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Research Article

PREVALANCE OF EXTRAINTESTINAL MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASE IN A TERTIARY CARE CENTRE

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A R T I C L E I N F O

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A B S T R A C T

Inflammatory Bowel Disease (IBD) is an immune mediated intestinal condition characterized by a remitting and relapsing course. In addition to the intestinal manifestations, the disease presents with numerous extra intestinal manifestations. Roughly 1/3rd of the patients with IBD have Extra intestinal manifestations. This study analyses the clinical presentation of IBD in our Tertiary Care Centre with special emphasis to the Extra Intestinal Manifestations of Inflammatory Bowel Disease (IBD).

INTRODUCTION

Inflammatory Bowel Disease (IBD) comprises of conditions characterized by atendency for chronic or relapsing immune activation and inflammation within the gastrointestinal tract. Crohn's Disease and Ulcerative Colitis are the two major forms of idiopathic IBD. The incidence of IBD ranges from 0-20 per 100000 persons worldwide for both Ulcerative Colitis and Crohn's Disease. The age of onset commonly being 2nd to 4th decade, it is most common among the people of Jewish ethnicity. The condition is familial in 5-10% of the patients. Both Ulcerative Colitis and Crohn's Disease have Male preponderance.IBD manifest mainly with intestinal manifestations but may have extra intestinal manifestations as well. Among the affected individuals, up to 1/3rd of the patients have at least 1 extra intestinal manifestation, the overall incidence being 20-40%. Blacks have high incidence of ocular and joint manifestations while Hispanics have skin manifestations. The various extra intestinal manifestations include musculoskeletal, mucocutaneous, hepatobiliary, hematologic, vascular, ocular, renal, genitourinary manifestations and others. Although many associations between IBD and Extra intestinal manifestations have been proposed, it is not fully elucidated. Some may share a common pathology with IBD.

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MATERIALS AND METHODS

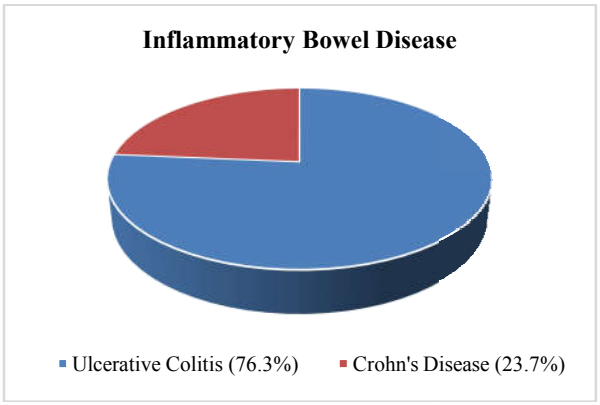
In this cross-sectional study, 93 patients attending the Medical Gastroenterology OPD at Govt.

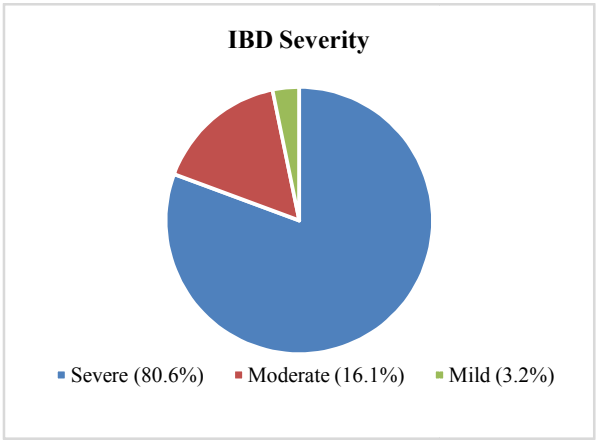
Rajaji Hospital, Madurai, presenting with complaints of bleeding PR, diagnosed with Inflammatory Bowel Disease and those who satisfied the clinical, colonoscopic and histologic criteria for IBD were included in our study. The selected patients were evaluated with detailed history of symptoms regarding intestinal and extra intestinal manifestations. Detailed clinical examination, Complete Blood Count, Routine Blood Biochemistry including Blood Glucose, Renal &Liver Function tests, Serum Amylase were estimated. Ultrasound Abdomen and Colonoscopy were done. Biopsy of the colon was done and stained with H&E. Urine Routine analysis, Stool for parasites, occult blood and culture were done. Slit lamp examination of eyes was done to look for the evidence of uveitis. Extent of the disease was determined by colonoscopy and was classified as distal proctitis, proctosigmoiditis, left-sided colitis (involvement up to splenic flexure) and pancolitis. Severity was assessed using Truelove &Witt's criteria. Cases were examined for other extraintestinal manifestations namely musculoskeletal, mucocutaneous, hepatobiliary, hematologic, vascular, ocular, renal, genitourinary and others. Patients who tested Positive for HIV, Hepatitis B or Hepatitis C antibodies were excluded from the study.

