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Original research article

Clinical Profile of Patients Treated for Inflammatory Bowel Disease in A Tertiary Care Hospital in South India- A cross-sectional study

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Abstract

Background: There are very few studies from South India about the epidemiology and clinical features of inflammatory bowel disease (IBD) exclusive to the region. This hospital based study was aimed to determine the clinical and epidemiological profile of IBD patients who had undergone in an apex tertiary gastroenterology centre in Madurai, South India. **Material and Methods**: 63 consecutive IBD patients were included in this cross sectional prospective observational study over a period of 18 months. Participants demographic and clinical profiles, disease activity, severity, extra intestinal manifestation, medical and surgical interventions and response to therapy were evaluated. **Results**: Of the 63 Inflammatory bowel disease cases, 24 had Crohn's disease(CD) (38%) and 39 had Ulcerative colitis(UC) (62%). Most common age group of UC was in fourth decade while CD had bimodal incidence. Systemic symptoms in both groups were by and large the same with few exceptions. Most of the patients with IBD had low normal Body mass index(BMI) with evidence of nutritional deficiency in form of low haemoglobin and serum albumin. Extra-intestinal manifestations, though uncommon were seen in both groups, Most UC had left sided colitis(E1&E2) while ilecolonic disease was most common in CD (L3) patients. Most of patients achieved remission with initial treatment, [UC (82%) & CD (67%)]. However, a significant minority (8% of UC & 20% of CD) patients required surgical intervention. The use of biologicals and novel interventions still remains in the nascent stage. **Conclusion**: There is rise in prevalence of inflammatory bowel disease in south India. The clinical profile of IBD here concurs more

or less with similar studies published from other parts of the country. Though most of the patients responded well to the initial treatment, there is definite lacunae in the acceptance of novel medical and surgical interventions.
Keywords: Inflammatory bowel disease; Ulcerative colitis; Crohn's disease

Introduction

The term inflammatory bowel diseases(IBD) encompass a spectrum of diseases, of which ulcerative colitis(UC) and Crohn's Disease(CD) are the most familiar entities. Although the exact etiology is unknown, its triggering and perpetuation have been ascribed to various genetic, environmental and immunological factors.Historically IBD was seen as the bane of Western countries , but rrecent reports suggest that numbers have been stealthily climbing up in Asia .A recent study, "The Asia-Pacific Crohn's and Colitis Epidemiologic Study (ACCESS)" , dealt with prevalence of IBD in eight Asian regions and Australia.It clearly suggested that amongst Asian nations, India has the highest disease burden[1].The IBD Task Force came into vogue in 2003 to combat the disease by the Indian society of gastroenterology(ISG), have done various clinicoepidemiological studies by questionnaire methods in this regard.Of 1159 questionnaires analyzed, UC: CD was 750:409 and zone wise break up was North 220 (148:72), East 159 (90:69), Central 255 (227:28), South 466 (235:231), and West 59 (50:9). Hence, there exists a north south divide in the demographic profile of IBD [2]. Interestingly, apart from various studies published from Vellore, there has not been much population based studies regarding IBD prevalence.[3]

Meenakshi mission hospital and Research Centre (MMHRC) is an 800 bedded tertiary care hospital and apex referral centre situated in Madurai, a major city in South India and caters to ten neighbouring districts of Tamilnadu. The gastroenterology department here is a center of excellence and has dedicated IBD ooutpatient department which provides comprehensive care in IBD, including endoscopic, surgical and novel medical therapies. This study was hence conducted to delineate the clinical and demographic profile of IBD patients in Southern Tamilnadu.

Materials and Methods:

This was, a hospital based prospective cross-ssectional observational analysis conducted in the departments of internal medicine and gastroenterology in MMHRC. All consecutive 63 patients from age 18 and above were enrolled in the study over a period of 18 months from September 2016 to April 2018.Excluded from the study, were paediatric IBD cases, patients with IBD-U(IBD Unclassified),patients with a diagnostic dilemma of Crohn's disease vs Intestinal Tuberculosis, and moribund cases with critical illness, All participants in the study were included after proper informed written consent and permission was obtained beforehand from the Institutional Ethics Committee .The diagnosis of CD was based on a amalgamation of clinical, endoscopic, histological, and/or radiological features and with sufficient exclusion of tuberculosis and infective etiologies. All information regarding demographics, clinical, endoscopic and radiological manifestations, disease activity, IBD family history, extra-intestinal manifestations, extent of the disease, treatmentt particulars and the need for surgery were taken into account.

