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Study of Extra Intestinal Manifestations of Inflammatory Bowel Disease Patients in a Tertiary Care Hospital

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Abstract
Crohn's disease cannot be distinguished from ulcerative colitis on clinical grounds, yet the two diseases are distinct syndromes with divergent treatment and prognosis. IBD presents mainly with intestinal and extraintestinal manifestations. The various extraintestinal manifestations include musculoskeletal, mucocutaneous, hepatobiliary, hematologic, vascular, ocular, renal and genitourinary manifestations. The study was conducted with the approval from the institutional Ethical Committee, Sree mookambika college of medical sciences . The duration of illness was upto 10 years, at different stages of Inflammatory bowel disease. Patients with the age group ranging from 15-70 years were studied. The selected patients were evaluated with detailed clinical history regarding duration of the disease and symptomatology. Aphthous ulcer is present in 5.12% of patients in our study. Sleisenger concluded that aphthous ulcers are common among patients with Crohn's disease, ulcerative colitis but also among healthy persons. At least 10% of patients with UC develop oral aphthous ulcers. These lesions usually occur with flares of colitis and resolve on control of the disease. It is present in 15.38% of the participants. Out of the 2 cases of CD, angular stomatitis was presentin one case. The aim was to study the clinical presentation of IBD in our hospital and the extraintestinal manifestations of the disease. All cases of bleeding PR who satisfied the clinical, colonoscopic and histologic criteria of IBD were included as well as cases of proven IBD. Thirty nine patients with inflammatory bowel disease were included in the study. Colonoscopic examination of these patients were done after taking proper consent.

INTRODUCTION

Idiopathic inflammatory bowel disease (IBD) comprises conditions characterised by a tendency for chronic or relapsing immune activation and inflammation within the gastrointestinal tract. Crohn's disease and ulcerative colitis are the two major forms[1] of idiopathic IBD. They share many clinical and epidemiologic characteristics, suggesting that underlying causation may be similar. Indeed, more than occasionally Crohn's disease cannot be distinguished from ulcerative colitis on clinical grounds, yet the two diseases are distinct syndromes with divergent treatment and prognosis. IBD manifest mainly with intestinal manifestations as well as with extraintestinal manifestations. The various extraintestinal manifestations include musculoskeletal, mucocutaneous, hepatobiliary, hematologic and vascular, ocular, renal and genitourinary manifestations and others. Among these, hepatobiliary manifestation in the form of fatty liver and musculoskeletal manifestation in the form of pauciarthralgia are the most commonly seen[2-4]. Crohn's disease (CD) is a condition of chronic inflammation potentially involving any location of the alimentary tract from mouth to anus, but with a propensity for the distal small bowel and proximal large bowel. Ulcerative colitis (UC) is a chronic inflammatory disorder of the gastrointestinal tract that affects the large bowel and is a major disorder under the broad group of inflammatory bowel diseases[5].

Aims and Objectives of the Study: To study the clinical presentation of IBD in our hospital, To study the extra intestinal manifestations of inflammatory bowel disease.

MATERIALS AND METHODS

The duration of illness was upto 10 years, at different stages of Inflammatory bowel disease. Patients with the age group ranging from 15-70 years were studied. The selected patients were evaluated with detailed history regarding duration of disease and symptomatology. This study was conducted at sree mookambika institute of medical sciences at general surgery department. Inclusion criteria are All cases of bleeding PR who satisfied the clinical, colonoscopic and histologic criteria of IBD were included, All cases of proven UC were also included. Exclusion criteria are Positive results rheumatological diseases, Patients with chronic alcoholism. Thirty nine patients of ulcerative colitis were selected from Surgery opd presenting with complains of bleeding PR and those who satisfied the clinical, colonoscopic and histologic criteria for IBD. Detailed clinical examination was done. Vitals and temperature of for stool culture, ova and parasites and clostridium difficile toxin, Patients with known patients were recorded. All systems are examined carefully . Colonoscopic examination of these patients were done after taking proper consent. Biopsy specimens were taken and sent for histopathological examination. Extent of the disease was determined by colonoscopy and was classified into distal proctitis, proctosigmoiditis, left-sided colitis (involvement up to splenic flexure) and pancolitis. Severity was assessed using Truelove and Witts criteria. Cases were examined for extraintestinal manifestations. Liver function tests of these patients were sent. Ultrasound scan of abdomen was done to know the incidence of fatty liver and gallstones. Musculoskeletal manifestations and Dermatological manifestations were noted. Slit lamp examination of eye was done to look for evidence of uveitis. Statistical analysis was done using the statistical package for social sciences (SPSS).Different statistical methods were used. Mean±SD was determined for quantitative data and frequency for categorical variables. The independent t-test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group difference for categorical variables.

