ORIGINAL ARTICLE

Epidemiology of Inflammatory Bowel Disease in Iran:

A review of 803 cases

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ABSTRACT

Aim: To gain recent characteristic information about inflammatory bowel disease (IBD) in Iran.

Background: Inflammatory bowel disease (IBD) was believed to be infrequent in Iran; however, during the recent years its prevalence has been continuing in our country.

Patients and Method: Between 1992 and 2007, a total of 803 IBD patients (671 ulcerative colitis (UC), 109 Crohn's disease (CD) and 23 indeterminate colitis (IC)) referred to our research centre. We evaluated the demographic data, extraintestinal manifestations, chief complaints and extension of disease in this group of patients.

Results: The mean age at diagnosis was 33.01, 33.18, and 34.52 years in UC, CD, and IC patients, respectively. The male to female ratio was 0.78 for UC patients while it was 1.18 in CD patients. Patients with UC chiefly presented by hematochezia (54.24%), whereas those with CD and IC complained of abdominal pain (55.96% and 47.82%, respectively). Totally, 67.51% UC patients, 70.64% CD patients and 73.90% IC patients reported extra intestinal manifestations. The most involved section was left colon in UC (90.49%) and colon in CD patients (75%).

Conclusion: The demographic and clinical picture of IBD is more or less the same as other developing countries; however, the rarity of CD in Iran is noted. Although the true epidemiologic profile of IBD in Iran is still unknown, it is not as rare as previously thought and it seems as if gradual adoption of a western lifestyle may be associated with continuing rise in IBD.

Keywords: *Ulcerative colitis, Crohn's disease, Epidemiology, Iran.*
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INTRODUCTION

The chronic inflammatory bowel diseases (IBD) include two distinct entities, ulcerative colitis (UC) and Crohn's disease (CD), although there is a small group of patients with an intermediate form. UC is an inflammatory process confined to the colon in all instances, which presents itself clinically with bloody diarrhea, mucus in the stools, abdominal pain, and weight loss. CD can affect any part of the digestive tract from the mouth to the anus. The terminal ileum is the commonest site for the disease. CD is clinically presented with abdominal pain, diarrhea and weight loss, however, it occasionally presents with

an abdominal mass, intestinal obstruction, or fistula (1). About 10% of the patients with colonic inflammation can not be classified as either CD or UC. These patients are categorized as "indeterminate colitis" (2,3).

Etiology of ulcerative colitis and Crohn's disease are still unknown. Knowledge of differing incidence rates of IBD in different geographic areas or among races may provide insights into possible etiologic factors. Similarly, temporal trends in the incidence rates in a given area can provide valuable clues towards etiology. Epidemiological studies from Western countries have reported that the incidence rates of IBD are higher in the northern part of the world and among whites than in nonwhite populations (4). The epidemiological data of the IBD prevalence in Europe are provided by the Western Europe countries (5). Only few and scattered reports come from the countries of the Eastern and Middle Europe (6).

Unfortunately, there have been only few studies on IBD in Iran. This is largely attributed to the lack of a national registry system as well as the idea of rarity of IBD in Iran.

We aimed to define the demographic features and clinical characteristics in a relatively large group of patients with IBD who had referred to our department during a 15-year period. These data may provide insight into the possible causes of IBD and in part could explain the differences between the IBD profile in Iran in comparison with other countries.

PATIENTS and METHODS

We used the database of Inflammatory Bowel Disease patients in the research center for Gastroenterology and Liver Diseases of Shahid Beheshti University of Medical Sciences, Tehran, Iran. The database is specially designed for IBD patients according to a prepared questionnaire. The questionnaire contains the patient's demographic

data, history of IBD or other associated diseases, date of onset, signs and symptoms and extraintestinal manifestations which were categorized as follow; mucocutaneous, musculoskeletal, liver and biliary, urinary tract and eye. Consultations were offered for extraintestinal manifestations when appropriate.

Data were gathered during a 15-year period (1992-2007) from the patients referring to Taleghani hospital (IBD research center) and 5 private clinics in Tehran that welcome patients from all other provinces of Iran. The diagnosis of IBD was verified on the basis of well-established clinical, endoscopical, radiological, histological, and surgical criteria as described by Lennard–Jones (7).

The patients were interviewed face to face by trained general practitioners. Whenever patients referred back, their disease data was updated by another interview. If the patient was illiterate and could not give exact answers to our questions, we referred to his medical records. Having completed the questionnaire, these data were entered to the IBD database.

Ethical Consideration:

Our project was approved by the ethical committee of RCGLD, while an informed consent was retrieved from patients before the interview.