Data Analysis

Measured parameters were elucidated as mean±standard deviation. Significance of differences between studied groups was measured by chi-square tests. Association analysis was performed by Pearson or Spearman correlation analysis. All statistical analysis was obtained using SPSS version 17 (SPSS Inc., Chicago IL). A p value<0.05 was taken as statistically significant.

Results

Out of 63 patients of inflammatory bowel disease, 39 patients (62%) had ulcerative colitis(UC) and 24 patients (38%) had Crohn's disease(CD). Most of the patients with UC were in the fourth decade (23.8%), and third decade (15. 9%).In contrast, there was bimodal distribution for CD with 15.9% patients in the third decade followed by second smaller peak in the sixth decade(7.9%).There was a male preponderance in both UC and CD.Among UC patients (n= 39), 22 were male (56%) and 17 female (44%). while in CD group (n= 24), 14 were male (58%) and 10 were female (42%).Around 75% of both UC and CD patients had normal Body mass index(BMI)(18.5-24.9),while the rest were underweight.

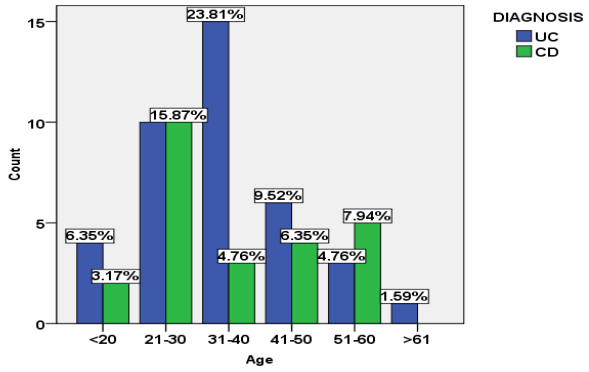

Figure 1: Graph depicting IBD prevalence in various age groups

Gastrointestinal bleeding, abdominal pain and diarrhoea were more common in UC patients (95%), which was slightly higher than in the CD group (92%,92% and 75% respectively) (p value<.001). weight loss and fever were more seen in CD, (15% and 8%) against 12% and 6% in the UC group (p value<.015).

Extra intestinal manifestations were more prevalent in CD than UC. The incidence of perianal and internal fistulas was twice in CD when compared to UC (12%vs 6%).However, dermatological manifestations like erythema nodosum and pyoderma gangrenosum were exclusively seen in UC patients.

Table 1: Table depicting Common presenting complaints in UC&CD patients

Variable	ulcerative colitis(UC) (n=39)	Crohn's Disease(CD) (n=24)	Total	P-Value
Fever				
Yes	6 (15%)	8 (33%)	14	0.096
No	33 (85%)	16 (67%)	49	
Bleeding/Melena				
Yes	37 (95%)	22 (92%)	59	0.612
No	2 (5%)	2 (8%)	4	
Diarrhea				
Yes	37 (95%)	18 (75%)	55	<0.001
	2 (5%)	6 (25%)	8	
Abdominal pain				
Yes	37 (95%)	22 (92%)	59	0.612
No	2 (5%)	2 (8%)	4	
Weight loss				
Yes	12 (32%)	15 (63%)	27	0.013
No	27 (68%)	9 (37%)	36	

The Montreal classification was applied to delineate the extent of UC&CD[4]. Among UC,84.6% had left sided colitis and proctitis (E1&E2), while, only 15.4% had pancolitis (E3). Whereas, combined small bowel and colonic involvement was most common (45.8%) site in CD patients (L3), followed by isolated colonic involvement (41.7%)(L2). Only 12.5% had isolated small bowel disease (L1),and none had isolated upper gastrointestinal involvement(L4).

