

Original Article

The profile of inflammatory bowel disease in natives of Western Himalayas

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ABSTRACT

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Background: To study the profile of Inflammatory Bowel Disease (IBD) in natives of Himachal Pradesh.

Material and Methods: A total of 101 patients of IBD were included. The clinical profiles, disease activity, severity and response to therapy were evaluated.

Results: Of the 101 patients, 82% were diagnosed with Ulcerative Colitis (UC), 12% with Crohn's Disease (CD) and 6% with Inflammatory Bowel Disease Unclassified (IBDU). The mean duration between onset of symptoms and diagnosis was 12.3 months for UC, 15 months for CD and 3 months for IBDU. Chronic diarrhea (98%) and blood in stools (94%) were most common symptom in UC and abdominal pain (83%) was most common in CD. E2(45.78%) disease was most common in UC, L2(50%) was most common in CD and Left sided colonic involvement was most common in IBDU (83%). Extra intestinal manifestations were noted in IBDU (67%), CD (50%) and UC (40%). Most of the patients had moderate disease activity and responded well to pharmacotherapy.

Conclusion: IBD is not uncommon in the rural hilly areas of India. There is predominance of ulcerative colitis rather than Crohn's disease.

KEYWORDS: Inflammatory bowel disease; Himalayas; colitis; diarrhea.

Introduction

The idiopathic Inflammatory Bowel Diseases (IBD) comprise three types of chronic intestinal disorders: Crohn's Disease (CD) Ulcerative Colitis (UC) and Inflammatory Bowel Disease Undifferentiated (IBDU)/ Indeterminate Colitis.¹ The incidence and prevalence rates of IBD in Asian countries are still low compared

with those of Western countries, but have been increasing rapidly during the past decades.² The incidence of IBD has dramatically increased during the 20th century, and in the developed nations is as high as 20 and 24 cases per 100,000 person-years for CD and UC, respectively.³ There are substantial variances in the incidence and

prevalence rates of IBD among different races or ethnic groups in Asia, with the highest rates in India, Japan, and some Arab world. In England studies have indicated that the incidence of UC among migrant South Asians is higher than that of Europeans, suggesting that South Asians are genetically predisposed to UC.² As developing countries, such as India and China, became industrialized, the incidence of IBD has risen in parallel.¹ In developing countries in which IBD is emerging; UC is typically more common than CD. In India, for example, there are reports of UC/CD ratio of 8:1.⁴

Himachal Pradesh is located between 30°22' and 30°12' north latitude and between 75°47' and 79°4' east longitude. It is a mountainous state in northern India, situated in western part of outer Himalaya in with altitudes ranging from 350 to 7000 meters above MSL. It is one of the least urbanized states in India, with predominantly agricultural economy. The life style and dietary habits of population in the area differs from those living in plains. The studies on IBD from this region not available thus this study was planned to know the profile of IBD from natives of this region.

Methods

The present study was conducted in Departments of Medicine and Department of Gastroenterology, Indira Gandhi Medical College, Shimla from 1st June 2014 to 31st May 2015. All consecutive patients of IBD above 18 years and who were natives of Himachal Pradesh were enrolled for the study. There were total of 101 patients enrolled, of these 43 were newly diagnosed (33 patients of UC, 8 patients of CD and 2 patients IBDU) and 58 old diagnosed patients on follow up (50 of UC and 4 each of CD and IBDU).

IBD diagnosis was based on the typical clinical course of the disease and endoscopic examination with histological confirmation of IBD. A diagnosis of IBDU was considered when the morphology included overlapping features of UC and CD regarded as inconsistent with either diagnosis. All information regarding disease was obtained in a prepared performa. The past records of patients were also used for retrieving information. The extent and severity of UC was classified

as per Montreal. The patients of CD were classified on basis Montreal classification and severity assessed by Harvey Bradshaw index.