RESULTS AND DISCUSSIONS

Table 1: Quantitative Parameters

Parameter	Normal cases		Abnormal cases		Range	Mean	S.D.
	No.	%	No.	%			
Hb.%	11	28.2	28	71.8	4.8-13.2	9.96	1.81
Total WBC	26	66.67	13	33.33	6.2-18.7	9.7	3.3

Table 2: Count

Erythrocyte sedimentation							
Rate	11	28.2	28	71.2	20-145	64.1	35.1
Platelet	28	71.2	11	28.2	1.25-5.17	2.82	0.86
Fibrinogen	39	100	-	-	114-450	186	75
Amylase	29	74.4	10	25.6	34-185	78.7	44.6
Bilirubin	39	100	-	-	0.3-1.1	0.85	0.14
Ast and alt	34	87.2	5	12.8	12-46	23.1	9.2
Alp	39	100	-	-	90-382	158.9	61.7
Total protein	32	82.1	7	17.9	4.4-7.5	6.45	0.79
Albumin	31	79.5	8	20.5	2.3-4.8	3.59	0.61
Globulin	34	87.2	5	12.8	2.1-3.5	2.86	0.35

In this study 71.8% of patients were anaemic and 71.2% were having elevated ESR. There was no significant elevation of alkaline phosphatase noted.

RESULTS AND DISCUSSIONS

Table 3: Biopsy Findings

Biopsy findings	Cases	
	No.	%
Non Caseating granuloma	2	5.1
Active Ulcerative Colitis	37	94.9
Total	39	100

Biopsy of the cases showed non caseating granulomas in Crohn’s disease and evidence of active Ulcerative colitis in the rest.

Table 4: Truelove and Witts Criteria for Disease Severity

Truelove and Witts	CASES	
	No.	%
Mild	1	2.7
Intermediate	6	16.2
Severe	30	81.1
Total	37*	100

Extent of Disease: Out of the 37 cases of UC, 51.3% had evidence of total colitis, followed by involvement upto splenic flexure in 23.1%, distal proctitis in 12.8% and distal proctosigmoiditis in 7.7%.

Table 5: Extent of Disease

Extent of disease	Cases	
	No.	%
Distal Proctitis (DP)	5	12.8
Distal Procto Sigmoiditis (DPS)	3	7.7
Splenic Flexure (SF)	9	23.1
Total Colitis (TC)	20	51.3
Terminal Ileum and Colon (TIC)	2	5.1
Total	39	100

Table 6: USG Findings

USG Findings	Cases			
	Normal		Abnormal	
	No	%	No	%
Fatty liver	30	76.9	9	23.1
Gall stones	35	89.7	4	10.3
Total			13	33.3

Fatty liver was the predominant hepatobiliary manifestation in our study in 23.1%.

