

## Epidemiological and Clinical Characteristics of Inflammatory Bowel Disease in Patients from Northwestern Iran

Kourosh Masnadi Shirazi<sup>1</sup>, Mohammad Hossein Somi<sup>2\*</sup>, Yoosef Bafandeh<sup>3</sup>, Firooz Saremi<sup>4</sup>, Nooshin Mylanchy<sup>5</sup>, Parisa Rezaeifar<sup>5</sup>, Nasim Abedi Manesh<sup>7</sup>, Seyed kazem Mirinezhad<sup>8</sup>

1. Assistant professor, Department of Internal Medicine, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
2. Professor, Department of Internal Medicine, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
3. Professor, Department of Internal Medicine, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
4. Internist, Department of Internal Medicine, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
5. Internist, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
6. Resident of Internal Medicine, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
7. Ph.D Student of Nutrition, Nutrition Faculty, Tabriz University of medical Sciences
8. Researcher, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran

**\* Corresponding Author:**

Mohammad Hossein Somi, MD  
 Department of Internal Medicine, Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran  
 Tel: + 98 411 3367473  
 Fax: + 98 411 3367499  
 Email: mhosseinsina@yahoo.com  
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### ABSTRACT

#### BACKGROUND

There are few reports from Iran about the epidemiology and clinical features of inflammatory bowel disease (IBD). This study aims to determine the epidemiologic profile and clinical features of IBD in Northwest Iran referral centers.

#### METHODS

In a cross-sectional setting, we evaluated 200 patients with definitive diagnoses of IBD who referred to Tabriz educational hospitals during the period of 2005 to 2007. Demographic characteristics as well as patients' clinical profiles were evaluated. Disease activity and severity were determined by the Crohn's Disease Activity Index and Truelove and Witt's classification of ulcerative colitis (UC). The related probable demographic factors were tested.

#### RESULTS

Of the 200 IBD patients, 183 (91.5%) were diagnosed with UC and 17 (8.5%) with Crohn's disease (CD). There was a positive first degree relative of IBD in 10.9% of UC and 11.8% of CD patients. Abdominal pain was the primary presenting symptom in 25.7% of UC patients and in 58.8% of those with CD. Among UC patients, left-sided colitis was the main feature (52.5%); while in patients with CD, colon involvement was predominant (52.9%). There was no significant contributor for activity or severity of disease noted among demographic factors.

#### CONCLUSION

The occurrence of UC was much higher than CD. The onset of IBD occurred in younger ages with a predominance in males. Left-sided colitis in UC and colon involvement in CD was common. Mostly, the pattern of IBD was mild to moderate with good response to pharmacotherapy. Disease activity and severity were unaffected by demographic features.

#### KEYWORDS

Inflammatory bowel disease; Iran; Demographic; Disease severity

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## INTRODUCTION

Inflammatory bowel diseases (IBD) encompasses a group of diseases, triggered and perpetuated by a variety of diverse genetic, environmental and immunologic factors that share similar clinical manifestations and which primarily affect the small intestine and colon.<sup>1</sup> The two most common entities of IBD, ulcerative colitis (UC) and Crohn's disease (CD) are more common in developed countries than developing countries.<sup>2,3</sup> According to recent studies, the incidence of IBD is increasing in developing countries.<sup>3-5</sup> In comparison to Western countries, there are limited data regarding the epidemiology, clinical features and causes of IBD in these regions.<sup>6,7</sup> Similar to other parts of Asia, previous reports from Iran have demonstrated an increasing incidence of IBD, particularly UC, in this region.<sup>8-11</sup> As Iran is a wide country with different ethnicities, therefore additional studies that emphasize epidemiologic and clinical features of IBD are needed to elucidate its pattern in Iran. The present study has assessed IBD cases from primary referral centers in Northwest Iran over a 24 month period with the intent to research the epidemiologic and clinical features of IBD and their relationship with disease activity and severity.

## MATERIALS AND METHODS

All patients diagnosed with IBD that were hospitalized or referred to public hospitals and main referral care centers in Tabriz, Northwest Iran between 2005 and 2007 were included. Patients in the surgical ward were not included in the study. IBD diagnosis was based on the typical clinical course of the disease and endoscopic examination with histologic confirmation of UC or CD. All information regarding demographics, family history of IBD, major extra-intestinal manifestations, extent of IBD, treatment details, need for surgical treatment, and coexistence of other diseases were obtained. A prepared questionnaire was completed by the interviewer. The activity and severity of the disease were determined by the Crohn's Disease Activity

Index and the Truelove and Witt's classification of UC. Study was approved by local Ethics Committee and informed consents signed by patients.

