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Editorial

# Inflammatory Bowel Disease in Pakistani Population: An Important Diagnosis, Not to be Overlooked

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Inflammatory Bowel Disease (IBD) includes Ulcerative Colitis (UC) and Crohn's Disease (CD). CD and UC have distinct as well as overlapping clinicopathological characteristics. Indeterminate colitis is the term used to describe a type of IBD where strict characterisation into UC and CD is not possible.[1] Aetiology and pathogenesis of IBD remains incompletely understood despite advances in clinical science. Multifactorial causation is postulated. Environmental factors, i.e., geographical location, ethnicity, diet and lifestyle contributes to disease onset in genetically susceptible individuals. Other aetiological factors are also postulated, e.g., inappropriate immune response to intestinal microbial infection (although no specific pathogen has been identified) and medications (e.g., NSAIDs).[2]

IBD, once considered the disease of developed western world, is now a global problem and there is growing evidence that the prevalence is increasing in less developed and newly industrialised parts of the world.[3,4,5] Although there is paucity of epidemiological studies on IBD from Pakistan, there is growing evidence to suggest rising incidence of IBD.[6] It is important for the clinicians to be aware of this fact and to consider IBD as a differential diagnosis in their patients with suggestive symptoms. This article will focus on recognising the symptoms of IBD and diagnostic pathways to establish the initial diagnosis in the clinical setting.

UC affects the large intestine and predominantly presents with diarrhoea and/or per-rectal bleeding in adults. Associated symptoms can also include abdominal pain, incontinence, and in severe disease systemic symptoms, e.g., fever, symptoms related to anaemia, evidence of nutritional compromise and weight loss can occur. If left untreated, it may progress to fulminant colitis leading to toxic megacolon and perforation. Patients who have pre-dominantly distal UC can also present with constipation.

CD can involve any part of digestive tract from oral cavity to anal/peri-anal region, although majority of patients have small intestinal with or without large intestinal involvement. CD limited to large intestine is present in less than one third of patients with CD. Upper gastrointestinal CD is relatively uncommon (<15%).[7] Perianal CD can present either along with involvement of other GI sites or as a distinctly disease involved site. Depending upon the location of disease it can either present with diarrhoea predominant symptoms (in case of intestinal involvement particularly large intestine) or symptoms of intestinal obstruction, constipation, bloating, nausea or vomiting, owing to transmural involvement of small bowel resulting in strictures. UGI tract involvement, albeit uncommon, can also present with symptoms of dyspepsia and acid reflux. Systemic features, e.g., weight loss, anaemia etc. may also be present depending upon location, extent and severity of disease.

As IBD is an inflammatory condition, it can also involve non-GI organs. Extra intestinal manifestations can be present in both CD and UC.[8] These could include symptoms either from associated inflammatory conditions; arthritis or arthralgia, eye involvement in the form of uveitis, iritis or episcleritis, skin disorders like erythema nodosum and pyoderma gangrenosum, Primary Sclerosing Cholangitis, or secondary to malabsorption and diarrhoea directly related to intestinal IBD, e.g., renal stones, metabolic bone disease.

IBD is predominantly a disease of young age and age of onset for many patients is between 15 to 30 years, although it can present at any age and there is some evidence to suggest a bimodal distribution with second peak seen at age between 50-80 years. Younger patients presenting with GI symptoms can easily be labelled as having irritable bowel syndrome (IBS) or functional

gut symptoms, particularly in early stages of the disease. It is especially true in case of Crohn's disease where they present with non-diarrhoeal symptoms. Furthermore, in a geographical location where IBD is thought to have low prevalence and infectious causes of diarrhoea are pre-dominant, there could be additional delays in diagnosis owing to local knowledge and perception of healthcare professionals, practice bias and lack of support on basis of histological differentiation, purely because of less practical and professional exposure to the cases of IBD.[9] Delays in diagnosis can lead to presentation with severe disease and can also be responsible for decreased quality of life and can affect mental health of the patients, especially younger age cohorts.[10] GI endoscopic investigations can be challenging due to several factors in Pakistan's health system, e.g., availability & expertise of endoscopists, GI specialist histopathologists to review specimens. There is also added difficult, perhaps, due to perception of local population to undergo these investigations, especially female patients. Hence it is important to rationalise available resources and reserve these invasive tests to patient who are more likely to have benefit and yield a positive diagnosis. This may also increase their compliance to recommendation for invasive investigations.[11]

