JOURNAL WATCH

1. The Use of Fecal Calprotectin Testing in Paediatric Disorders: A Position Paper of the European Society for Paediatric Gastroenterology and Nutrition Gastroenterology Committee

Koninckx CR, Donat E et al. The Use of Fecal Calprotectin Testing in Paediatric Disorders: A Position Paper of the European Society for Paediatric Gastroenterology and Nutrition Gastroenterology Committee. J Pediatr Gastroenterol Nutr. 2021 Apr 1;72(4):617-640. doi: 10.1097/MPG.0000000000003046.

The role of fecal calprotectin (FC) in the clinical practice to get clues about inflammatory bowel disease (IBD) or functional gastrointestinal disorders (FGD) is well known. Calprotectin a complex protein, is present in tissues and fluids which are abundant in neutrophils and monocytes. In inflammatory conditions there is influx of inflammatory cells mainly neutrophils and monocytes. Activation followed by death of aggregated inflammatory cells release large amount of calprotectin which can be measured in faeces. Various conditions as Crohn disease (CD), ulcerative colitis (UC), cystic fibrosis, rheumatoid arthritis, bacterial infections etc. demonstrate high fecal calprotectin. This position paper reviews the evidence through a literature search in PubMed and Cochrane databases, determining the value of FC in different gastrointestinal disorders and formulate a recommendation. A stool weight of 50-100 gm preferably early morning sample is sufficient for the test. Most of the literature suggest that the sample can be kept at room temperature for 3-7 days but most analysis methods recommend to keep faecal samples for up to 2 to 3 days at room temperature, 5 to 7 days in a fridge or frozen if long-term storage is required. False positive results may be seen in samples collected from diaper, after bowel enema, post colonoscopy and in blood mixed stool. Commonly used drugs as nonsteroidal anti-inflammatory drugs and proton pump inhibitors can also lead to falsely high levels of FC. The normal range of FC is stated as less than 50µg/g of faeces and a cut-off of more than 100 µg/g of faeces has better diagnostic value for IBD. FC levels are higher in children as compared to adults however specific ranges for various age groups have not been established. Preterm and younger children may have higher levels. High FC levels are indicators of IBD and can help decide whether a colonoscopy is required or not. However, levels of FC cannot be used to differentiate between IBD and non IBD conditions. FC may be used to confirm remission or diagnose relapse in view of clinical symptoms and should be measured every six monthly during follow up. FC can be used to differentiate FGD from organic ones. In irritable bowel syndrome FC levels are observed to be higher than healthy children but lower than that seen in children with IBD. Children with constipation have normal FC levels whether functional or organic. FC levels show a great range of variability in food allergies, cow's milk protein allergy and celiac disease, so it cannot be used as a diagnostic or prognostic marker in these conditions. There is no evidence which corelates FC levels and clinical or laboratory findings of enteropathy, so FC levels should be used with caution in conditions with enteropathy as cystic fibrosis. Similarly, it has low utility in acute gastroenteritis and appendicitis. It is helpful in predicting the risk of necrotising enterocolitis (NEC) if there are rising levels in serial FC estimations. It is also useful in monitoring patients with NEC. Juvenile polyps are associated with high FC but a normal level doesn't rule out polyp. FC levels should always be analysed based on the clinical presentations.

2. The Value of Obtaining Colonic Mucosal Biopsies of Grossly Normal Tissue in Pediatric Patients

Glass J, Alcalá HE, Tobin M. The Value of Obtaining Colonic Mucosal Biopsies of Grossly Normal Tissue in Pediatric Patients. J Pediatr Gastroenterol Nutr. 2021 May 1;72(5):677-682. doi: 10.1097/MPG.0000000000003038. PMID: 33399330.

Endoscopic mucosal biopsy plays an important role in the diagnosis of a number of gastrointestinal conditions. However, there is no guideline regarding the necessity and yield of mucosal biopsy from grossly normal colonic mucosa. This paper describes a retrospective study with an aim to assess the value of mucosal biopsy from grossly normal tissue. In this study the agreement between the endoscopist and the histopathogist was examined whether they both reported normal or abnormal tissue. After exclusion 237 endoscopies were analysed. The predictive value of agreement between the endoscopist and pathologist was 81%. Abnormal histology was observed in 46 out of 237 patients (19.4%) with normal appearing colonic mucosa on endoscopy. Out of 46, 17 patients were known case of IBD, 11 had histological evidence of inflammation and rest had non-specific or clinically non-significant histological findings. These findings proposed that colonic mucosal biopsies may not be required from patients with grossly normal mucosa on colonoscopy. Biopsy should be obtained from patients with significant clinical or laboratory features.