## Statistical analysis

All statistical analyses were performed using SPSS version 17 (SPSS Inc., Chicago IL.). Measured values were expressed as mean±standard deviation. Significance of differences between studied groups was calculated by the independent samples t- and chi-square tests. Association analysis was performed by Pearson or Spearman correlation analysis.  $p < 0.05$  was considered statistically significant.

## RESULTS

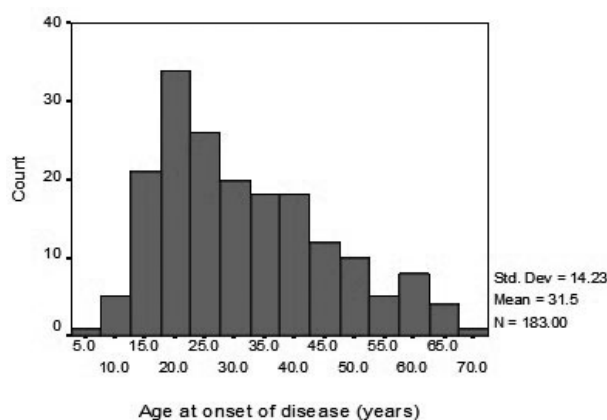
A total of 200 IBD patients were included in this study (mean age: 36.87±14.88 years). Epidemiologic characteristics of the studied population are presented in Table 1. There were 183 (91.5%) patients diagnosed with UC and 17(8.5%) patients with CD. The UC/CD ratio was greater than 10:1. The mean age at onset of IBD in CD cases was 27.00±14.15 years, for UC it was 31.54±14.23 years ( $p=0.211$ ). There was a male predominance, with a male/female ratio of 1.08 for UC and 1.83 for CD. A first degree relatives of IBD was present in 11.8% of CD patients and 10.9% of those with UC. Only 5 UC patients underwent appendectomies. The median age of patients was 34 years (range: 12-76). Symptoms appeared before 40 years of age in 75% of patients (Fig. 1). The median time interval from initiation of symptoms to diagnosis in UC was 14 months; for CD, it was 12 months. There were no significant differences between the two groups ( $p=0.50$ ).

The predominant form of UC was left-sided colitis, which affected almost 52.5% (96) of the studied population. Pancolitis was present in 32 (17.5%) patients. Both small and large bowel involvement was seen in 29.4% of patients with CD. However 52.9% of patients had Crohn's colitis, while isolated small bowel involvement was seen in 17.6% of patients. The extent of IBD was age-dependent, yet there were no significant differences related to

**Table 1:** Epidemiological characteristics of study patients.

Parameters		Ulcerative colitis (n=183)	Crohn's disease (n=17)	p-value*
Gender	Male	95	11	0.312
	Female	88	6	
Age (years)		37.24±14.97	32.82±13.67	0.243
University education		115	11	0.332
Married		116	12	0.379
Family income	Low	9	1	0.979
	Middle	122	11	
	High	52	5	
Smoking history		27	1	0.313
Oral contraceptive pill use		17	2	0.111
Breastfed		164	15	0.859
First degree relatives of IBD		20	2	0.916
Residence	Urban	102	14	0.342
	Rural	81	3	

\* Independent sample t- and chi-square tests.

**Fig. 1:** Age at onset of Inflammatory bowel disease (IBD)

the extent of IBD with regards to sex, education and employment ( $p>0.05$ ).

There were extra-intestinal manifestations in 23% of UC patients and in 29.4% of those with CD. Among the extra-intestinal manifestations of IBD, hepatobiliary disorders were most frequent as observed in 30 (16.39%) UC and 2 (11.8%) CD patients (Table 2).

Approximately 28 (14%) patients had coexisting disorders such as hyperlipidemia, high blood pressure, diabetes, autoimmune hepatitis, coronary heart disease, and hypo- and hyperthyroiditis.

The majority of patients with CD (41.2%) and UC (76%) were treated with only 5-amino salicylic acid (5-ASA).