Diagnosis of IBD needs comprehensive review and correlation between clinical, biochemical, endoscopic, histological, and radiological investigations. A comprehensive medical history and clinical examination is a backbone of good medical practice, and its importance can not be emphasised enough with regards to IBD also. Both UC and CD are generally chronic diseases. Some patients can present as acute disease flare for the first time, but usually majority present with long standing un-resolving or re-current symptoms. History and examination should focus on; (i) ruling out differentials e.g., travel history (infectious causes), recent antibiotic use (antibiotic associated diarrhoea, Clostridium Difficile infection), any history of high risk medications use like NSAIDs, any evidence of immunocompromised states (Cytomegalovirus infection can mimic UC), previous history of radiation therapy (radiation proctitis, colitis and enteritis), any food intolerances (Coeliac, lactose intolerance etc.), any evidence of atherosclerotic diseases (ischemic colitis), known history of diverticulosis (diverticulitis), previous history of tuberculosis or contact history, difficult to flush fatty stools (pancreatic exocrine insufficiency), previous history of cholecystectomy or ileal resections (Bile associated diarrhoea), long standing or poorly controlled Diabetes (autonomic neuropathy) and screening for extra-intestinal manifestations of IBD (ii) assessing the disease activity and severity e.g., severity of diarrhoea (number and type of stools on Bristol chart), associated per rectal bleeding and severity of it, presence of abdominal pain, nausea or vomiting, evidence of malabsorption (anaemia, weight loss etc.). Use clinical scoring systems to standardise assessment of disease severity, e.g., Truelove and Witts Criteria, simple clinical colitis activity index, Harvey Bradshaw index etc.[12] (iii) exploring family history of IBD and colorectal cancer (iv) assessing co-morbidities and current immunisation status which will have implications in the treatment of disease, if diagnosed.

Every patient should have baseline biochemical assessment[13] in the form of Full Blood Count (FBC), inflammatory markers (CRP, ESR), electrolytes, liver enzymes, coeliac screen, and stool analysis to rule out infectious causes. Faecal Calprotectin (FCP) is a neutrophil derived protein that is a sensitive marker of intestinal inflammation. A negative or normal FCP level in a young patient with GI symptoms can help differentiate between IBD and IBS. Patients with positive FCP should have further investigations to rule out IBD. There is no rigid cut off between positive and negative FCP values. Higher values are more sensitive. A cut off of 150ug/g has been suggested by ECCO-ESGAR guidelines.[13] FCP is also useful in monitoring of disease activity in patients diagnosed with IBD. Use of FCP is not recommended for diagnosis of IBD in elderly patients and those deemed high risk of colorectal pathology or cancer after clinical evaluation, and this cohort of patients should be offered endoscopic evaluation.

High risk patients identified after above assessment should be offered further investigations to reach or exclude the diagnosis of IBD. Histological confirmation of IBD is the gold standard and ileo-colonoscopy should be offered as 1st line investigations to patients where there are no contra indications to procedure. This is especially true in patients with diarrhoea or colonic predominant symptoms, as it will not only help establishing the diagnosis of IBD, but also to exclude other causes of diarrhoea and bowel symptoms, e.g., microscopic colitis, ischemic colitis and diverticulosis/ diverticulitis. Furthermore, endoscopy will help in identifying extent and severity of disease. Several endoscopic severity scores are being used in clinical practice to standardise endoscopic reporting in patients with IBD e.g., Mayo Score, UCEIS, UCCIS scores for UC, and CDEIS, SES-CD scores for CD. Biopsies specimen should be assessed by Histopathologist with interest and expertise in GI diseases' reporting to enhance diagnostic yield.[14]

Radiological investigations are usually complementary to endoscopic investigations in IBD. These are particularly useful in evaluation of small bowel disease non-invasively. Several modalities can be used, e.g., MR enterorrhaphy (MRE), CT enterorrhaphy (less preferred

than MRE due to radiation risk) and intestinal ultrasound (cheaper but is operator dependent and validity is not fully known). MRI pelvis can establish extent and severity of peri-anal CD and can outline fistulas and collections. Barium meal and follow through, and barium enemas are the investigations which are being rapidly replaced in modern practice owing to availability of these more sophisticated modalities.

Small bowel capsule endoscopy (SBCE) can be offered to evaluate & monitor small bowel disease and can be more sensitive in diagnosing and assessing mild mucosal disease. On the other hand, MRE can be the preferred modality, if there are contraindications to SBCE, e.g., structuring small bowel disease. Invasive small bowel endoscopy (enteroscopy) is usually reserved where histological sample is required from small bowel in case a diagnostic dilemma exists, or a therapeutic intervention is required.