Results

During study period 101 patients of IBD presented to our hospital. UC was noted in 83 (82%) patients followed by CD in 12(12%) patients and IBDU was noted in 6 (6%) patients. Fifty eight (57.42%) were old cases seen on follow up and 43 (42.58%) were newly diagnosed.

The age ranged from 18-76 years with a mean age of 43.56±14.13 years (UC- 43.87±13.67yrs, CD- 43.5±15.93 yrs and IBDU-36.5±15.06 yrs) Forty three (42%) were aged < 50 yrs. Half of patients of CD and IBDU were aged < 50yrs. The overall females to male ratio in study group were 1.02:1. The sex distribution was almost equal in UC however CD had more (66%) males and IBDU group had more (66%) female patients. Majority of patients were from rural background in all three groups. Thirty two (32%) belonged to lower middle class, 28(28%) upper lower and upper middle class and 12% belonged to upper class (Modified Kuppuswamy Scale).

As per BMI classification for Asians in UC group 39 (47%) had normal BMI, 32(38%) were underweight, 10 (12%) were overweight. In CD group 9 (75%) had normal BMI and in IBDU 2(33%) patients were underweight, normal and overweight each.

The vegetarianism (UC-58%, CD-75%, IBDU-66.67%), smoking (UC-23%, CD-42%), use of NSAIDs in preceding 3 months (UC-23%, CD-17%, IBDU-17%), consumption of alcohol (17% in all groups), use of tobacco (UC-13%, CD-8%, IBDU-17%) were main factors associated.

In UC patients, 66 (79%) patients were diagnosed within one year of the onset of symptoms. In CD group, 9 (75%) patients were diagnosed within 9 months of onset of symptoms. In IBDU group, 5 (83%) patients were diagnosed with in one year of onset of symptoms.

Table 1 delineates different symptoms and their occurrence in types of IBD at presenting complaints. Intestinal obstruction was noted in 7 (7%) patients, of total 3 (4%) patients of UC (1 patient had dynamic

Table 1: Symptoms at onset of inflammatory bowel disease

Symptoms	Total		Ulcerative Colitis		Crohn's Disease		IBDU	
	n=101	%	n=83	%	n=12	%	n=6	%
Diarrhea	94	93	81	97	8	67	5	83
Blood in stool	92	91	78	94	9	75	5	83
Weight loss	72	71	61	73	8	75	3	50
Mucus in stool	88	87	75	90	8	67	5	83
Abdominal pain	62	61	48	58	10	83	4	67
Tenesmus	53	52	50	60	2	17	1	17
Urgency	50	49	46	55	2	17	2	33
Fever	17	17	14	17	1	8	2	33
Intestinal Obstruction	7	7	3	4	4	33	0	0

obstruction and was subjected to extended hemicolectomy for subacute intestinal obstruction and 2 patients had adynamic (hypokalemia) obstruction), whereas 4 (33%) patients of CD had dynamic intestinal obstruction and 1 of them was subjected to surgery for stricture in colon.

Ulcerative Colitis

In UC patients, the extent of disease was noted as per Montreal classification. E1 disease was seen in 23 (27.71%), E2 in 38 (45.78%) and E3 in 22 (26.5%). The severity of UC at onset was also graded as per Montreal classification. S1 disease was seen in 8(9.63%), S2 in 42 (50.60) and S3 in 33 (39.76%). Of the 40 old UC patients with follow up of more than one year at least, 21 (42%) had intermittent flares, 17 (34%) had single episode and 12 (24%) had chronic continuous disease. In UC, 70(84%) achieved remission with ASA, 11 (13%) needed ASA and steroids and 2 (2%) patients needed ASA, steroids and azathioprine.