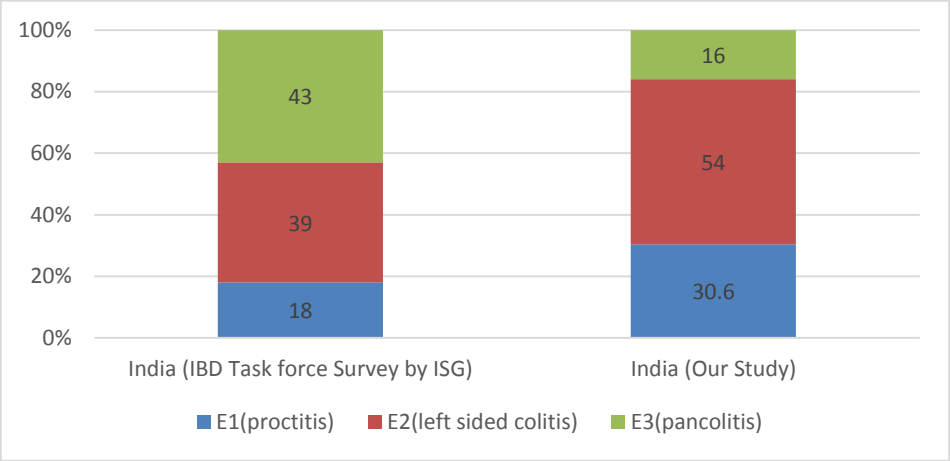

Figure 2: Comparison of disease extent of ulcerative colitis between IBD task force study and our study

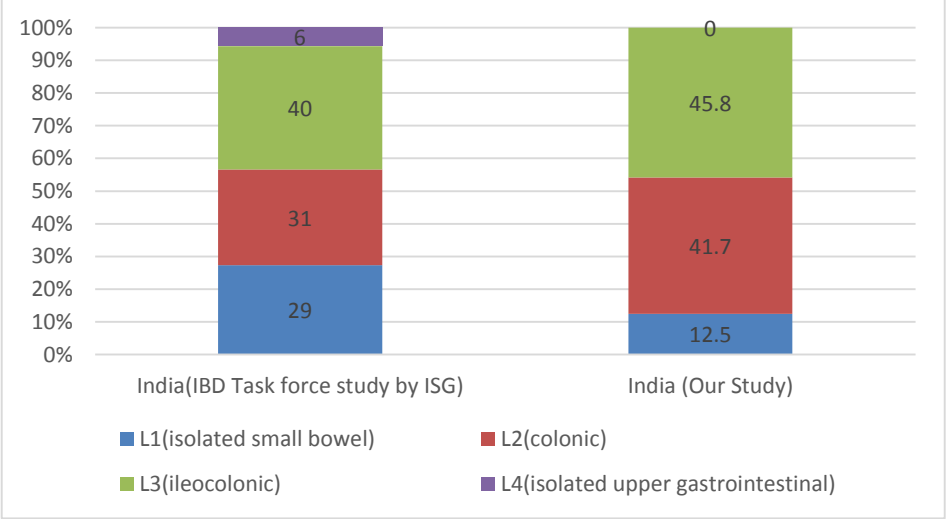

Figure 3: Comparison of disease location of Crohn's disease between IBD task force study and our study

The severity of both UC and CD were assessed using Truelove Witts criteria & Harvey Bradshaw index respectively[5,6].38.5% of UC patients had severe ,33.3%moderate and 28.2% mild disease. In contrast,66.7% of CD patients had moderate disease, while the rest (33%) had mild, and none had severe disease

Most of the UC patients were treated with mesalamine and steroids (46.2%), while a minority required steroids and immunosuppressant (28.2%). Most of CD patients had to be treated with steroids and azathioprine (61.5%), 16% (L2 disease) received mesalamine treatment. Most of patients achieved remission (82% of UC & 67% of CD) with 1st line of treatment, out of which few (10%) were lost to follow up after few months and around 5% in both groups were eventually steroid dependent. Only a small minority required biological therapy (8% of patients with CD and none with UC) while surgical intervention was needed in 21% of the

CD and 8 % of UC patients. All three surgical UC patients had acute severe colitis with toxic megacolon and underwent total proctocolectomy,while of the eight CD patients, four had small bowel resection because of recurrent intestinal obstruction, two underwent fistulectomy, one had colectomy and one had ileocolectomy. One death was documented as result of venous tthromboembolism in the CD group.

Table 2: Table depicting prevalence of common extraintestinal manifestations seen in the CD and UC groups.

Extra intestinal Manifestations	Ulcerative Colitis	Crohn's Disease
Arthritis& Arthralgia	9.6%	9.6%
Fistula & Perianal Involvement	6.3%	12.8%
Oral Ulcers	3.2%	4.8%
Growth Retardation	3.2%	3.2%
Renal Involvement	1.6%	1.6%
Dermatological Manifestation	6.3%	-
Gall Stone	-	1.6%
Thromboembolism	-	1.6%

Table 3: illustrating Comparison of nutritional laboratory indicators in both UC&CD groups before and after treatment