3. Diagnostic Value of Persistently Low Positive TGA-IgA Titers in Symptomatic Children With Suspected Celiac Disease

Trovato CM, Montuori M, Morelli A, Alunni Fegatelli D, Vestri A, Giordano C, Cucchiara S, Caio G, Oliva S. Diagnostic Value of Persistently Low Positive TGA-IgA Titers in Symptomatic Children With Suspected Celiac Disease. J Pediatr

Gastroenterol Nutr. 2021 May 1;72(5):712-717. doi: 10.1097/MPG.0000000000003047.

The role of high titers of serum tissue transglutaminase 2 IgA (TGA-IgA) is undisputable in the screening of celiac disease in symptomatic as well as asymptomatic children. But the diagnostic value of persistently low positive titers in children with suspected CD is not known. This retrospective study in 281 children tries to find the answer and describes the diagnostic outcome of suspected CD children with persistently low positive anti-TGA IgA who underwent upper gastrointestinal endoscopy and duodenal biopsy. All of the patients had one or more gastrointestinal or extra gastrointestinal manifestations of CD. Three groups were made: Group A (Low positive) with TGA levels more than ULN but less than 5ULN; Group B(moderate positive) with TGA levels more than 5ULN but less than 10ULN; Group C (TGA negative) as controls. Out of 281 patients a repeat test showed positive TTG in 224 whereas as 57 had negative reports. Mucosal changes compatible with CD was observed in 204 children out of 224, who had positive TTG and the median level of TTG was 3ULN. In group A 87% (n=142) were diagnosed as CD. Endomysial antibody (EMA) was performed in 138 in group A and was found to be negative in 21% (n=29). Almost 80% had mucosal changes in second part of duodenum and beyond. Only 15% exhibited changes in the duodenal bulb. Out of 20 with normal mucosal findings, 14 were designated as potential CD on the basis of symptoms, positive TTG and EMA, and HLA predisposition. In group B all were diagnosed as CD on the basis of biopsy and only 3% had isolated duodenal bulb changes and EMA was positive in only 3%. The study concluded that a mean value of TTG 1.7ULN may be considered as threshold for duodenal biopsy.

4. Noninvasive biomarkers for the diagnosis and management of autoimmune hepatitis

Harrington, C, Krishnan, S, Mack, CL, Cravedi, P, Assis, DN, Levitsky, J. Noninvasive biomarkers for the diagnosis and management of autoimmune hepatitis. Hepatology. 2022; 00: 1–18. https://doi.org/10.1002/hep.32591

The diagnosis and management of autoimmune hepatitis (AIH) still continues to intrigue gastroenterologists. Lack of predictors for response to the treatment and identification of high-risk individuals for relapse adds to the struggle. This review based on PubMed literature search tries to look for biomarkers that can help predict the clinical course and early relapse in patients with AIH. Currently the biomarkers used to speculate the response and relapse are aminotransferases (AST and ALT); IgG and total immunoglobulins, and 6-thioguanine (6-TG). ALT levels less than half the upper limit of normal (ULN) and IgG level less than 1200 mg/dL when sustained for 2 years, decreases the risk of relapse by almost 40% after cessation of treatment and improves the histology in terms of disappearance of interface hepatitis. Liver enzymes are good predictors of biochemical remission but not histological remission. In the preclinical stage, DRB1*03:01, SH2B3, and CARD10 can be of help in screening children with other autoimmune features. The frequency of T cells secreting IL-17 and TNF-α increases significantly in active AIH and correlates with liver injury, and the levels of Th1 and Th17 cells significantly decreased after immunosuppression withdraw. These markers may have utility in detection of the disease before serological changes are evident and can also keep a track of the disease activity. High levels of adenosine deaminase, serum TGF-ß1, vitamin 25(OH)-D and ferritin have been found to match up with interface hepatitis and active histological process in children with AIH. High levels of Treg cells and serum DNAse1 have been shown to corroborate with histological remission. For relapse prediction anti-asialoglycoprotein receptor (ASGPR) titers may be helpful as their levels increase prior to elevation of liver enzymes thus it can predict relapse after withdrawal of immunosuppression.

Compiled by **Dr Rimjhim Shrivastava**