Crohn's Disease

The disease distribution of CD was classified as per Montreal classification is given in **Table 2**. As per Harvey Bradshaw Index, 67% had moderate disease, 17% had mild disease and remaining 17% patients were in remission. Of the 4 old patients of CD with follow up of more than one year at least, 2 (50%) had single episode and 1 (25%) each had intermittent flares and chronic continuous disease. In

Table 2: Disease classification of Crohn's Disease (Montreal Classification)

Variable	n=12 (%)
A1 (<16years)	not included in study
A2 (Age 17-40years)	7 (58)
A3 (Age >40years)	5 (42)
L1 (ileum)	3 (25)
L2 (colon)	6 (50)
L3 (ileocolic)	3 (25)
L4 (isolated upper disease modifier)	0 (0)
B1 (non stricturing non penetrating)	8 (67)
B2 (stricturing)	4 (33)
B3 (penetrating)	0 (0)
Perianal disease modifier (p)	0 (0)

CD, 11 (92%) improved with ASA and 1(8%) needed ASA, steroids and azathioprine.

Inflammatory Bowel Disease Undifferentiated

Left sided colon involvement was seen in 5 (83%) patients and 1 (17%) patient had right sided involvement in IBDU. Three (75%) had single episode and 1 (25%) had intermittent flares remaining 2 patients were newly diagnosed. None of the patients had fulminating disease. In all, 6 (100%) patients of IBDU remission was achieved with ASA alone.

Table 3 shows various extra-intestinal manifestations (EIMs) in the study group. At least one EIM was present in 43 (42%) of the patients, 2 EIMs were present in 20 (20%) and ≥ 3 EIMs were present in 8 (8%). In UC group, one patient had colorectal carcinoma and suffered from UC for 25 years and one patient had cholangiocarcinoma.

Discussion

The ratio of UC:CD was 1.82:1 in a study by Makharia et al.⁵ This ratio in this study was 6.9:1 in present study. The ratio though is higher than the survey in India but in sub analysis of survey this ratio of UC:CD was 2.05:1 for north zone and 8.1:1 in central zone of India. There were only 0.4% cases of IBDU in the survey, but in this study the proportion was higher with 5.9% which is in consistency with Chinese study by Zhou et al.^{1,5} In the present study 80% patients belonged to rural and 20% belonged to urban areas and could be since in Himachal Pradesh about 90% population resides in rural areas. In this study, maximum number of patients in UC were (44.19%) in the age group 31-45 years as seen in study. The mean age of the patients was 43.52 \pm 13.67, which was higher than 38.5 \pm 13.5 seen in study by Makharia et al.⁵ The mean age of the patients of CD was 43.5 \pm 15.93 years with mean age of females was 44 years and 43.25 years for males. In another study by Das et al from

the mean age of onset was 33.2 \pm 13.6 years.⁶ The median age of patients of IBDU 29.5 years as compared to 40.22 years in study by Zhou N et al.¹ The average BMI of IBD was 19.69 kg/m² in our study which was like 19.8 kg/m² seen in a study by Ghoshal et al.⁷ Most patients in this study were vegetarian however 93% patients of UC were non-vegetarian in a study conducted in South of India by Gunishetty et al.⁸ In UC patients, 23% were smoker compared to 14 % in a study by Russel et al. In CD group 42% were smokers and in the study by Russel et al, 27% smoked.⁹ This shows consistency with association of smoking with decreased risk of UC and increased risk of CD. In another Indian study by Gunishetty et al 5% of UC patients were smokers compared to 12% in controls.⁸

There were 23% patients of UC and 17% of CD with history of NSAIDS use in preceding 3 months, which was higher in UC (19%) but lower in CD (30%) as reported by Bernstein et al.¹⁰ A study by Ozin et al reported that 33% patients of CD were current NSAIDS users.¹¹ In present study 16% patients of UC and 17% of CD had history of consumption of alcohol, comparable to Makharia et al, the history of consumption of alcohol was noted in 13% of patients of UC and in 12% patients of CD.⁵ Gunisetty et al reported alcohol use in 29% patients of UC.⁸ In this study, in 2 % patients of UC and none in CD group had undergone appendectomy. Russel et al reported that 5% patients of UC and 11% in CD group had history of appendectomy.⁹ Makharia et al reported