Differentiating between intestinal tuberculosis and CD can be a challenge in the developing world due to prevalence of TB and relatively low incidence of CD. In this scenario, histological differentiating characteristics (e.g., caseating, confluent, large granulomas are common in intestinal TB vs microgranuloma common in CD) should complement clinical evaluation (e.g., diarrhoea, per rectal bleeding, perianal disease in CD vs fever and night sweats which are common in intestinal TB) and endoscopic investigations (e.g., cobble stoning of mucosa, longitudinal and aphthous ulcerations seen commonly in CD vs transverse ulcerations seen in intestinal TB). Furthermore, radiological evaluation, particularly of lungs, for any evidence of active or latent TB, serological markers and microbiological investigations for tuberculous infection should also contribute to decision making[15]. It is important to establish to correct diagnosis at start as usual anti-tuberculous therapy regimen in intestinal TB often includes steroids which may treat and mask the IBD diagnosis and may lead to long term morbidity because of late-stage complications of the disease due to lack of maintenance treatment.

A simplified diagnostic algorithm is shown in Figure-1 to investigate GI/bowel symptoms and stepwise approach to help establish the diagnosis of IBD. Following this approach may result in early diagnosis of IBD and may decrease physical and mental harm associated with delay in diagnosis of IBD. Detailed evaluation of other causes of diarrhoea is out of scope of this article but has been briefly summarised in the flow chart.