Table 7: Mucocutaneous Manifestations

Mucocutaneous	Cases			
	Present		Absent	
	No	%	No	%
Angular Stomatitis (AS)	6	15.3	33	74.62
Pyoderma Gangrenosum (PG)	1	8	38	97.4
Aphthous ulcer (AU)	2	2.56	37	94.87
Erythema Nodosum(EN)	1	5.12	38	97.4
		2.56		
Total skin (EN+PG)	2		37	94.8
Total mucosal (AU+AS)	8	5.12	31	79.5
		20.5		

Angular stomatitis was the most seen mucocutaneous manifestation in our study. We had 2.56% each of erythema nodosum and pyoderma gangrenosum in our study. 39 patients of IBD from General surgery Department were analysed. Our study has 37 cases of UC and 2 cases of CD.Of the 37 cases of UC,81% of cases are severe, 16% intermediate and 2.6% classified as mild according to the Truelove and Witts criteria. Total colitis is seen in 51.3% of cases followed by left sided colitis in 23.1%, distal proctitis in 12.8%, distal proctosigmoiditis in 7.7%[6-9]. Sex ratio of IBD in this study is 1:2.5 . The sex ratio for UC is 1:2.4. Sleisenger Text Book of Gastroenterology shows a small excess risk of Crohn's disease among women and a female-to-male ratio between unity and 1.2:1. Most studies have not shown any gender difference in the occurrence of UC and a male-to-female ratio of nearly 1:1 applies to all age groups. The age group with maximum prevalence of disease in our study is 31-40 years. The peak incidence of UC occurs in the 2nd and 3rd decades of life and had a second peak incidence above 50 years of age. According to Sleisenger, UC may present at all ages, although diagnosis before the age of 5 years or after 75 years is uncommon .Studies have reported a second, smaller peak in the elderly, between the ages of 60 and 70 years. This second peak is less pronounced than that for Crohn's disease. Crohn's disease is diagnosed mostly among persons aged 15-30 years, although the age of diagnosis may range from early childhood through the entire lifespan. Population-based studies have shown the median age of diagnosis to be approximately 30 years. Of the 39 patients, 25 patients have anyone of the extraintestinal features, which is 64% in our study. Below is the list of frequency of extraintestinal manifestations in our study compared with published data[10,11,12]. In a study by Navaneethan U, Remzi FH *et al* ,a total of 545 Ileal Pouch Anal Anastomosis patients with underlying IBD which included 346 patients with ulcerative colitis, 25 with indeterminate colitis and 2 with Crohn's colitis, a total of 17.4% had abnormal LFTs. Of these patients[15] 13.9% had abnormal transaminases. The most common cause of an abnormal LFT was transient elevation in 49.2% patients, followed by fatty liver (fatty change on imaging with body mass index (BMI) >/=25 kg/m(2) in the absence of other causes, including alcohol abuse and drug-induced hepatitis) in 15.4%, drug-induced abnormal LFTs in 7 (10.7%) and chronic hepatitis B or C in 6 (9.2%)[13,14]. Harrison says Fatty liver is detected in >50%of abnormal liver biopsies in IBD.In our study the incidence is 23.1% and is comparable to the above data.Our study, the gall stone incidence is 10.3%. Gall stones are present in both cases of CD and percentage of UC patients with Gallstones is 5.4%. In a study by Kurchin A, *et al* ,a retrospective study of 152 ileostomates with inflammatory bowel disease (IBD) revealed that 10.5 per cent had diagnoses of cholelithiasis. The remaining patients, were followed for possible cholelithiasis, with sonographic examination and 23.2 percent were found to have cholelithiasis, usually in an asymptomatic stage. Among women over 50 years old, (63.6 per cent) had gallstones[15,16]. Harrison says 10-35%of patients with ileitis or ileal resection have gall stones and that it is more associated with CD.In a study by Bargiggia S, Maconi G, et al ,of over three hundred and eleven patients with CD and 200 patients with UC, hepatobiliary abnormalities were found at Ultrasound in 54.2% and 55.9% of CD and UC patients, respectively. Liver enlargement and mild-to-moderate to severe liver steatosis were found in 25.7% and 39.5% of CD patients and in 25.5% and 35.5% of UC patients, respectively. The prevalence of gallstones among CD patients was 11%, higher than that among UC patients (7.5%). In a study by Orchard TR, *et al,* 976 patients with ulcerative colitis and 483 patients with Crohn's disease were reviewed. Type 1 arthralgia occurred in 3.6% of patients with UC and in 6.0% of those with CD.Type 2 occurred in 2.5% of patients with UC and 4.0% of those with CD .Brynskov J, Binder V. *et al* reported mild arthritis/arthralgias as the most frequent extraintestinal manifestation in inflammatory bowel disease (IBD) and to occur in 10-35% of patients. D'Incà R, Podswiadek M, *et al* in a cohort of 651