RESULTS

Totally, 803 patients were registered in our database, 671 UC, 109 CD and 23 IC patients. The mean age at diagnosis was 33.01 (a range, 3-80 years) in UC, 33.18 (a range, 7-73 years) in CD, and 34.52 years (a range, 17-70 years) in IC patients. In all IBD subgroups, most of the patients aged 20-29 years. In figure 1 the age-specific frequency rates by IBD type are shown.

The male to female ratio in UC patients was 0.78, where women were predominant; in contrary,

male to female ratio in CD patients was 1.18. We also had one transsexual patient suffering from ulcerative colitis.

Five-hundred and one (74.66%) UC, 80 (73.39%) CD and 13 (56.52%) IC patients had history of breast feeding. Forty-six (6.85%) UC, and 16(14.67%) CD patients were smokers. Fifty-two (7.74%) UC and 12 (11%) CD patients consumed alcohol. Appendectomy and tonsillectomy were carried out in 4.60% and 4.47% of UC patients, comparing with 15.59% and 3.66% of CD patients, respectively.
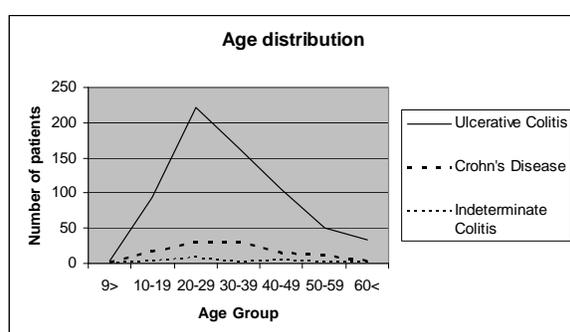

Figure 1. *Age distribution of Iranian patients with inflammatory bowel disease*

Totally, 139 (20.71%) UC patients had a positive family history; of whom 91 (13.56%) were first- and 48 (7.15%) were second-degree relatives. The rate of positive family history in CD patients was almost similar to UC patients, affecting 13 (11.92%) first- and 7 (6.42%) second-degree relatives.

Table 1. *Predominant chief complaints of patients with ulcerative colitis (UC), Crohn's disease (CD), and indeterminate colitis (IC)*

	UC	CD	IC
Diarrhea	54.24*	48.62	34.78
Hematochezia	48.88	22.01	34.78
Bloody Diarrhea	45.00	22.93	30.43
Tenesmus	43.07	41.28	26.08
Abdominal pain	40.53	55.96	47.82
Weight loss	33.38	44.03	26.08
Weakness	46.79	41.28	47.82
Anorexia	24.44	33.94	30.43
Constipation	17.43	14.67	30.43

*Given as percentages of the number of patients in the different disease groups.

As presented in table 1, the major chief complaints of UC patients were diarrhea (54.24%), hematochezia (48.88%), weakness (46.79%) and bloody diarrhea (45.00%). On the other hand, the predominant chief complaints of CD patients were abdominal pain (55.96%), diarrhea (48.62%), weight loss (44.03%) and weakness (41.28%). IC patients complained more commonly of abdominal pain (47.82%), weakness (47.82%), diarrhea (34.78%), hematochezia (34.78%), anorexia (30.43%), bloody diarrhea (30.43%) and constipation (30.43%).

Perianal diseases were detected in 26 (23.85%) patients with Crohn's Disease: 13 (11.92%) fistula, 12 (11%) hemorrhoid, 2 (1.83%) anal abscess, 1 (0.91%) fissure, and 1 (0.91%) anal stenosis.

Totally, 21 (3.12%) UC and 15 (13.76%) CD patients had undergone colectomy.

Extra intestinal manifestations are shown in figure 2. Totally, 67.51% of UC, 70.64% of CD and 73.9% of IC patients reported extraintestinal manifestations. Muscoloskeletal manifestations were, by far, the most common extraintestinal site of involvement. The frequency of primary sclerosing cholangitis, pyoderma gangrenosum and erythema nodosum in UC patients were 37 (5.51%), 11 (1.63%) and 20 (2.98%), respectively. These extraintestinal manifestations were also appeared in patients with Crohn's disease: primary sclerosing cholangitis in 2 (1.83%), pyoderma gangrenosum in 4 (3.66%) and erythema nodosum in 7 (6.42%) patients. Primary sclerosing cholangitis and pyoderma gangrenosum did not appear in IC patients, however, 2 (8.69%) had erythema nodosum.

