**Research Article**

# Incidence of Ulcerative Colitis Relapse: A Prospective Cohort Study in Southern Iran

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## Abstract

**Background:** The epidemiology of inflammatory bowel disease (IBD) is changing globally and there is disagreement between studies about the prevalence of relapse of ulcerative colitis (UC) as a type of IBD.

**Objectives:** The current study aimed to find out the incidence of relapses in patients with UC in Southern Iran.

**Patients and Methods:** In a prospective cohort study in a period of one year (from October 2012 to October 2013) 157 patients with UC who were in clinical remission for at least three months and were registered in the IBD registry of Shiraz University of Medical Sciences, Shiraz, Iran were enrolled. The sample size was calculated according to the formula to determine a ratio. Clinical relapse was described as deterioration of bowel movements, lower intestinal bleeding or worsening of abdominal pain and diarrhea leading to changes in previous treatment. Age and gender distribution and the frequency of relapse in a one-year follow-up were recorded.

**Results:** Among the 1273 registered patients with UC, 157 patients were enrolled in the survey by systematic sampling. Among patients, 48.7% were female and no significant difference was observed between the mean age of two gender groups (P = 0.70). Seventy-four patients, 48.1% (33 males and 41 females), relapsed during the 12-month follow-up period and the main medication of the 64 non-relapsing (80%) and 62 relapsing (83.8%) patients was mesalazin (P = 0.65).

**Conclusions:** Although, the reported incidence was almost equal to previous reports from other regions of the world, relapsed and non-relapsed UC patients received mesalazin as treatment without any significant differences.

*Keywords:* Ulcerative Colitis, Relapse, Mesalazin, Incidence

## 1. Background

Inflammatory bowel disease (IBD) is a chronic gastrointestinal disease which has two types, the Crohn disease (CD) and ulcerative colitis (UC). The UC is a chronic idiopathic type of IBD characterized by continuous mucosal inflammation that starts in the rectum and extends proximally (1). Typical symptoms include bloody diarrhea, abdominal pain, urgency, and tenesmus (2). The course of UC consists of intermittent exacerbations alternating with periods of complete asymptomatic remission (3). A small percentage of patients, however, have continuous symptoms and are unable to achieve remission (4). Indeed, the natural history of UC is characterized by a relapsing-remitting course and less often by a continuous active course. More than half of patients will inevitably relapse within a calendar year following a flare of disease (5). It is believed that both genetic and environmental factors contribute to the pathophysiology of IBD. Also, geographical variations existed in the dominant type of IBD. The epidemiology of IBD is changing globally. Incidence and prevalence may have stabilized in high-incidence areas such as North America and Europe but they continue to rise in previously low-incidence areas such as Eastern Europe, Asia, and a great part of the developing world (6). The annual incidence of UC in Europe is 24.3 per 100,000 persons (7). It is reported that UC is more common in Iran (8). In addition, previous reports demonstrated increasing incidence of UC in Iran (9, 10). Most patients with chronic UC run a relapsing course and it is suggested that UC relapse may follow a seasonal pattern (11). In order to prevent relapse and severe complications in patients with anticipated relapse, and also reduce over-treatment in patients who do not require severe treatment, it is critical to find and present the picture of relapse incidence in each population.

## 2. Objectives

The current study aimed to find out the incidence of relapses in patients with UC in Southern Iran.

## 3. Patients and Methods

### 3.1. Ethical Statement

The study was evaluated and accepted by the ethics committee of Shiraz University of Medical Sciences (code number: 6495). All patients read the study objectives or had them explained for them and signed written informed consent before enrolment in the study. The obtained data were secured and only the authors could reach them just for analysis. These points were discussed for all objectives and were followed in the study period and also after that.

