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TASK FORCE REPORT

Survey of inflammatory bowel diseases in India

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Abstract
Introduction Inflammatory bowel disease (IBD), both ulcerative colitis (UC) and Crohn's disease (CD), once thought to be uncommon, is now seen commonly in India. The Indian Society of Gastroenterology (ISG) Task Force on IBD decided to collate data on the clinical spectrum of IBD currently prevailing in India.

Methods An open call to members of ISG was given through publication of a proforma questionnaire in the Indian Journal of Gastroenterology and the web portal of ISG. The proforma contained questions related with demographic features, family history, risk factors, clinical manifestations and characteristics, course of disease, and pattern of treatment of IBD.

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Results Of 1,255 filled questionnaires received, 96 were rejected and 1,159 (92.3 %) were analyzed. This comprised data on 745 (64.3 %) patients with UC, 409 (35.3 %) with CD, and 5 with indeterminate colitis. The median duration of illness was longer in patients with CD (48 months) compared to those with UC (24 months) (p=0.002). More than one half of patients (UC 51.6 %, CD 56.9 %) had one or more extraintestinal symptoms. A definite family history of IBD was present in 2.9 % (UC 2.3 % and CD 4.6 %; p= 0.12). The extent of disease in UC was pancolitis 42.8 %, left-sided colitis 38.8 %, and proctitis alone in 18.3 %. The extent of disease involvement in CD was both small and large intestine in 39.6 %, colon alone in 31.4 % and small intestine alone in 28.9 %. Stricturing and fistulizing disease were noted in 18.8 % and 4.4 % of patients with CD respectively. Chronic continuous and intermittent disease course were present in 35.5 % and 47.2 % of UC patients respectively, and in 23.1 % and 68.8 % of CD patients. Four percent of patients with UC had undergone colectomy, while 15.2 % of patients with CD underwent surgical intervention.
Conclusions The present survey provides a reasonable picture of the demographic features and clinical manifestations of Indian patients with IBD, their risk factors, course of disease, and the treatment given to them.

Keywords Crohn's disease · Extraintestinal manifestations · Treatment · Ulcerative colitis

Introduction

Ulcerative colitis (UC) was first reported from India in the late 1930s, but large case series were reported only from the 1960s onwards [1–10]. Two studies, both from northern India, reported a population prevalence of ulcerative colitis (UC) of approximately 42 per 100,000 persons with a crude incidence rate of 6 per 100,000 population [11, 12]. The first report of Crohn's disease (CD) from India appeared in the literature in 1972, approximately 30 years after the first recorded UC reports, and dealt with the surgical pathology of operated cases [13]. Subsequent Indian publications on CD focused on diagnostic differentiation of CD from tuberculosis, but included several small and two larger case series [14–24]. There are no population-based data on the incidence or prevalence of CD in India.

The Indian Society of Gastroenterology (ISG) established a Task Force on Inflammatory Bowel Disease (IBD) in 2003. Its aim was to obtain a representative picture of the current demographic and clinical profile of patients with IBD in the country and to develop guidelines for management of IBD.

Methods

The core committee of the ISG-IBD Task Force drafted a prospective data collection questionnaire for IBD, which was published in the *Indian Journal of Gastroenterology* (2006;25:110–8) and posted on the ISG website (www.isg.org.in/admin/myuploads/Inflammatory_Bowel_Disease.pdf). An open call was given to all members of the ISG to participate in the data collection. Hard copies of the questionnaire were distributed to those who requested it. Participating physicians were requested to complete the questionnaire for consecutive patients with UC and CD seen by them, diagnosed on the basis of a standard combination of clinical, endoscopic and histological features [25, 26]. The Ethics Committees of the All India Institute of Medical Sciences, Delhi and the Christian Medical College, Vellore approved the study plan.

The data in this manuscript were generated from those who responded to the invitation; all the respondents were qualified gastroenterologists. All completed questionnaires were dispatched to the coordinator (GKM) who screened them for completeness of data. Questionnaires that had inadequate information were rejected. Identifying data of patients were removed from the completed questionnaires after coding in order to maintain confidentiality. The data were entered in a datasheet by a data-entry operator; each entry was double checked by the first author. Data on diet were available in less than a half of questionnaires and were not considered for analysis.