Of 803 IBD patients, the extension of disease was determined in 367 (45.07%) with total colonoscopy and upper GI endoscopy. Of 305 UC patients, 2 (0.65%) had sigmoiditis, 276 (90.49%) had left colon colitis, and 27 (8.85%) presented with pancolitis. The extension of disease was determined in 48 (44.03%) CD patients: colon 36 (75%), ileum 7 (14.58%), ileum and colon 2 (4.16%) and upper GI tract 1 (2.08%). Extension of

disease in 14 (60.86%) IC patients were as follow: 12 (85.71%) left colon, 1 (7.14%) sigmoid and 1(7.14%) transverse colon.

Colorectal cancer was developed in 14 UC (2.08%) patients and one CD (2.1%) patient.
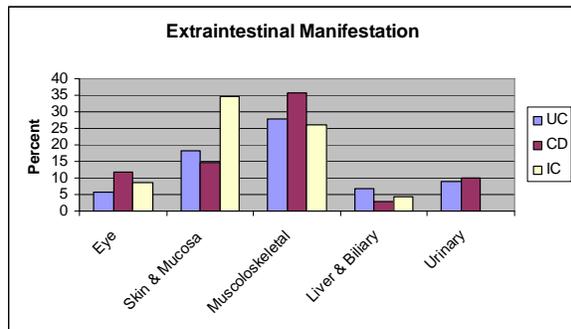

Figure 2. Frequency of extra-intestinal diseases in ulcerative colitis (UC), Crohn's disease (CD) and indeterminate colitis (IC) patients

DISCUSSION

There are a variety of reasons as to why it is essential to pursue epidemiological studies in IBD. First, it is important to quantify the magnitude of the problem. This helps health planners understand the resources that are necessary to manage these patients. Trends in the epidemiology, more importantly, can lead to disease etiology clues.

The peak age of onset of UC and CD has varied among different studies but appears to be broadly similar to the Western experience. In a Japanese nationwide survey, the peak age of onset was 20–29 years for UC and 15–24 years for CD (8), whereas the median age of diagnosis in a Korean study was 35 years (9). In the Leong et al. study from Hong Kong and China the mean age of diagnosis of CD was 33.1 years and 37.2 years, respectively (10). Similarly, in a more recent review from China, the mean age of CD was 37.7 years, and 44.0 years for UC (11). Also a recent study in Lebanon showed that the peak age of diagnosis both in CD and UC was 20-30 and the mean age of diagnosis was 32 for UC and 28.8 for CD (12). In our study the mean age of diagnosis

and the peak age of diagnosis were almost similar to our previous study with 457 IBD patients in Iran (13) and also other Asian countries.

In the Morita et al. survey in Japan, CD was twice as common in male as in female subjects (8). In the Leong et al. study, CD was 2.5-fold more common in male subjects (10). In our previous study on 457 IBD patients (13) also there was a predominance in male CD patients. Our study showed similar results, where more men were affected by CD. Unlike other studies, we have found a slight female predominance in UC which is similar to our previous study.

We found a relatively high prevalence of a positive family history of IBD, significantly more so in patients with UC than in patients with CD (20.71% versus 18.34%).

Diarrhea was the most prevalent chief complaint of our UC patients, a finding that is not only differed from our previous study (13), but also disagreed Sang Hyoung Park et al. study on 304 Korean UC patients and Russel et al. study in Netherland which explained rectal bleeding as the most predominant chief complaint (14,15). On the other hand, abdominal pain was the most prevalent chief complaint among CD patients. This is in agreement with previous studies (13,15)

Results revealed that there are not significant differences between the extent of disease in Asian and Western UC patients, although great variability has been reported. Both Yang et al. from Korea and Ling et al. from Singapore reported approximately equal proportions of patients with distal, left-sided and extensive disease (9,16), however, Jiang and Cui reported that 70% of UC patients had proctitis (11). In our study, 90.49% of UC patients had left side colitis.

Disease involvement in CD patients is predominantly ileocolonic with approximately 30% of patients having colonic involvement and 10–20% having only small intestinal involvement (17). In our study, 75% of CD patients had colonic involvement.

Extra-intestinal manifestations have been reported in 2–34% of Asian UC patients (17). In our study, 67.51% of UC, 70.64% of CD and 73.9% of IC patients reported extraintestinal manifestations. This is, by far, greater than the reported 6.1% in Chinese UC patients (18) and 6.2% in Bernstein et al. study; however, in the latter study, those with peripheral arthritis have been deliberately excluded (19). Our data are ,however, comparable to Indian population (34.7%), Korean patients (24.1%), and other Western studies (21-41%) (20-22). Early diagnosis, in addition to a consistent therapy and regular check-ups, may lead to a significant reduction in extra-intestinal diseases. Moreover, establishing the associations of immunomediated diseases in extra-intestinal sites may lead to a better understanding of the pathogenesis of IBD.