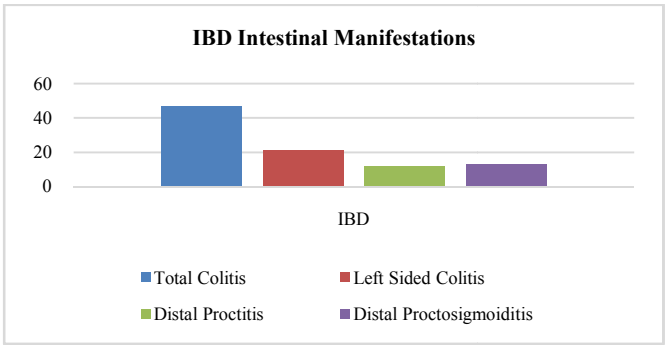
RESULTS

Out of the 93 patients of IBD were analyzed, 71 cases were diagnosed with Ulcerative Colitis and 22 cases diagnosed as

Crohn's Disease. Out of 93 patients, 68 were males and 25 were females, the sex ratio was 2.7:1 male to female. The age range with maximum prevalence of disease in our study was 31-40 years with the mean age being 33.8. On the whole, 75(80.6%) cases were classified as severe, 15(16.1%) intermediate and 3(3.2%) classified as mild. Total Colitis was seen in 47(50.5%) cases followed by Left Sided Colitis in 21(22.6%), Distal Proctitis in 12(12.9%), Distal Proctosigmoiditis in 13(14%).







59 cases out of 93 (63.4%) patients had at least any one extra intestinal feature (Statistically Significant). Fatty liver was seen in 21(22.6%) patients, Gall stones 10(10.8%), 1(1.1%) had Pancreatitis, 7(7.5%) had Nephrolithiasis, Pauciarthralgia 26(30%), Polyarthralgia 8(8.1%), Low backache 23(24.7%), Erythema nodosum 3 (3.2%), PyodermaGangrenosum 2(2.2%), Angular stomatitis 14(15.1%), Aphthous Ulcer 5(5.3%), Conjunctivitis 4(4.3), Anterior Uveitis 2(2.2%) formed the extraintestinalmanifestations.

Ulcerative colitis is more prevalent than Crohn's Disease in our study. Sex ratio of Inflammatory Bowel Disease, M:F = 2.7:1. The peak age group affected by IBD is 31-40 years, the mean age being 33.8 years. Total Colitis is the predominant colonoscopy finding in our study. The majority of Ulcerative Colitis cases are having severe disease (80.6%) based on Truelove & Witt's criteria. Extra intestinal manifestations of IBD in our study are 63.4 %. 18% of the study group had >1 extra intestinal manifestation. The most common extra intestinal manifestations are Pauciarthralgia (30%) & Fatty liver (22.6%). No cases of Primary Sclerosing Cholangitis were found in our study. The extra intestinal manifestations in our study are comparable to published literature worldwide.

Extra Intestinal Manifestation	No. of Patients	Percentage
Fatty Liver	21	22.6%
Gall Stones	10	10.8%
Pancreatitis	1	1.1%
Nephrolithiasis	7	7.5%
Pauciarthralgia	26	30%
Polyarthralgia	8	8.1%
Low Back Ache	23	24.7%
Erythema Nodosum	3	3.2%
Pyoderma Gangrenosum	2	2.2%
Angular Stomatitis	14	15.1%
Aphthous Ulcer	5	5.3%
Conjunctivitis	4	4.3%
Anterior Uveitis	2	2.2%

DISCUSSION

The Extra Intestinal manifestations are common in patients with Inflammatory Bowel Disease occurring in nearly 1/3rd of the patients [1]. The incidence was much higher in our study (63.4%). These can affect multiple organs which proves that the consequence of the disease is not limited to the intestine only. The pathogenesis is not fully established, the close postulate being an aberrant adaptive immune response directed against extra intestinal sites due to common epitopes in consequence of the loss of intestinal barrier integrity in genetically predisposed individuals. Inflammatory manifestations of the skin, eyes, liver and joints were considered as primary manifestations. Extra intestinal manifestations were common in patients with Crohn's disease with HLA-A2, HLA-DR1 & HLA-DQw5 and in patients with Ulcerative Colitis with HLA-DR103 [2]. Most of the Extra intestinal manifestations parallels the disease activity of IBD and will respond to the treatment of the underlying bowel disease [3]. Extra intestinal manifestations are a proof that IBD is not only limited to the gut. Sometimes these can be more debilitating than the intestinal disease.