All the study variables were compared between the two categories of IBD, namely, UC and CD. Quantitative characteristics were compared using Student's t test or Wilcoxon rank sum test as appropriate. Categorical information was compared between the two groups using the chi-square test.

Results

Completed questionnaires were received from the north (Chandigarh, Delhi, Ludhiana), central (Bhilai, Indore, Jodhpur, Lucknow), west (Mumbai), east (Guwahati, Kolkata, Cuttack) and south zones (Chennai, Manipal, Vellore) of the country (Table 1). Of the 1,255 completed questionnaires received, 96 were rejected because of grossly incomplete data.

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Table 1 List of cities from which institutions provided data on IBD

Region	City	Total	UC	CD
North Zone	Delhi	220	148	72
	Chandigarh			
	Ludhiana			
East Zone	Guwahati	159	90	69
	Kolkata			
	Cuttack			
Central Zone	Lucknow	255	227	28
	Jodhpur			
	Bhilai			
	Indore			
West Zone	Mumbai	59	50	9
South Zone	Chennai	466	235	231
	Manipal			
	Vellore			
Total		1,159	750	409

Table 2 Clinical features of patients in this survey

Feature	UC	CD	*p*-value
Chronic diarrhea	611/743 (82.2)	263/407 (64.6)	<0.001
Blood in stool	622/720 (86.4)	168/398 (42.2)	<0.001
Mucus in stool	441/584 (75.5)	76/203 (37.4)	<0.001
Abdominal pain	481/721 (66.7)	299/399 (74.9)	0.004
Constipation	94/534 (17.6)	33/180 (18.3)	0.825
Perianal disease	35/532 (6.6)	17/144 (11.8)	0.037
Anorectal pain	176/536 (32.8)	39/182 (21.4)	0.004
Anal fissure	25/566 (4.4)	14/198 (7.1)	0.144
Perianal fistula	21/696 (3)	56/383 (14.6)	<0.001
Weight loss	453/732 (61.9)	269/407 (66.1)	0.16
Fever	183/715 (25.6)	170/396 (42.9)	<0.001
Pallor	376/582 (64.6)	86/203 (42.4)	<0.001
Pedal edema	94/584 (16.1)	10/204 (4.9)	<0.001
Abdominal mass	4/579 (0.7)	9/203 (4.4)	<0.001

Data are as *n* (%) Denominator in each cell indicates number where data were available

UC ulcerative colitis, *CD* Crohn's disease

The 1,159 (92.3 %) questionnaires analyzed included 708 with complete data and 451 with incomplete data but containing vital information. The 1,159 patients with IBD included 745 (64.3 %) with UC, 409 (35.3 %) with CD, and five (0.4 %) with indeterminate colitis; the last group was excluded from final analysis.

Demographic characteristics

The mean (SD) age of patients with UC and CD was 38.5 (13.5) and 35.9 (13.9) years, respectively (p=0.002). The male-to-female ratio was 1.4 in UC and 1.3 in CD (p=0.32).

Duration of illness

Median (range) duration of illness in patients with CD (48 [1–516] months) was higher than in those with UC (24 [1–612] months) (p=0.002). There was no difference in the median (range) time interval from onset of symptoms to the first diagnosis in patients with UC (96 [1–456] months) and CD (12 [1–288] months) (p=0.08).

Clinical manifestations

Chronic diarrhea, blood in stool, anorectal pain and pedal edema were significantly more common in patients with UC in comparison to CD (Table 2). On the other hand, abdominal pain, perianal fistula, fever and presence of abdominal mass were significantly more common in CD compared to UC. Data on extraintestinal manifestations were available in 738 questionnaires. More than a half of the patients surveyed had one or more complaints referable outside the gastrointestinal (GI) tract; in about 40 % of those with extraintestinal symptoms, more than one manifestation was noted (Table 3). Joints pain with or without arthritis was present in 33.2 % and 26.3 % of patients with UC and CD, respectively (Table 3).