Variables	Before Treatment	After Treatment	% Change	P-Value
	Mean ± SD	Mean ± SD		
Hemoglobin levels	10.09 ± 2.63	11.27 ± 1.98	11.69	**<0.001**
CD Group	10.33 ± 1.89	10.66 ± 2.11	3.19%	0.471
UC Group	9.93 ± 3.07	11.68 ± 1.88	17.62	**<0.001**
Albumin	2.36 ± 0.89	3.29 ± 0.63	39.41%	**0.001**
CD Group	2.40 ± 1.37	3.03 ± 0.78	26.25%	0.328
UC Group	2.34 ± 0.76	3.38 ± 0.58	4.44%	**0.003**

The average haemoglobin in our study population was 10.09 ± 2.63(10.33 ± 1.89 in CD &9.93 ± 3.07in UC group) (p value<.001).The incidence of bleeding manifestation is more in UC and this may explain the lower level of haemoglobin than CD group. The average serum albumin was 2.36 ± 0.89 mg/dl. It was seen that prompt treatment, led to a significant improvement in laboratory parameters like Haemoglobin and serum albumin (p value<.001), the change was more noticeable in the UC group. While we could not document C reactive protein (CRP) variations in all the patients, it was noted that around 1 /3rd of patient had CRP positivity at time of diagnosis.

Discussion

This present study strives to illustrate the clinic epidemiological profile of IBD and the correlation with disease activity of the IBD patients in Southern Tamilnadu who attended our department. It is considered that the magnitude of UC is twice that of CD in Asia in comparison to the Western world [7.] The ACCESS study, reasons that prevalence of UC was twice that of CD in the included Asian countries. In the future India could observe a paradigm change in the UC/CD prevalence,as happening in the west.[1]

Table 4: Comparison of the present study with clinical profile of inflammatory bowel disease in India by IBD task force

Variable	Ulcerative colitis		Crohn's disease	
	Our Study	ISG Survey by IBD task force	Our Study	ISG Survey By IBD task force
Mean Age	35	38.5	33.2	35.9
Male:Female	1.38	1.4	1.27	1.3
Diarrhea	95%	82.2%	75	64.6%
Hematochezia/melena	95%	86.4%	92	42%
Abdominal pain	92%	66.7%	95	74.9%
Fever	6%	25%	8%	42%
EIM(one or more)	30.2%	51%	35.1%	57.5%

In concordance with other Indian studies, ours showed male predominance in both UC and CD group. The IBD task force survey documented that the male: female ratio was 1.4 and 1.3 for UC and CD, respectively[2].Likewise, the scholarly article on CD from three Indian centers demonstrated a male: female ratio of 1.8 [8]. This male preponderance can be due to a either a relatively low incidence in comparison to the Western world or a manifestation of socio referral gender bias, in which women may be underrepresented in getting proper medical attention. The age of presentation also had differences in both the groups. We found that UC patients were predominantly in 4th decade whereas CD had a bimodal age distribution. This mirrors the IBD pattern in the west, [9]. In most of the Indian studies, including the largest one by Makharia et al, the mean age at first detection of UC and CD was 38.5 and 35.9 years, respectively, however CD incidence was not accompanied by a second peak[2].

Most of our patients with UC presented with bleeding and diarrhoea, while , significant number of CD patients had constitutional symptoms like weight loss & fever.This is in concordance with data from Bryce Perler et al, who conducted the study among IBD patients in the Ocean State Crohn's and Colitis Area Registry (OSCCAR), a community-cohort.[10]Interestingly, the incidence of hematochezia was very high(92%) in our CD patients. While in the data from the western, rectal bleeding is less common in CD than UC, Indian scenario is slightly different. Studies by Amarapurkar et al and Pugazhendhi et al describes hematochezia percentages around 30 and 47 respectievely[3],[11]while Makharia et al and Ghoshal et al, have recorded 72% and 68%,the incidence of bleeding in CD.[2,8] The relatively higher number of cases may be due to low sample size and selection bias.The average BMI of IBD was 23.2kg/m2 in our data which was slightly more than 19.8 kg/m2 described by by Ghoshal et al. In the present study, overall extra intestinal manifestations(EIM) were seen in 28%of UC and 33% CD patients., Most studies indicate that the overall prevalence of EIMs in Indian patients is more or less similar to the western scenario. Studies by Kedia et al from AIIMS Delhi revealed the overall prevalence of single and multiple EIMs in UC and CD was 33.2 versus 38.3% and 6.9 versus 4.7%, respectively. The commonest EIM noted in both IBD groups was peripheral arthropathy[7].Unlike western data , where Primary sclerosing cholangitis (PSC)&other hepatobiliary manifestations has been described as varying from 2.4 to 7.4%[13,] the prevalence of PSC in our study was nil in both groups. This is not surprising because The frequency of PSC in UC patients from other Indian studies varied from 1.3 to 3.9%. The probable reason for this low prevalence of PSC may be due to the overall low prevalence rate of coexisting autoimmune liver pathology in Indian subjects, which accounts for only 1.7-5.7% of all cases of chronic liver disease in Indian reports.[14]