Factors responsible for extra intestinal organ involvement in IBD are diverse and sometimes it can be difficult to differentiate the true extra intestinal manifestations (EIMs); i.e. primary systemic affection by the disease itself, from secondary extra intestinal complications of the disease, caused for example by malnutrition, chronic inflammation or side effects of therapy. Some of these EIMs may not correlate with disease activity (e.g., primary sclerosingcholangitis) but in general EIMs tend to follow the clinical course of IBD [4].Extra intestinal manifestations can be grouped into 1. Reactive manifestations often associated with intestinal inflammatory activity and reflecting a pathogenic mechanism common with intestinal disease (arthritis, erythema nodosum, pyoderma gangrenosum, aphthous stomatitis, iritis/uveitis); 2. Other autoimmune diseases independent of the bowel disease that reflect only a major susceptibility to autoimmunity. They are not considered (apart for primary sclerosingcholangitis) as specific IBD features but only as autoimmune associated

diseases such as ankylosing spondylitis, primary biliary cirrhosis, alopecia areata, and thyroid autoimmune disease and others [5].

Both Crohn's disease and Ulcerative colitis are associated with extra intestinal manifestations among which in Crohn's Disease it is around 40% and in Ulcerative colitis the rate is significantly lower. Our study also indicates the same. According to the pattern of involvement the extra intestinal manifestations can be broadly divided into 3 groups., the first group involving the skin, eye, joints and mouth. These activity parallels the activity of the disease. The second group includes manifestations that are secondary to complications of or a direct extension of bowel disease. These are more common with Crohn's disease than Ulcerative colitis. The third group contains other non-specific extra intestinal manifestations [6].
Mucosal T-cells are important in maintaining intestinal homeostasis, defined as the balance between the mucosal epithelium, intestinal microbes, and host immune response. Abnormal T-cell response to microbial antigens can disrupt this equilibrium and is believed to be the mechanism that triggers the chronic inflammation and excessive secretion of cytokines that lead to the development of IBD. It has been proposed that some EIM's seen with IBD manifest as a result of immune dysregulation resulting in a lymphocyte mediated destructive process. IBD patients with hepatic EIMs could be explained by mucosal T-cells in the gut aberrantly travelling to the liver, becoming exposed to hepatic antigens, and ultimately causing liver damage. Similar mechanism could possibly explain the pathogenesis of other EIM's (including the skin) in patients with IBD [8].

Among the dermatologic manifestations Erythema nodosum occurs in up to 15% of CD & 10% of UC patients. Attacks correlate with bowel activity. The lesions of EN are hot, red, tender nodules 1-5 cm over anterior surface of the legs, thigh, calves and arms. Pyoderma gangrenosum is more common with UC than CD and is associated with severe disease [7]. The course is independent of the intestinal disease. It begins as a pustule and spreads concentrically to undermine the healthy skin and they contain necrotic tissue at the centre. Others include Pyoderma vegetans, pyostomatitisvegetans and Sweet syndrome (neutrophilic dermatosis). Oral mucosal lesions include Aphthous Ulcers and Angular stomatitis. These have cobble stone lesions of the buccal mucosa.

Peripheral arthritis is more common with CD and correlates with intestinal disease. It is asymmetric, poly/pauci articular, migratory and involves the large joints. Ankylosing spondylitis occurs commonly in CD and sacroiliitis is equal in both UC and CD. They do not correlate with the bowel disease activity. Ocular manifestations include conjunctivitis, iritis/uveitis, episcleritis. Prompt intervention is necessary to prevent permanent visual loss. Therefore, evaluation of the eye should be a routine component in the care of patients with IBD [9]. Hepatic steatosis is more common with IBD and usually presents with hepatomegaly. Fatty liver is due to chronic illness, malnutrition & steroid therapy. Gallstone formation is caused by malabsorption of bile acids, resulting in depletion of the bile salt pool and the secretion of lithogenic bile and is more common with Crohn's disease [10]. Primary SclerosingCholangitis (PSC) in patients with UC is ~5% but 50-75% of patients with PSC have IBD. This frequently leads to biliary cirrhosis and hepatic failure. Gall bladder polyps are also seen occurring and gall bladder surveillance is mandatory as they have a lifetime risk of cholangiocarcinoma.