Personal history and relevant past history and prior surgery

There was no difference in the number of patients with UC and CD who reported smoking (21.3 % vs. 24.2 %; p=0.28), consumption of alcohol (13.3 % vs. 11.7 %; p=0.44) or use of oral contraceptive pills (9.7 % vs. 7.8 %; p=0.63). A greater percentage of patients with CD had undergone appendicectomy compared to those with UC (8.2 % vs. 2.1 %; p<0.001). More patients with CD had undergone intraabdominal surgery (other than appendicectomy) in comparison to those with UC (23.3 % vs. 11.2 %; p<0.001). A history of hemorrhoids or surgery for the same was equally common in CD and UC (8.9 % vs. 8.8 %; p=0.95).

Family history

A definite history of IBD in one or more family members was present in 2.9 % overall (UC 2.3 % and CD 4.6 %; p=0.12). An additional 1 % reported that one or more members of their family were suspected to have IBD (UC 1.35 %, CD 0 %).

Investigations for evaluation of extent of disease

Nearly all (98.6 %) patients with UC had undergone colonoscopy for evaluation of extent of their disease (Table 4). The terminal ileum was intubated in 34.5 % of colonoscopies

Table 3 Extraintestinal symptoms in patients in this survey

		UC	CD	*p*-value
No. of manifestations	None	268/543 (49.4)	84/195 (43.1)	0.470
	1	161/543 (29.6)	68/195 (34.9)	
	2	96/543 (17.7)	36/195 (18.5)	
	3	18/543 (3.2)	7/195 (3.6)	
Type of manifestation	Arthralgia	195/586 (33.27)	54/205 (26.3)	0.066
	Backache	225/715 (31.46)	145/398 (36.4)	0.09
	Skin lesions	14/588 (2.38)	7/206 (3.4)	0.434

Data are as *n* (%). Denominator in each cell indicates number where data were available

UC ulcerative colitis, *CD* Crohn's disease

and colonic biopsies were done in 84 %. A minority (1.4 %) of patients underwent barium enema for evaluation of disease extent. For evaluation of the extent of CD, 90.3 % underwent colonoscopy and in 41.9 % the terminal ileum was intubated. A variety of procedures were used for small bowel evaluation, including barium meal follow-through or small bowel enema, CT scan, enteroscopy and capsule endoscopy. Nearly two-fifths of patients underwent upper gastrointestinal endoscopy. In 16 of 202 patients, the diagnosis of CD was confirmed on surgically resected specimens.

Extent of disease

Among 714 patients with UC (where report on extent of the disease was available), the disease extent reported most commonly was pancolitis (n=306, 42.8 %), followed by left-sided colitis (277, 38.8 %), while proctitis alone was least common (131, 18.3 %). Among 394 patients with CD (where report on extent of the disease was available), the most common pattern of disease was involvement of both small and large intestine (156, 39.6 %) followed by isolated colonic involvement (124, 31.4 %) and isolated small intestinal involvement (114, 28.9 %). Involvement of the upper GI tract was reported in 23 (5.8 %). Seventy-five of 398 (18.8 %) CD patients had stricturing disease, while 9/203 (4.4 %) had fistulizing disease; 6.9 % patients were reported to have perianal disease as a disease modifier.

Course of disease

The course of both diseases was characterized by intermittent flares in many patients. Disease with intermittent flares was more common in CD than in UC, while a pattern of chronic continuous disease was more common in UC than in CD (Table 5). More than 80 % of patients with both diseases remained on indefinite medical treatment. Discontinuation of medical treatment was more common in UC (17.5 %) compared to CD (6.9 %). Only 4 % of patients with UC had undergone colectomy while 15.2 % of patients with CD underwent surgical intervention.

