 9.7(4) years), who presented with inflammatory bowel disease symptoms as per European Crohn's and Colitis Organization guidelines [1,2]. The presenting complaints necessitating FCP testing and colonoscopy/endoscopy were: chronic abdominal pain (52, 98.1%), chronic diarrhea (51, 96.2%), mucoid stools (38, 71.7%), blood in stools (28, 52.8%), prolonged fever (6, 11.3%), pallor (9,17%), oral ulcers (4, 7.5%), glossitis (2, 3.8%) and angular cheilitis (2, 3.8%). Many patients presented with combination of symptoms mentioned above.

FCP using enzyme-linked immunosorbent assay by LIAISON Calprotectin Assay (negative <6.2 mg/kg) was performed at baseline for all enrolled patients along with radiological investigations as deemed appropriate. Colonoscopy along with endoscopy was performed on all patients the subsequent day before the results of the FCP were available and a final confirmation with tissue biopsy reports was done for diagnosis of inflammatory bowel disease.

Of the 53 children, 17% had biopsy-confirmed diagnosis of inflammatory bowel disease; eight (15.1%) had Crohn's disease and one (1.9%) had Ulcerative colitis. Receiver Operating Characteristics (ROC) curve revealed an optimal cut-off for FCP level of 68 mg/kg to discriminate between IBD and non-IBD causes of inflammation and this value had sensitivity of 100%, specificity of 70%, positive predictive value of 40%, negative predictive value of 100%, and likelihood ratio for a positive test of 3.4. The area under the curve of the ROC

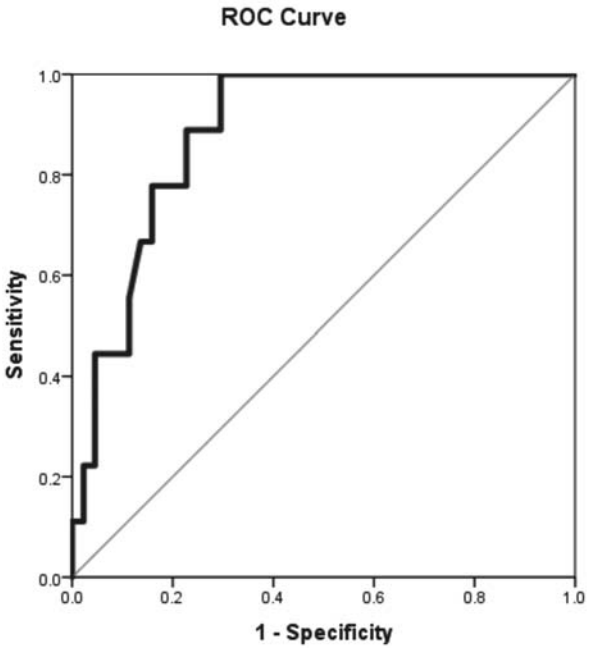

FIG. 1 *ROC curve showing area under the curve of 0.88 (95% CI 0.79-0.97) for FCP value of 68 mg/kg***.**

was 0.88 (95% CI 0.79-0.97) (***Fig.* 1**). In our cohort of 53 patients, by considering FCP cut-off of 68 mg/kg, we had nine True Positives, 13 False Positives, no False Negative, and 31 True Negatives. Mean (SD) FCP in false positive cases was 502.7 (469) µg/g and Mean (SD) FCP among IBD cases was 818.8 µg/g (873.2).

Studies with larger cohort from published literature suggest the usefulness of calprotectin as a screening marker for inflammatory bowel disease [3,4]. In IBD, FCP is often used to predict mucosal healing while the patient is on therapy [1]. Endoscopy and histology remain the current gold standard method for detecting and monitoring bowel inflammation. A meta-analysis by Rheenen, *et al*. [5] suggested FCP to be a useful screening tool for patients who were most likely to need endoscopy for suspected IBD. Raised FCP may be associated with other inflammatory conditions apart from inflammatory bowel disease like rectal polyp, non-specific colitis and eosinophilic procto-colitis [6].

We had few limitations in our study. There were no controls. Though the levels of FCP were not known before doing the endoscopy, we had a positive FCP in all cases, and the histopathology showed inflammatory changes in entire cohort; though not necessarily IBD changes. We did not have patients with negative FCP results, rendering our study not useful to evaluate its role in all gastrointestional inflammatory conditions. In Indian settings, infective etiologies causing inflammatory changes are lot more common than western population and this might result in children going through invasive procedures unnecessarily. Therefore, FCP should be used in conjunction with more robust non-invasive investigations before arriving at a decision to do endoscopy.

Our pilot study in an Indian setting adds to the growing evidence from around the world that presence of FCP in stool highlights the need to rule out inflammatory causes for gastrointestinal symptoms, and higher values are associated with diagnosis of IBD. Studies with larger cohort with control group will be needed to enhance the usefulness of this biomarker in IBD.

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