The most frequent genitourinary complications are calculi [4], ureteral obstruction and ileal bladder fistula. The highest frequency of Nephrolithiasis (10-20%) is seen with CD [3]. Calcium oxalate stones develop secondary to hyperoxaluria. Metabolic bone disorders are common due to malabsorption, increased inflammatory mediator activity (IL-1, IL-6, TNF) which contribute to low bone density. The absolute risk of an osteoporotic fracture is about 1% per person per year. Patients with IBD have increased risk of both venous and arterial thrombosis even if the disease is not active due to the existing state of hypercoagulability. A spectrum of all small medium and large vessel vasculitides are common. Other manifestations include endocarditis, ILD, secondary amyloidosis, renal failure. Pancreatitis is a rare manifestation and results from duodenal fistulas, ampullary CD, gall stones, PSC, autoimmune or due to drugs.

As the incidence of extra intestinal manifestations is large and the variability far and wide, these manifestations may cause more debilitating illness with morbidity and mortality than the disease per se. Therefore, it becomes an object of necessity to diagnose and treat these manifestations as early as possible. For than a multimodality approach involving various specialties has become mandatory.

References

1. Extra intestinal manifestations of inflammatory bowel disease: Clinical aspects and pathogenesis. Sandro da Costa Ferreira, Bernardo Bezerra Martins de Oliveira, André MarussiMorsoletto, Ana de Lourdes Candolo Martinelli, Luiz Ernesto de Almeida Troncon. Review Article - Journal of Gastroenterology and Digestive Diseases (2018) Volume 3, Issue1 Extra intestinal Manifestations of Inflammatory Bowel Disease. Stephan R Vavricka, MD, Alain Schoepfer, MD, Michael Scharl, MD, Peter L. Lakatos, MD, Alexander Navarini, MD, and Gerhard Rogler, MD*. Lippincott Williams & Wilkins Open Access Jul 2. 2015.
2. Extra intestinal Manifestations of Inflammatory Bowel Disease Jonathan S. Levine, MDand Robert Burakoff, MD, MPH Gastroenterology &Hepatology 2011 April 7.
3. Extraintestinal manifestations and complications in inflammatory bowel diseases, Katja S Rothfuss, Eduard F Stange, and Klaus R Herrlinger. World J Gastroenterol. 2006 Aug 14.
4. Extraintestinal manifestations in inflammatory bowel disease; SilvioDanese, Stefano Semeraro, Alfredo Papa, Italia Roberto, Franco Scaldaferri, Giuseppe Fedeli, Giovanni Gasbarrini, and Antonio Gasbarrini World J Gastroenterol. 2005 Dec 14; 11(46)
5. Extra intestinal manifestations of inflammatory bowel disease Chinyu G Su MD, Thomas A Judge MD, Gary R Lichtenstein MD. Gastroenterology Clinics of North America Volume 31, Issue 1, March 2002, Pages 307-327
6. Pyoderma gangrenosum among patients with inflammatory bowel disease: a descriptive cohort study. Adam V. Weizman, MSc, MD, Brian Huang, MD, Stephan Targan, MD, Marla Dubinsky, MD, Phillip Fleshner, MD, Manreet Kaur, MD, Andrew Ippoliti, MD, DeepaPanikkath, Eric Vasiliauskas, MD, David

Shih, MD, PhD, Dermot P.B. McGovern, MD, PhD, and Gil Y. Melmed, MD, MPH Author Manuscript. J Cutan Med Surg. 2014 Oct; 18(5): 361.

7. Skin Manifestations of Inflammatory Bowel Disease Brian L. Huang,1 Stephanie Chandra,2 and David QuanShih2 Frontiers in Physiology. 2012; 3: 13. Published online 2012 Feb 6.
8. Ocular manifestations of inflammatory bowel disease. Mintz R1, Feller ER, Bahr RL, Shah SA. Inflamm Bowel Dis. 2004 Mar; 10(2):135-9. PubMed
9. Incidence and risk factors for gallstones in patients with inflammatory bowel disease: a large case-control study. Parente F1, Pastore L, Bargiggia S, Cucino C, Greco S, Molteni M, Ardizzone S, Porro GB, Sampietro GM, Giorgi R, Moretti R, Gallus S. Hepatology. 2007 May;45(5):1267-74.

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