### 3.2. Study Design

A descriptive prospective cohort study was performed on patients with UC who were in clinical remission for at least three months. They were registered in a 14-month study from Aug. 2010 to Sep. 2012 in the inflammatory bowel diseases (IBD) registry of gastroenterohepatology research center in Shiraz, Fars province (population 4,597,000), Iran (12). According to the sample size calculation formula to determine one ratio and frequency of relapse in previous studies, the sample size was calculated as157 patients. Systematic sampling was employed to select a calculated sample size (sampling frame: 1273; calculated sample size: 157, with sampling interval (K = 1273/157 = 8) from the registered patients. Follow-up was over one year from 1 October 2012 to 1 October 2013. The patients were visited at intervals of three months. All patients were followed-up to the end of the study and those who had a relapse were detected. Indeed, the study population was stratified into two different groups including relapsers and non-relapsers.

### 3.3. UC, Remission and Relapse

UC was diagnosed according to the Truelove and Witts criteria (13). Clinical remission was characterized by normal baseline stool frequency and lack of bloody stool (14). Clinical relapse was described as deterioration of bowel movements accompanied by lower intestinal bleeding or worsening of abdominal pain and diarrhea leading to changes in previous treatment included increase in dose or change of drugs, added steroids, and admission to hospital or surgery (14, 15). The exclusion criteria were using non-steroidal anti-inflammatory drugs (NSAIDs) within the three months prior to the study and also pregnancy.

### 3.4. Statistical Analysis

To determine the significant differences of quantitative and qualitative variables between the two groups, student t-test and $\chi^2$ test were used respectively. Descriptive

analysis included calculation of incidence and report of disease related variables such as age, gender and the used drugs performed using the SPSS statistical software, version 16 (Inc. Chicago, IL).

## 4. Results

The study trend and overall findings are presented in Figure 1. As demonstrated, the primary sampling frame included all registered patients, 1273 with ulcerative colitis. Among them, 157 patients were enrolled in the survey by random sampling. Two patients did not complete the study because of relapse due to arbitrary cut-off drugs. The patients included 48.7% female with mean ± SD of age of 42.48 ± 11.22 years (range: 20 - 69 years) and 51.3% male with mean ± SD of age of 41.81 ± 10.82 years (range: 21 - 83 years). No significant difference was observed between the age of the two groups (P = 0.70); there was a significant difference between the relapsers and non-relapsers regarding age, but no significant difference was observed in the gender (P < 0.001 and P = 0.1, respectively) (Table 1).

**Table 1.** Comparison Between Relapsers and Non-Relapsers Regarding Age and Gender

| Variable | Non-Relapsers | Relapsers | P Value |
|---|---|---|---|
| **Age, y, mean ± SD** | 46.97 ± 10.56 | 36.90 ± 8.89 | < 0.001 |
| **Gender, No. (%)** | | | 0.1 |
| Male | 46 (58.20) | 33 (41.8) | |
| Female | 35 (45.3) | 41 (54.7) | |

The incidence of relapse in one year follow-up was 48.1% per year. They were 33 males and 41 females. The mean age was 42 years; mean number of previous relapses before the study, mean duration of disease and mean duration of remission before the study were 3.7, 99 and 46 months, respectively. The main medication of the 64 non-relapsing (80%) and 62 relapsing (83.8%) patients was mesalazin (p=0.65). Also, asacol and sulfasalazine were used in relapsing (12.2% and 4.1%) and non-relapsing (12.5% and 7.5%) subjects. However, the differences between relapsing and non-relapsing groups using these two drugs were not statistically significant (P > 0.05).

## 5. Discussion

In the current preliminary study, the incidence of UC relapse in the sample of IBD registry of gastroenterohepatology research center affiliated to Shiraz University of Medical Sciences, Shiraz, Iran was evaluated. It was found
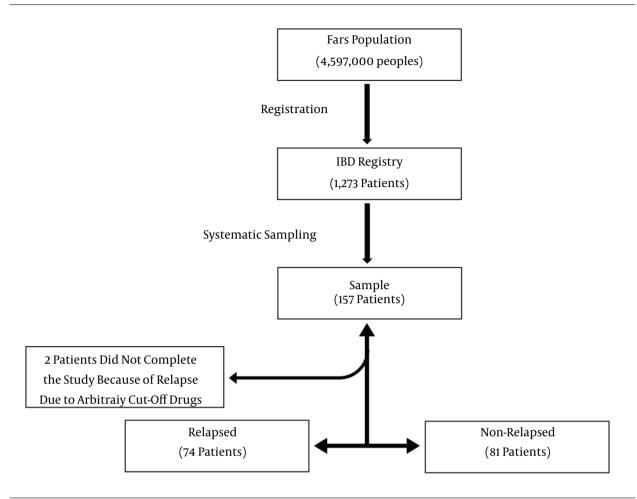
**Figure 1.** The Trends of the Study and Overall Findings