Table 3: Extra-intestinal manifestations in inflammatory bowel diseases

Extra-intestinal Manifestations	Total		Ulcerative Colitis		Crohn's Disease		IBDU	
	n=101	%	n=83	%	n=12	%	n=6	%
Peripheral Arthralgia	35	35	26	31	6	50	3	50
Central Arthralgia	22	22	19	23	2	17	1	17
Episcleritis	14	14	10	12	2	17	2	33
Erythema nodosum	6	6	4	5	1	8	1	17
Thromboembolism	2	2	2	2	0	0	0	0
Reactive Arthritis	2	2	0	0	1	8	1	17
Iritis	2	2	1	1	1	8	0	0
Malignancy of colon	1	1	1	1	0	0	0	0
Ankylosing Spondylitis	1	1	1	1	0	0	0	0
Cholangiocarcinoma.	1	1	1	1	0	0	0	0

a definite family history of IBD in one or more family members in (3%) patients of IBD.⁵ In present study, none had family history of IBD. This difference could largely be because of unawareness of IBD in rural areas.

Ulcerative Colitis

The findings of present study in UC are in agreement with Makharia et al who observed blood in stool present in 86% patients, diarrhea in 82%, mucus in 75%, abdominal pain in 67%, weight loss in 62% and fever in 22% patients.⁵ The extent of disease in this study were similar to Sood et al reported that 47% patients presented with left sided colitis, 27% had pancolitis and 25% had proctosigmoiditis.¹²

In study by Makharia et al EIMs were present in 50.6% of UC patients, 1 EIM in 29.6%, 2 EIMs in 17.7% and 3 EIMs in 3.2%.⁵ In the study by Bandyopadhyay et al at least one extra-intestinal manifestation was present in 40% patients of UC, Two extra-intestinal manifestation was present in 12% and ≥ 3 were present in 7% patients.¹³ In the study by Singh B et al, EIMs were seen in 33.2% of UC patients.¹⁷ Kochhar R et al reported EIMs in 34.7% patients of UC and musculoskeletal manifestations

were most common followed by ocular manifestations (8%).¹⁸ In the present study 40% of UC patients had at least 1 EIM, 13% had 1 EIM, 16% had 2 EIMs and 11% had ≥ 3 EIMs. Most common EIM was in musculoskel et al symptoms as arthralgia peripheral in 31% and central in 23%. In the study by Bandyopadhyay et al arthritis was present in 21% patients, ankylosing spondylitis in 16%, episcleritis in 14% and mucocutaneous lesions in 12% patients.¹³ Makharia et al observed arthralgia in 33% patients, backache in 31% and skin lesion in 2% patients.⁵

Of the total 58 patients with follow up of at least 1 year 22 (37.9%) had single episode and were in remission, 23 (39.7%) number had intermittent flares and 13 (22.4%) patients had chronic continuous disease. Of 50 old UC patients 42% had intermittent flares, 34% had single episode and 24% had chronic continuous disease. In the study by Makharia et al 47% patients had intermittent flares, 35% had chronic continuous disease and 17.2% had single episode.⁵

Crohn's Disease

In the present study, the patients with CD disease had similar presentation with pain abdomen, weight loss and

Table 4: Comparison of the present study with survey of inflammatory bowel disease in India

Variable	Ulcerative colitis		Crohn's disease	
	Present study	ISG Survey	Present study	ISG Survey
Mean Age(SD)	43.8(13.67)	38.5(13.5)	43.5(15.9)	35.9(13.9)
Male:Female	0.93	1.4	2	1.3
Diarrhea	97	82.2	67	64.6
Blood in stool	94	86.4	75	42.2
Weight loss	73	61.9	75	66.1
Mucus in stool	90	75.5	67	37.4
Abdominal pain	58	66.7	83	74.9
Fever	17	25.6	8	42.9
No EIM	60	49	50	43.1
Single EIM	13	30	17	34.9
Two EIMs	16	18	25	18.5
Three or more EIMs	11	3	8	3.6
Single episode	38	17	50	8.1
Intermittent flare	40	36	25	23.1
Chronic continuous disease	22	47	25	68.8