Treatment received

Data on prior treatment with antitubercular drugs were available in 1,066 patients. A higher number of patients with CD (139/378; 36.7 %) had received such treatment, compared with 54 of 688 (7.8 %) with UC (p<0.001). Different forms of disease-specific treatment had been received by the patients and these are summarized in Tables 6 and 7. Approximately two-thirds of patients with UC and CD had received corticosteroids in the past; 29.1 % and 26.9 % of them were receiving corticosteroids at the time of

Table 4 Investigations for evaluation of extent of disease

Investigation	UC	CD	*p*-value
Colonoscopy	583/591 (98.6)	187/207 (90.3)	<0.001
Retrograde ileoscopy	183/531 (34.5)	70/167 (41.9)	0.081
Gastroduodenoscopy	85/581 (14.6)	79/203 (38.9)	<0.001
Enteroscopy	4/581 (0.7)	23/201 (11.4)	<0.001
Capsule endoscopy	1/571 (0.2)	5/200 (2.5)	0.005
Barium follow-through	18/585 (3.1)	93/198 (47)	<0.001
Barium enema	14/588 (2.4)	23/204 (11.3)	<0.001
Abdominal CT	31/547 (5.7)	52/186 (27.9)	<0.001
Biopsy	497/591 (84.1)	158/207 (76.3)	0.012
Surgical resection	7/586 (1.2)	16/202 (7.9)	<0.001

Data are as *n* (%). Denominator in each cell indicates number where data were available. The data collection form did not differentiate between surgery for cure and surgery for diagnosis

UC ulcerative colitis, *CD* Crohn's disease

Table 5 Course and outcome of disease in patients in this survey

		UC	CD	*p*-value
Course	Single episode	95/552 (17.2)	14/173 (8.1)	<0.001
	Chronic continuous	196/552 (35.5)	40/173 (23.1)	
	Intermittent flares	261/552 (47.2)	119/173 (68.8)	
Outcome	Discontinued medical therapy	89/508 (17.5)	12/174 (6.9)	<0.001
	Indefinite medical therapy	410/508 (80.7)	149/174 (85.6)	
	Colectomy/other surgery	21/530 (4)	21/138 (15.2)	
Complications		49/460 (10.6)	28/128 (21.8)	0.001

Data are as *n* (%). Denominator in each cell indicates number where data were available

UC ulcerative colitis, *CD* Crohn's disease

inclusion in the study. More patients with CD (62.9 %) than with UC (28 %) had received azathioprine; other immunosuppressants such as methotrexate were used in only a minority of patients. Infliximab also was used in only a minority of patients with UC and CD. Probiotics had been used in 25.7 % and 10.4 % of patients with UC and CD either in the past or currently.

Discussion

The present study is the first nationwide survey of patients with IBD in India. The proportion of patients with UC reported here was higher than that of CD; in fact, the proportion of CD in the community may actually be lower than the 36 % in this survey, which may reflect referral bias to specialist gastroenterologists interested in IBD.

Traditionally IBD is thought to be uncommon in India; UC is seen more often, but CD is being reported now from every part of India. Two earlier prevalence studies in the community [11, 12] done 15 years apart suggested that the prevalence of UC has been static; there is a subjective impression among Indian gastroenterologists that there has been an increase in occurrence of CD in the recent past in India [27]. Fifty percent of patients from the southern zone had CD, compared to only 26 % in all the other zones combined. This may reflect the possibility that CD is more common in southern India than in the northern parts of India. However, these data should be interpreted with caution as the data came from specialist gastroenterologists interested in IBD management and could reflect a degree of referral bias.

IBD in the West is characteristically associated with a bimodal age distribution pattern, with a peak at age 20–39 years and a second smaller peak at 60–79 years; such