In a comparison between the clinical characteristics and presentation of CD and UC (Tables 3 and 4), it was noted that patients with CD had a significantly higher incidence of abdominal cramping ( $p=0.009$ ) and weight loss ( $p=0.017$ ). The majority of patients were in remission, 66.12% for UC patients and 58.82% for CD patients, with mild to moderate severity (91.80% for UC and 88.24% for CD patients; Table 3).

**Table 2:** Extra-intestinal manifestations of study patients.

	Ulcerative colitis n (%)	Crohn's disease n (%)	<i>p</i> -value*
Skin disorders	7 (3.8)	0 (0)	0.999
Arthritis	11 (6)	1 (5.9)	0.999
Eye disorders	2 (1.1)	1 (5.9)	0.235
Hepatobiliary	30 (16.39)	2 (11.8)	0.872
Urologic disorders	17 (9.3)	2 (11.8)	0.667
Fistula	1 (0.5)	1 (5.9)	0.163
Urinary stones	12 (6.6)	1 (5.9)	0.999

\* Independent samples t-test.

**Table 3:** Clinical characteristics of the study patients.

		Ulcerative colitis	Crohn's disease	<i>p</i> -value*
Disease activity	Active	62	7	0.545
	Remission	121	10	
Disease severity	Severe	15	2	0.080
	Moderate	28	6	
	Mild	140	9	
Colon cancer		3	1	0.232
Onset of extra-intestinal manifestations before intestinal symptoms		6	1	0.468
Disease situation	Controllable with therapy	148	11	0.039
	Uncontrollable with therapy	7	3	
	Intermediate	28	3	

\* Independent samples t-test.

**Table 4:** Comparison of the clinical presentation of study patients.

Clinical feature	Ulcerative colitis n (%)	Crohn's disease n (%)	<i>p</i> -value*
Abdominal cramping	47 (25.7)	10 (58.8)	0.009
Diarrhea	36 (19.7)	6 (35.3)	0.208
Bloody diarrhea	22 (12)	1 (5.9)	0.699
Rectal bleeding	45 (24.6)	3 (17.6)	0.767
Vomiting	12 (6.6)	3 (17.6)	0.122
Fever	7 (3.8)	1 (5.9)	0.515
Anorexia	22 (12)	3 (17.6)	0.452
Weight loss	15 (8.2)	5 (29.4)	0.017
Other	20 (10.9)	2 (11.8)	0.999

\* Independent samples t-test.

We assessed the association between severity and activity of disease with demographic variables however there was no significant correlation ( $p > 0.05$ ).

## DISCUSSION

The present study aimed to describe the epide-

miologic profile and clinical presentations of IBD and its correlation with disease activity and severity among IBD patients in Northwest referral centers of Iran.

Most previous reports from Iran have discussed an increasing rate of UC and rarity of CD.<sup>9-11</sup> Similarly, in this study, a higher rate of UC was observed among the 200 patients who referred to the referral care centers from the Northwest urban and rural regions over a 24-month period. In comparison with previous studies, the UC to CD ratio was higher (>10:1).<sup>12-15</sup> In this regard, results from other Asian countries were inconsistent, but our findings were similar to two reports of Wang and Ishibashi and et al.<sup>6,15</sup> and the most recent report from Iran.<sup>16</sup> Geographic and ethnic differences might be the main reason.

The ratio of male to female patients was 1.08:1 in UC and 1.83:1 in CD in our study, which showed a male gender dominance for IBD that agreed with studies in some Asian countries,<sup>10,14,15,17-19</sup> but differed from most previous studies in Iran which have shown slightly more frequent IBD in females.<sup>9-11,20</sup> In Western countries, UC tends to be slightly more common in males, whereas CD is marginally more common in females.<sup>21</sup> Differences in sample sizes and the numbers of patients in each group (UC and CD) possibly account for this inconsistency.