chronic diarrhea being common symptoms as reported by Makharia et al.⁵ Another study by Ghoshal et al reported bloody diarrhea in 68% patients, abdominal pain in 62%, weight loss in 57% and intestinal obstruction in 28% patients.⁷ In study by Santana et al, with respect to age at diagnosis, 70% were classified as A1 and 30% as A2 as per Vienna classification. In this study as per Montreal classification 58% patient were from 17-40 years of age. 50% had L2 disease and 67% had B1 disease. In that study as per Vienne classification 19.1% had L1, 21% were classified as L2, 38% as L3 and 21% as L4. According to the disease behavior, 47% were classified as B3, 13% as B2 and 40% as B1.¹⁴

The severity of CD at the time of initial presentation was assessed as per Harvey Bradshaw Index. In present 67% had moderate disease and 17% were in remission and mild disease each compared to study by Plevy et al, 66% were in remission, 17% had mild disease and 16% had moderate/severe disease.¹⁵

It was observed in study by Bandyopadhyay et al, 24% patients had arthritis, 19% had ankylosing spondylitis, 13% had ocular manifestations and mucocutaneous lesion in 7% patients.¹³ In study by Makharia et al backache was seen in 36% patients, arthralgias in 26% and 3% patients had skin lesions, similarly in this study 50% of CD patients had EIMs and arthralgias were seen most commonly.⁵ In study by Singh B et al EIMs were seen in 38.3% of CD patients, peripheral arthropathy and erythema nodosum were more common in CD than in UC.¹⁷ Of the 4 old patients of CD 50% had single episode and 25% each had intermittent flares and chronic continuous disease. Makharia et al observed that 69% patients of CD had intermittent flares, 23% had chronic continuous disease and 8.1% had single episode.⁵

Inflammatory Bowel Disease Undifferentiated

In the present study patients of IBDU presented with diarrhea, blood in stool and mucus in stool in 83% patients each, abdominal pain in 67%, weight loss in 50%. In a study by Zhou N et al and Bermejo et al also had abdominal pain the most common symptom was abdominal pain, diarrhea, weight loss and fever as most common presenting features in IBDU.^{1,16}

In this study, left sided colon involvement was seen in 5 (83%) patient and 1 (17%) patient had terminal ileum involvement. In a study of the 27 patients by Zhou et al, 11% had pancolonic involvement, 15% had primarily left sided and right sided involvement respectively, 52% had small bowel involvement and 7% had extensive involvement.¹ In study by Bermejo et al, 46% had extensive colitis, 29% had distal colitis, 8% had colitis with rectal sparing and 17% had variable location.¹⁶ Extra-intestinal manifestations were present in 67% patients in the present study. One and two extra-intestinal manifestations were present in 33% patients each. Zhou et al et al reported arthralgia, erythema nodosum and mucocutaneous abscess in 11%.¹ In total 74 (73%) patients had anemia at presentation, 64 (77%) patients of UC, 6(50%) patients of CD and 4 (67%) patients with IBDU had anemia. This paper highlights the similarities and differences of demographics and clinical characteristics of IBD patients in this region of India compared to other studies from different region of India and Asia. The limitation of this study included limited number of CD and IBDU patients and short study period.

In conclusion IBD is not uncommon in western Himalayas and rural areas. UC is the most common IBD seen. In every patient presenting with chronic diarrhea, chronic pain abdomen, blood in stools, weight loss, anemia and hypoalbuminemia, it should be a strong differential.