that the rate of relapse in the 12month follow–up in these patients who used mesalazin was 48.1%.

In a study, it was reported that 73% of UC patients treated by mesalazine for up to 12 months were relapsed (16). Also, Bitton et al. evaluated and followed 74 patients with clinically and endoscopically determined inactive UC for one year. They reported that 27 patients (36.5%) were relapsed with significant predictive factors of younger age and female gender (14). In another old cohort study, 92 patients with clinically inactive UC had been followed up for over 48 weeks. Among them, 35 patients (38%) relapsed who had a significant higher previous relapse rate than non-relapsers (11). Other reported relapse rates from different studies were 37.3% (17), 20% (18), 26.2% (19) and 26.5% (20). Also, Park et al. in a retrospective study of 84 patients reported that the relapse rate was 24% and 79% in one and six years, respectively (21). In a 10-year prospective cohort study in USA, the relapse rate of 67% was reported in the 771

UC patients (22). Finally, in two retrospective studies, the relapse rate was 38% in 92 American patients (11) and 14% in Japanese patients (23). The relapse rate in the current study was approximately equal to other reported rates, and in agreement with the range reported in controlled clinical trials in quiescent UC. The annual relapse rate of placebo-treated patients was ranged from 38% to 76 % (5). These variations may be due to differences in geographical regions, populations' characteristics, type of the study and also the therapeutic strategies used to treat UC. However, due to the rate of incidence of relapse in the12-month follow up, it is recommended that all patients receive maintenance therapy. Also, it may be an option for very mild course of disease intermittent therapy.

As another finding of the study, no significant difference was detected in treatment with mesalazin between relapsing and non-relapsing patients. Although the effects of new drugs on the relapse of UC were reported recently (24-

30), this effect was not observed in the current study about mesalazin. It is highly recommended to use new generations of UC drugs and increase visits of high risk patients for relapse in the region under study.

As a limitation of the current study, it should be expressed that one of the factors that may determine relapse times is extension of the primary disease. Unfortunately, the study did not consider the extension of UC and its difference among patients and its impact on relapse rates due to lack of appropriate or complete data.

Conclusively, the current study reported the relapse rate of 48.1% in UC patients (M/F= 1.2/1) of IBD registry of gastroenterohepatology research center which was almost equal to many previous reports from other regions of the world. Both relapsed and non-relapsed UC patients received mesalazin as treatment without any significant differences. However, performing further studies on comparison of the effects of different therapeutic strategies on UC patients are highly recommended.

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### Footnotes

**Authors' Contribution:** Study concept and design: Seyed Vahid Hosseini, Seyed Alireza Taghavi, Maryam Moini; acquisition of data: Ali Reza Safarpour, Manoosh Mehrabi, Masood Sepehrimanesh; analysis and interpretation of data: Ali Reza Safarpour, Peyman Jafari, Abbas Rezaianzadeh; drafting of the manuscript: Ali Reza Safarpour, Masood Sepehrimanesh; critical revision of the manuscript for important intellectual content: Seyed Vahid Hosseini, Seyed Alireza Taghavi, Peyman Jafari, Abbas Rezaianzadeh, Maryam Moini, Manoosh Mehrabi, Masood Sepehrimanesh, Ali Reza Safarpour; statistical analysis: Ali Reza Safarpour, Masood Sepehrimanesh; administrative, technical and material support: Seyed Vahid Hosseini, Seyed Alireza Taghavi, Maryam Moini; and study supervision: Seyed Vahid Hosseini, Seyed Alireza Taghavi.

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