Table 6 Treatment received by patients in this survey

		UC	CD	*p*-value
Mesalamine	Never	15/510 (2.9)	6/161 (3.7)	<0.001
	Previous	37/510 (7.2)	61/161 (37.9)	
	Current	458/510 (89.7)	94/161 (58.4)	
Other 5-aminosalicylates	Never	145/255 (56.8)	38/59 (64.41)	0.268
	Previous	41/255 (16.1)	4/59 (6.8)	
	Current	69/255 (27.1)	17/59 (28.8)	
Sulfasalazine	Never	186/254 (73.2)	53/80 (66.2)	0.415
	Previous	35/254 (13.8)	15/80 (18.7)	
	Current	33/254 (13)	12/80 (15)	
Corticosteroids	Never	34/444 (7.6)	5/130 (3.8)	0.058
	Previous	281/444 (63.3)	90/130 (69.2)	
	Current	129/444 (29.1)	35/130 (26.9)	
Azathioprine	Never	208/325 (64)	27/116 (23.3)	<0.001
	Previous	20/325 (6.1)	16/116 (13.8)	
	Current	97/325 (29.8)	73/116 (62.9)	
Other immunosuppressant	Never	252/257 (98)	74/77 (96.1)	0.189
	Previous	2/257 (0.8)	0/77 (0)	
	Current	3/257 (1.7)	3/77 (3.9)	
Infliximab	Never	282/283 (99.6)	87/91 (95.6)	0.010
	Previous	1/283 (0.3)	2/91 (2.2)	
	Current	0/283 (0)	2/91 (2.2)	

Data as *n* (%). Denominator in each cell indicates number where data were available

UC ulcerative colitis, *CD* Crohn's disease

Table 7 Other treatment received by patients in this survey

		UC	CD	*p*-value
Probiotics	Never	220/296 (74.3)	83/92 (90.2)	0.001
	Previous	58/296 (19.6)	2/92 (2.8)	
	Current	18/296 (6.1)	7/92 (7.6)	
TPN	Never	259/292 (88.7)	86/92 (93.5)	0.390
	Previous	32/292 (11)	6/92 (6.5)	
	Current	1/292 (0.3)	0/92 (0)	
Elemental diet	Never	245/251 (97.6)	82/85 (96.5)	0.854
	Previous	4/251 (1.6)	2/85 (2.3)	
	Current	2/251 (0.8)	1/85 (1.2)	
Blood transfusion	Never	163/248 (65.7)	23/41 (56.1)	0.344
	Previous	75/248 (30.2)	17/41 (41.5)	
	Current	10/248 (4)	1/41 (2.4)	
Antidepressant/anxiolytic	Never	291/297 (98)	90/91 (98.9)	0.313
	Previous	5/297 (1.7)	0/91 (0)	
	Current	1/297 (0.3)	1/91 (1.1)	

Data as *n* (%). Denominator in each cell indicates number where data were available

UC ulcerative colitis, *CD* Crohn's disease, *TPN* total parenteral nutrition

bimodal distribution has not been consistently observed in Asian studies [28–30]. The mean age of patients with UC in this survey was slightly higher than that of those with CD. In European and North American studies, UC is reported to be equally frequent in men and women at all ages, while CD has consistently revealed a greater incidence in women [28]. A male predominance has been reported in UC in a few Asian studies [29–31]. In the present study, a slight male preponderance was noted in both UC and CD; this may possibly reflect a bias of males reporting more often for medical care.

Approximately one in five patients in this study, almost equally among UC and CD, were smokers. As compared with people who never or rarely smoked, current smokers are thought to have a reduced risk whereas ex-smokers have a greater risk for development of UC; on the other hand, smoking aggravates the activity of CD [32]. The association of smoking with CD is ascribed to a specific genetic background [33]. A recent Indian case–control study did not find an association between smoking and CD [24]. The present study was not designed as a case–control study with normal controls and so the effect of smoking in our patients cannot be assessed.

Appendicectomy has been negatively associated with UC and this protective effect is explained on an immunological basis [34]. A recent meta-analysis found, however, that while most studies found a protective association of appendicectomy, some studies showed a positive association between the two [35]. In the present study, 4.3 % of patients with IBD had undergone appendicectomy, the surgery being more common among CD patients than those with UC; we have no information about whether the surgery was performed before or after the onset of IBD. The higher rate of appendicectomy in patients with CD may be due to a mistaken diagnosis of appendicitis.

One or more extraintestinal symptom(s) were reported in more than half the patients in this survey; the most common were arthralgia (with or without evidence of arthritis) and backache. We have no data on their correlation with disease activity; there also was no documentation of radiological evidence of sacroiliitis. While previous reports from India have shown variable results [36, 37], the present study suggests that extra intestinal symptoms are common in Indian patients with IBD, and are found almost equally in UC and CD.