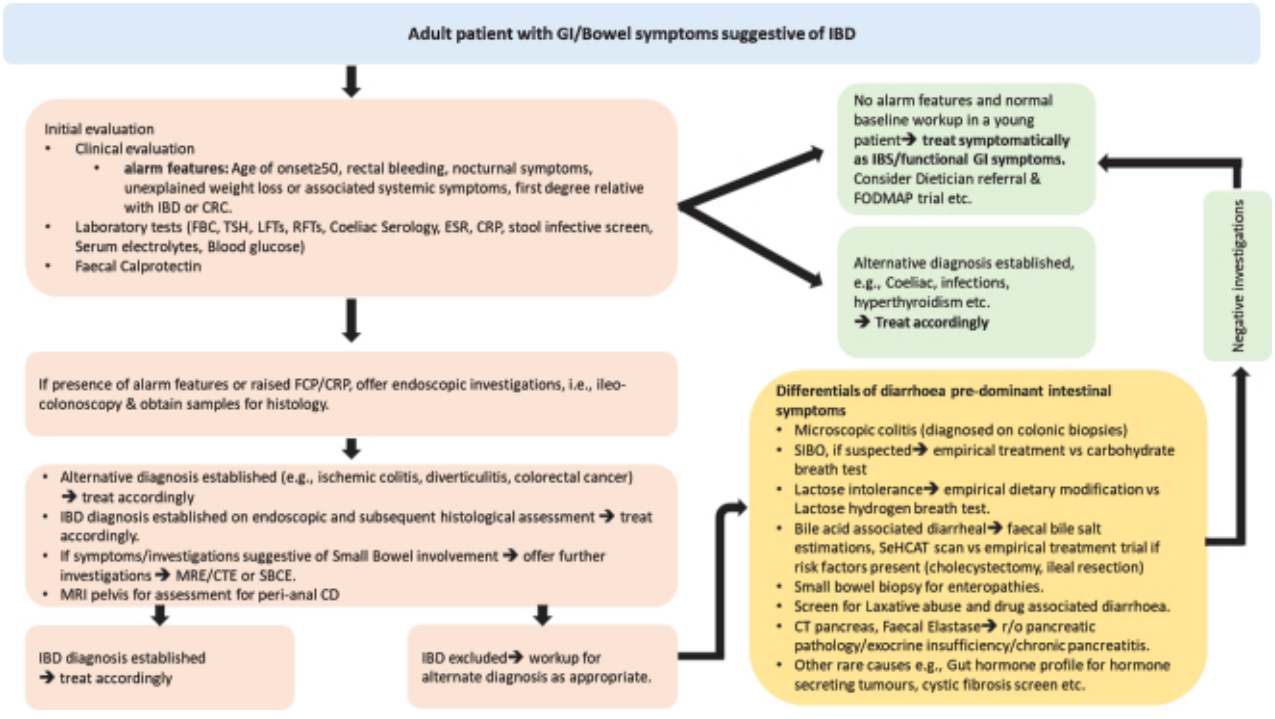


**Figure-1:** *Diagnostic algorithm for evaluation of patients with gastrointestinal or bowel symptoms*

*IBD: Inflammatory Bowel Disease, CRC: Colorectal cancer, FBC: Full Blood Count, TSH: Thyroid Stimulating Hormone, RFTs: Renal Function Tests, ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive Protein, MRE: Magnetic Resonance Enterography, CTE: Computed Tomography Enterography, SBCE: Small Bowel Capsule Endoscopy, FODMAP: Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols, SIBO: Small intestinal Bacterial Overgrowth, SeHCAT: 23-Seleno-25-Homotaurocholic Acid, Selenium Homocholic acid taurine or Tauroselcholic Acid.*

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## References

1. Mitchell PJ, Rabau MY, Haboubi NY. Indeterminate colitis. Tech Coloproctol. 2007;11(2):91-6.
2. Danese S, Fiocchi C. Etiopathogenesis of inflammatory bowel diseases. World J Gastroenterol. 2006; 12(30): 4807-12.
3. Windsor JW, Kaplan GG. Evolving Epidemiology of IBD. Curr Gastroenterol Rep. 2019;21(8):40.
4. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, Panaccione R, Ghosh S, Wu JCY, Chan FKL, Sung JJY, Kaplan GG. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet. 2017;390(10114):2769-78.
5. Ng SC, Tang W, Ching JY, Wong M, Chow CM, Hui AJ et al. Asia–Pacific Crohn's and Colitis Epidemiologic Study (ACCESS) Study Group. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. Gastroenterol. 2013;145(1):158-165.
6. Nasim S, Chawla T, Sheikh GM. Surgical management of inflammatory bowel disease: A low prevalence, developing country perspective. J Pak Med Assoc. 2016; 66(3):247.
7. Gajendran M, Loganathan P, Catinella AP, Hashash JG. A comprehensive review and update on Crohn's disease. Dis Mon. 2018;64(2):20-57.
8. Rogler G, Singh A, Kavanaugh A, Rubin DT. Extra-intestinal Manifestations of Inflammatory Bowel Disease: Current Concepts, Treatment, and Implications for Disease Management. Gastroenterol. 2021; 161(4): 1118-32.
9. Barnes EL, Loftus EV Jr, Kappelman MD. Effects of Race and Ethnicity on Diagnosis and Management of Inflammatory Bowel Diseases. Gastroenterol. 2021; 160(3):677-89.
10. Carroll MW, Kuenzig ME, Mack DR, Otley AR, Griffiths AM, Kaplan GG, Bernstein CN, Bitton A, Murthy SK, Nguyen GC, Lee K, Cooke-Lauder J, Benchimol EI. The Impact of Inflammatory Bowel Disease in Canada 2018: Children and Adolescents with IBD. J Can Assoc Gastroenterol. 2019;2(1):S49-S67.
11. Hasan F, Mahmood Shah SM, Munaf M, Khan MR, Marsia S, Haaris SM, Shaikh MH, Abdur Rahim I, Anwar MS, Qureshi KS, Iqbal M, Qazi S, Kasi BA, Tahir M, Ur Rehman SI, Fatima K. Barriers to Colorectal Cancer Screening in Pakistan. Cureus. 2017; 9(7): e1477.
12. Sturm A, Maaser C, Calabrese E, Annese V, Fiorino G, Kucharzik T et al. European Crohn's and Colitis Organisation [ECCO] and the European Society of Gastrointestinal and Abdominal Radiology [ESGAR]. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 2: IBD scores and general principles and technical aspects. J Crohns Colitis. 2019;13(3):273-284.
13. Maaser C, Sturm A, Vavricka SR, Kucharzik T, Fiorino G, Annese V et al. European Crohn's and Colitis Organisation [ECCO] and the European Society of Gastrointestinal and Abdominal Radiology [ESGAR]. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. J Crohns Colitis. 2019; 13(2):144-64.
14. Fléjou JF. Histoseminar on inflammatory bowel diseases (IBD). Introduction - pathologist's role in diagnosis and surveillance in 2017. Ann Pathol. 2017; 37(4): 279-80.
15. Kedia S, Das P, Madhusudhan KS, Dattagupta S, Sharma R, Sahni P, Makharia G, Ahuja V. Differentiating Crohn's disease from intestinal tuberculosis. World J Gastroenterol. 2019;25(4):418-32.