Ulcerative Colitis

84% of our patients had left sided colitis and proctosigmoiditis(E1&E2) while only 16% had pan colitis(E3).The findings were similar to study by Sood et al reported that 47% patients had left sided colitis, 27% pancolitis and 25% with proctosigmoiditis in a north Indian IBD cohort[17].We had almost an equal distribution of mild, moderate and severe ulcerative colitis patients.Most of the UC patients were treated with mesalamine and steroids(46.2%),and more severe ones with steroids and immunosuppressant's(28.2%).Interestingly, even though none of the patients were treated with biologicals, surgical intervention in form of colectomy was done in 8%.The overall colectomy rate was 12% in a UC cohort from Oxford, UK .[15] The consensus of opinion is that overall colectomy rates among Indian patients is much low as compared to the developed west, which may indicate slightly benign course . Other plausible explanations for lesser colectomy numbers in India may be attributed to socioeconomic factors with lesser number being receptive for the same[2] However the long term colectomy rates has not been compiled in our study and is expected to be much higher than the above figure.In the IBD task force survey, approximately two thirds of all UC patients were treated with steroids, 30% with azathioprine (AZA), and miniscule fraction of 1% of received biological therapy[2] .

Crohns Disease

Most of the patients with CD had combined ielocolonic(45.8%),followed by isolated colonic disease,while. isolated small bowel disease(L3) was found to be less common.Perianal Crohns(P) disease was seen in three patients(8%).The ACCESS study cited the similarity of location of disease in Australasians, with L1, L2, L3, and L4 disease being seen in 31,24,45 ,and 5 of all patients, respectively .This falls in line with the overall consensus that, L3 disease is the most common disease location across India, Asia, and the West, followed by varying percentages of L1 and L2 locations.[1] In a multicentric study on 182 patients from three centers, perianal manifestations of the disease was observed in around 17% cases[8.]. Most of the patients had robust clinical and endoscopic outcome with steroids and immunosuppressant's(67%),even though surgical intervention was needed in 21% and, biological(infliximab) were given in three cases(8%). The largest study from three centres in India reported that 37% of all patients required surgery.The medications used were 5-aminosalycylic acid (5-ASA) compounds in 78% , steroids in 42%, AZA in 29% , and methotrexate and biologicals in and around 2% of all patients [8].Although sulfa derivatives were ineffective in preventing relapse inquiescent CD, it is well known that large number of physicians and gastroenterologists worldwid use aminosalicylates for treatment of CD both for induction and maintenance ,and this explains the relatively high use of mesalamine in our CD patients [16].The lower use of biologicals among our population exposes the lack of affordability and insurance cover for our patients. The low levels of Haemoglobin and serum albumin noted in our patients mirrored the study by Ghoshal et al , who postulated that the CD patients had a lower hemoglobin levels (median 9.2 g, range 7-11 vs. 10.8 g,; $p<0.05$) and total serum proteins (median 6 g, range 3-7 vs. 7 g, ; $p<0.05$)[12.].

This paper demonstrates the similarities and vagaries of demographic and clinical details of the IBD patients in Southern India compared to other studies from north of the country. The limitations of the current study are a limited sample size, short study period and the study being a hospital based one than a community based one. Also significant family history could not be elicited in most cases and the risk of malignancy and other chronic sequeale could not be assessed. Because of all these, a larger community based study recruiting more patients with a longer duration of follow up is necessary for a better understanding of the disease and to arrive a definite

Conclusion:

To conclude, IBD can no longer be considered as a rare entity in Southern India, with a slow but sustained creep in both the disease burden and morbidity. The clinical profile and long term prognosis of IBD in India is as grim as in the West and calls for a muti disciplinary approach. On the other hand, practical constraints include delayed diagnosis, treatment expenses, paucity of medical insurance coverage, lesser acceptability among patients for surgery, improper follow-up and lack of comprehensive and dedicated care. Also with the rise in disease burden, our geographical region shows burgeoning opportunity for elucidating possible etiopathogenetic factors. Research should aim on the evolving novel and cost effective remedies which would may be helping the patients not only in the Indian subcontinent, but also the whole developing world.

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