A familial aggregation of IBD has been reported in 8 % to 14 % of patients from the West [38, 39]. Studies from Japan and Korea have shown that the risk of having UC in first-degree relatives of patients with UC is approximately 25-fold higher than that in the general population, which is comparable to that reported from Western countries [40, 41]. In an earlier report from Delhi, 5 % of patients with UC reported to have another family member with UC [42]. In the present study, a history (definite as well as possible) of IBD in one or more family members was present in approximately 4 % of patients with IBD (CD>UC). These data suggest that the familial occurrence in Indian patients is less than that reported in the West.

The extent of UC in this study was proctitis alone in 18 %, left-sided colitis in 38 % and pancolitis in 42 %, which is similar to that reported in another study from India [43] and from Singapore [44] and Korea [45]. In contrast, a multicenter retrospective study from China including 10,218 patients with UC reported that 70 % had proctosigmoiditis, 23 % left-sided colitis, and only 7 % had pancolitis [46]. The reasons for the difference in disease distribution between these various reports is not clear. The report from China clearly has a low prevalence of pancolitis compared to most other reports. These could reflect differences in population genetics or immune responses rather than

differences in diagnostic criteria, which are universally accepted and robust for UC.

Involvement of both small and large intestine (ileocolonic) was seen in 39.6 % of patients with CD, while 314 % and 28.9 % had isolated colonic and small intestinal involvement, respectively; upper GI involvement was reported in 5.8 %. In a report of 182 patients with CD from India, the location of disease was colon 41 %, terminal ileum 32 %, and ileo-colon 23 %; the upper GI tract was involved in 4 % [23]. In another report of 200 patients with CD, involvement was ileocolonic in 40 %, colonic in 26 %, ileal in 26 %, and upper GI in 8 % [24]. In the present study 19 % had stricturing disease; fistulizing disease was rather uncommon (4.4 %). In contrast, two studies from India reported higher prevalence of both stricturing (24 % and 23.5 %) and fistulizing (25 % and 17.5 %) disease [23, 24]. Both those studies were from tertiary care centers and may reflect a referral bias.

A third of patients with UC in our report had a chronic active course and one-half had remissions and relapses, while 17 % had had only a single episode of illness and remained well thereafter. In a study from the UK [47], 50 % of Asian origin patients experienced continued remission after an initial episode of UC, whereas 77 % of Caucasians suffered from relapsing disease. In a study from Turkey, an unusually high proportion (74 %) of patients had only a single attack of UC with subsequent complete remission [48]. Contrary to that, the cumulative probability of relapse after UC diagnosis for Korean patients was 30 % after 1 year, 59 % after 3 years, 72 % after 5 years, and 88 % after 10 years [49]. A Japanese hospital-based cohort of 844 patients with a median follow up of 7 years reported a relapsing-remitting pattern in 61 %, chronic-continuous course in 23 % and a single attack in only 16 % [50], very similar to the statistics in this report.

In addition to the nature of the disease, the level of education, compliance, and affordability of treatment are factors that affect the course of the disease [51]. In a recent study from Mumbai, up to 80 % of patients with IBD were not completely compliant with treatment; the non-compliant ones had three times higher risk of development of a relapse [51]. In the present survey, 17.5 % of patients with UC had discontinued their medications; the factors that led to discontinuation of medication and the outcome of this were not evaluated. Current use of mesalamine was more common in UC than in CD, while the reverse was true for the use of azathioprine.

The importance of this present survey is the prospective collection of data from every region in India that provides a reasonable picture of the demographic features and clinical manifestations of patients with IBD, their risk factors and course, and pattern of treatment given to them. The shortcomings of the study include incomplete data completion in some patients, and the fact that most patients were surveyed in urban clinics and tertiary-care centers; the lack of follow up is another shortcoming of the present study. Future studies, including population-based registries for IBD, may provide useful epidemiological and clinical data.

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