In this study the mean age at onset for UC and CD were relatively similar. The mean age at onset was about 31.5 years, which was in accordance with other studies,<sup>10,20</sup> however in two other studies from Iran the mean onset for IBD was greater than 36 years of age.<sup>11,14</sup> Younger patients seem to have a more aggressive, severe pattern of disease. In the present study there was no significant correlation between onset of IBD to disease activity ( $p=0.868$ ) and severity ( $p=0.940$ ). The average age of patients with CD (32.82 years) was similar to China and Western countries.<sup>22,23</sup> Our study, in agreement with other studies from the Middle East and previous studies conducted by Malekzadeh and Vahedi et al. did not reveal a second peak among patients over the age of 50 years.<sup>9,24,25</sup> This finding contrasted a study by Aghazadeh et al.<sup>10</sup> We demonstrated a pre-

dominance of IBD patients in the urban population, which was similar to previous results in Iran.<sup>20</sup>

It was found that 10.9% of UC and 11.8% of CD patients had positive histories of IBD in their first degree relatives. This proportion for UC was similar to a study by Aghazadeh et al.<sup>10</sup> but was higher than reports from some Western countries and China.<sup>12,18</sup> Reports from various countries in this regard are inconsistent, therefore more genetic studies are required to reveal a definite familial tendency in IBD. Correlation analysis in this study did not show an association between familial history to disease activity and severity.

There was a predominance of left-sided colitis (52.5%) in this study. In agreement with previous reports from Iran pancolitis was much less frequent.<sup>9,10</sup> The findings of present study demonstrated that the location of disease significantly correlated ( $p=0.033$ ) with age at onset of UC. Pancolitis was more frequent in patients who developed UC at a younger age. This finding agreed with the results of a study by Wiercinska-Drapalo et al.<sup>12</sup> Severe UC was observed in 8.2% of patients, 15.3% had moderate UC and 76.5% had mild UC. In Western countries and China, severe UC was higher than our results.<sup>23,26</sup> Colon involvement in CD patients was more frequent in the current study, which confirmed the results of a study by Aghazadeh et al., however this was in contrast to results from other studies.<sup>10,23</sup> In our study, 52.9% of patients had mild CD, 35.3% had moderate CD and 11.8% were diagnosed with severe, the latter were less than observed in Western countries (31.9%) and China (27%).<sup>23,27</sup> The difference between our results and these reports might be explained by the small number of patients with CD in our study.

In accordance with several reports, 90.5% of patients were prescribed 5-ASA, whereas approximately 33.0% took steroids and 27.5% were prescribed immunosuppressors.<sup>23</sup> None of our patients with CD required surgical treatment, whereas 2.7% of UC patients underwent IBD-related surgeries. Others reported a high rate of surgery.<sup>23</sup> The differences between our results were related to the limited number of CD patients, the study period and

the exclusion of hospitalized patients in the Surgery Department in the current study. In this study, the majority of UC patients responded to pharmacotherapy treatment.

Among extra-intestinal manifestations, hepatobiliary disorders were predominant in both UC and CD patients in our study which contrasted previous Iranian reports.<sup>9,10</sup> Primary sclerosing cholangitis was the main extra-intestinal complication in a study by Yazdanbod et al.<sup>20</sup> Development of extra-intestinal manifestations prior to the onset of intestinal complications were reported in 6 UC patients and 1 CD patient. There was no significant association between development of extra-intestinal manifestations and disease severity in this study. In support of other reports, the predominant clinical presentation in our patients was abdominal pain. Other frequent complications among UC patients were rectal bleeding and diarrhea. Diarrhea and weight loss were common problems in patients with CD.<sup>9,22</sup>

In this study 14.8% of UC patients and 5.9% of patients with CD were either active or passive smokers which approximated the results of previous reports from Iran, but contrasted those from Western countries.<sup>10,28</sup> This difference might be related to the fact that smoking is uncommon in Iranian women. As with Jiang et al.,<sup>18</sup> we could not find any correlation between smoking and disease extent in the present study. Several studies have reported an inverse association between smoking and UC.<sup>20,28</sup>

This paper demonstrated the similarities and differences of demographic and clinical characteristics of IBD patients in this region of Iran compared to other studies from different regions of Iran. The limitations of the current study included a limited number of patients with CD and short study period.

In conclusion, the occurrence of UC was much higher than CD. The age of onset for IBD was mostly before 30 years, with a predominance of male patients. The most common clinical form of UC was left-sided colitis and colon involvement in patients with CD. Mostly, the pattern of IBD was mild to moderate, with fewer patients who underwent surgery. Demographic features were not associated with disease activity and severity.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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