patients reported that arthropathy was axial in 52%, oligoarticular in 16% and polyarticular in 23%. In our study the percentage of pauciarthralgia and polyarthralgia are 25.6% and 7.69 % respectively[17-20]. Our study has one case of erythema nodosum. Prevalence of EN in our study is 2.6%. EN was diagnosed in a female patient with Crohn's disease in our study. In a study by Farhi D, *et al* among 2402 patients with Crohn disease (63.3%) and ulcerative colitis (31.0%), 5.8% had at least 1 skin manifestation. The most frequent dermatologic symptom was erythema nodosum (4.0%). Erythema nodosum was significantly and independently associated with a diagnosis of Crohn's disease and female sex. Yüksel I, *et al,* out of 352 patients studied, 9.3% had at least 1 major cutaneous manifestation. The prevalence of EN in IBD was 7.4%. Erythema nodosum was more common in Crohn's disease than in ulcerative colitis. 21. In a study by Moravvej H *et al,* the prevalence of cutaneous manifestations in ulcerative colitis was 4.07% and more frequent in females (52%) than in males (48%) . Also, Erythema nodosum was diagnosed only in female patients with Crohn's disease in that study. Yüksel I, *et al,* studied 352 patients and 34 patients (9.3%), who presented with at least 1 major cutaneous manifestation. The prevalence of Pyoderma gangrenosum in their study was 2.3%. In a study by Moravvej H, *et al,* the prevalence of cutaneous manifestations was 5.9%. These manifestations were higher in Crohn's disease (7.29%) than in ulcerative colitis (4.07%), more frequent in females (52%) than in males (48%) and pyoderma gangrenosum was seen more often in ulcerative colitis. In our study the frequency of PG is 2.56%and is associated with UC. The percentage of UC patients with PG is 2.7%[22,23]. Aphthous ulcer is present in 5.12% of patients in our study. Sleisenger says aphthous ulcers of the mouth are common among patients with Crohn's disease and ulcerative colitis but are also frequently seen among otherwise healthy persons. At least 10% of patients with UC develop oral aphthous ulcers. These lesions usually occur with flares of colitis and resolve on control of the bowel disease. It is present in 15.38% of patients examined in our study. Out of the 2 cases of CD, angular stomatitis is found in one case. Angular stomatitis is seen in nearly 8% of patients with Crohn's disease according to Sleisenger. In a study by Moravvej H *et al,* the prevalence of cutaneous manifestations in ulcerative colitis was 4.07% and was more frequent in females (52%) than in males (48%). Aphthous stomatitis was observed more frequently in Crohn's disease.

CONCLUSION

Our aim was to study the clinical presentation of IBD in our hospital and the extraintestinal manifestations of the disease. All cases of bleeding PR who satisfied the clinical, colonoscopic and histologic criteria of IBD were included along with proven cases of IBD. Thirty nine patients with inflammatory bowel disease were included in the study. Colonoscopic examination of these patients were done after taking proper consent. Extent of the disease was determined by colonoscopy. Biopsy specimens were taken and sent for histopathological examination. Severity of disease was assessed by Truelove and Witts criteria. Selected patients underwent clinical and laboratory evaluation to detect the extraintestinal manifestations. Analysis of data shows that Ulcerative colitis is more prevalent than Crohn's disease in our study and that IBD manifestations are seen predominantly in females. The age group with maximum prevalence of disease in our study is 31-40 years. Total colitis is the most common colonoscopic finding seen. Of the 39 patients, 25 patients have at least one extraintestinal feature, which accounts to 64% in our study. Pauciarticular arthralgias and Fatty liver are the most frequently found extraintestinal manifestations. Our study had only 39 patients and a larger patient population could throw more light on the extraintestinal manifestations.

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