References

1. Zhou N, Chen W, Chen S, Xu C, Li Y. Inflammatory bowel disease unclassified. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*. 2011;12(4): 280-6.
2. Yang SK, Loftus EV Jr., Sandborn WJ. Epidemiology of inflammatory bowel disease in Asia. *Inflamm Bowel Dis*. 2001;7(3):260-70.
3. Froklics A, Dieleman LA, Barkema HW, Panaccione R, Ghosh S, Fedorak RN et al. Environment and the Inflammatory Bowel Diseases. *Can J Gastroenterol*. 2013;27(3): 18-21.
4. Bernstein CN, Fried M, Krabshuis JH, Cohen H, Eliakim R, Fedail S et al. Inflammatory Bowel Disease: A Global Perspective. *WGO Global Guidelines*. 2009.
5. Makharia GK, Ramakrishna BS, Abraham P, Choudhuri G,

- Misra SP, Ahuja V et al. Survey of inflammatory bowel diseases in India. *Indian J Gastroenterol.* 2012;31(6): 299-306.
6. Das K, Ghoshal UC, Dhali GK, Benjamin J, Ahuja V, Makharia GK. Crohn's disease in India: a multicenter study from a country where tuberculosis is endemic. *Dig Dis Sci.* 2008;54: 469.
 7. Ghoshal UC, Shukla A. Malnutrition in inflammatory bowel disease patients in northern India: frequency and factors influencing its development. *Tropical Gastroenterol.* 2008;29(2): 95-7.
 8. Gunisetty S, Tiwari SK, Bardia A, Phanibhushan M, Satti V, Habeeb MA et al. The epidemiology and prevalence of Ulcerative colitis in the South of India. *Open J Immunology.* 2012; 2(4):144-8.
 9. Russel MG, Dorant E, Brummer RJM, Kruus MAV, Muris JW, Bergers JM et al. Appendectomy and the risk of developing ulcerative colitis or crohn's disease: results of a large case-control study. *Gastroenterol.* 1997;113:377-82.
 10. Bernstein CN, Rawsthorne P, Cheang M. A population-based case control study of potential risk factors for IBD. *Am J Gastroenterol.* 2006;101:993-1002.
 11. Ozin Y, Kilic MZY, Nadir I, Cakal B, Disibeyaz S, Arhan M et al. Clinical features of ulcerative colitis and crohn's disease in Turkey. *J Gastrointestin Liver Dis.* 2009;18(2): 157-62.
 12. Sood A, Midha V, Sood N, Puri S, Kaushal V. Profile of ulcerative colitis in a north Indian hospital. *Journal of Indian Academy of Clinical Medicine.* 2000;5(2):124-8.
 13. Bandyopadhyaya D, Bandhyopadhyay S, Ghosh P, De A, Bhattacharya A, Dhali GK et al. Extraintestinal manifestations in inflammatory bowel disease: prevalence and predictors in Indian patients. *Indian J Gastroenterol.* 2015;34(5):387-94.
 14. Santana GO, Souza LR, Azevedo M, Carolina A, Bastos CM, Lyra C. Application of Vienna Classification for crohn's disease to a single centre from Brazil. *Arg Gastroenterol.* 2008;45(1):64-8.
 15. Plevy S, Silverberg MS, Lockton S, Stockfish T, Croner L, Stachelski J et al. Combined serological, genetic, and inflammatory markers differentiate non-IBD, crohn's disease, and ulcerative colitis Patients. *Inflamm Bowel Dis.* 2013;19(6):1139-48.
 16. Bermejo F, Algaba A, Cuno JL, Botella B, Taxonera C Lopez-Serrano P et al. Inflammatory bowel disease unclassified (IBDU) in real practice: prevalence, clinical course and therapy requirements. European Crohn's and Colitis Organisation. Poster presentation: Clinical: *Diagnosis and outcome.* 2013:P216.
 17. Singh B, Kedia S, Konijeti G, Mouli VP, Dhingra R, Kurrey L et al. Extraintestinal manifestations of inflammatory bowel disease and intestinal tuberculosis: Frequency and relation with disease phenotype. *Indian J Gastroenterol.* 2015;34(1):43-50.
 18. Kochhar R, Mehta SK, Nagi B, Bhatia V, Goenka MK, Malik AK. Extraintestinal Manifestations of Idiopathic Ulcerative Colitis. *Indian J Gastroenterol.* 1991; Vol 10(3):88-89.