Perianal disease occurs in 2–30% of Asian patients, but it is generally less common than Western population (17). In our study, perianal diseases were detected in 26 (23.85%) CD patients.

Only a limited incidence of colon cancer among UC patients was observed in this study. These low rates could be partly explained by low incidence rate of colorectal cancer among the general Iranian population. These figures are similar to that found in studies conducted in Asia (9) but it was much less than that reported by Western countries (23,24).

REFERENCES

1. Bing XIA, Crusius JBA. Inflammatory bowel disease: definition, epidemiology, etiologic aspects, and immunogenetic studies. World J Gastroenterol 1998;4(5):446-58.

2. Price AB. Overlap in the spectrum of non-specific inflammatory bowel disease: 'colitis indeterminate'. J Clin Pathol 1978;31:567-77.

3. Wells AD, McMillan I, Price AB, et al. Natural history of indeterminate colitis. Br J Surg 1991;78:179-81.

4. Whelan G. Epidemiology of inflammatory bowel disease. Med Clin North Am 1990;74:1–12.

5. Shivananda S, Lennard-Jones J, Logan R, and the EC-IBD Study Group. Incidence of inflammatory bowel disease across Europe; is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Disease. Gut 1999;39:690-97.

6. Wiercinska-Drapalo A, Jaroszewicz J, Flisiak R, et al. Epidemiological characteristics of inflammatory bowel disease in North-Eastern Poland. World J Gastroenterol 2005;11(17):2630-33.

7. Lennard-Jones JE. Classification of inflammatory bowel disease. Scand J Gastroenterol Suppl 1989;24:2–6.

8. Morita N, Toki S, Hirohashi T, et al. Incidence and prevalence of inflammatory bowel disease in Japan: nationwide epidemiological survey during the year 1991. J Gastroenterol 1995;30 (Suppl. 8):1–4.

9. Yang SK, Hong WS, Min YI, et al. Incidence and prevalence of ulcerative colitis in the Songpa-Kangdong District, Seoul, Korea, 1986–1997. J Gastroenterol Hepatol 2000;15:1037–42.

10. Leong RW, Lau JY, Sung JJ. The epidemiology and phenotype of Crohn's disease in the Chinese population. Inflamm Bowel Dis 2004;10:646–51.

11. Jiang XL, Cui HF. An analysis of 10218 ulcerative colitis cases in China. World J Gastroenterol 2002;8:158–61.

12. Abdul-Baki H. Clinical epidemiology of inflammatory bowel disease in Lebanon. Inflamm Bowel Dis 2007;13(4):456-8.

13. Aghazadeh R, Zali MR, Bahari A, et al. Inflammatory bowel disease in Iran: A review of 457 cases. J Gastroenterol Hepatol 2005;20:1691–95.

14. Park SH. Clinical features and natural history of ulcerative colitis in Korea. Inflamm Bowel Dis 2007;13(3):345-9.

15. Russel MJ. High incidence of inflammatory bowel disease in the Netherlands. Dis Colon Rectum 1998;41:33-40.

16. Ling KL, Ooi CJ, Luman W, et al. Clinical characteristics of ulcerative colitis in Singapore, a multiracial city-state. J Clin Gastroenterol. 2002;35:144–8.

17. Quyang Q. Management consensus of inflammatory bowel disease for the Asia–Pacific region. J Gastroenterol Hepatol 2006;21:1772–82.

18. Bernstein CN, Blanchard JF, Rawsthorne P, et al. The prevalence of extraintestinal diseases in inflammatory bowel disease: A population-based study. Am J Gastroenterol 2001;96:1116–22.

19. Kochhar R, Mehta SK, Nagi B, et al. Extraintestinal manifestations of idiopathic ulcerative colitis. Indian J Gastroenterol 1991;10:88–9.

20. Park SM, Han DS, Yang SK, et al. Clinical features of ulcerative colitis in Korea. Korean J Intern Med 1996; 11: 9–17.

21. Monsen U, Sorstad J, Hellers G, et al. Extracolonic diagnoses in ulcerative colitis: An epidemiological study. Am J Gastroenterol 1990;85:711–16.

22. Olsson R, Danielsson A, Jarnerot G, et al. Prevalence of primary sclerosing cholangitis in patients with ulcerative colitis. Gastroenterology 1991;100: 1319–23.

23. Gyde SN, Prior P, Allan RN, et al. Colorectal cancer in ulcerative colitis: A cohort study of primary referrals from three centers. Gut 1988;29:206–17.

24. Ekbom A, Helmick C, Zack M, et al. Ulcerative colitis and colorectal cancer. A population-based study. N Eng J Med 1990;323:1228–33.