



# Risk Factors for Ulcerative Colitis in Shahrekord, Iran: A Case-Control Study

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## Abstract

**Background and aims:** Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) which involves the rectum and colonic mucosa, and is often constantly expanding. Few data are available on risk factors in Chaharmahal and Bakhtiari province. Therefore, the aim of this study was to investigate the association between potential risk factors and UC in Shahrekord.

**Methods:** A case-control study was conducted on patients diagnosed with UC. Overall, 27 new cases of UC and 54 healthy controls in the age range of 20–80 years were studied. Participants were recruited from Pathologic Centers in Shahrekord in 2018. Chi-square test and t test and were used. Logistic regression model was employed to analyze the association between risk factors and UC disease.

**Results:** The mean age at diagnosis was 41.74 years (SD: 7.16 years) and 44.94 years (SD: 6.67 years) for case and control subjects, respectively. Moreover, univariate and multiple odds ratio (OR) showed that there was no significant association between UC and any of the risk factors including gender, marital status, education, diastolic blood pressure, history of diabetes, history of hypertension, permanent use of piped water, night shift work, history of thyroid diseases, depression, history of fatty liver disease, history of kidney stones, and sleep time and wake-up time in the morning.

**Conclusion:** Generally, no significant association was observed between UC and the variables in the present study. Thus, further studies with larger sample size are necessary to better understand the other risk factors and environmental determinants of UC.

**Keywords:** Ulcerative colitis, Inflammatory bowel disease, Risk factors, Case-control

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## Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) which involves the rectum and colonic mucosa, and is often constantly expanding.<sup>1</sup> UC is characterized by diarrhoea, weight loss, pain in the lower left abdomen, rectal bleeding,<sup>2</sup> and remission and frequent relapses.<sup>3</sup> The disease can also lead to complication, surgery, hospitalization, and death. Moreover, it greatly influences the activity and quality of life of the patients.<sup>4,5</sup> Although the etiology of UC has not yet been well known, it seems that genetic, environmental, and immunoregulatory factors affect it.<sup>6,7</sup> The worldwide incidence and prevalence of IBD is rising, and the incidence is higher in industrialised countries compared to developing countries, despite limited information from developing countries.<sup>8</sup> The geographical variability and rising incidence of UC suggest

that environmental factors are involved in the etiology of the IBD<sup>8,9</sup>; however, limited information is available in this regard.<sup>10</sup> Furthermore, few data are available on the risk factors associated in Chaharmahal and Bakhtiari Province. Therefore, the purpose of this study was to investigate the association between prediagnostic risk factors and the risk of UC in Shahrekord, Chaharmahal and Bakhtiari province, Iran.

## Materials and Methods

A case-control study was conducted on the patients diagnosed with UC. Overall, 27 new cases diagnosed with UC and 54 healthy controls in the age range of 20–80 years were studied. Participants were recruited from Pathologic Centers in Shahrekord in 2018. The medical records of all cases were reviewed by gastroenterologists to confirm the

diagnosis. Control subjects were neighbours of UC patients and people who had referred to Shahrekord Cohort Study. In addition, controls were frequency-matched to cases by age and sex. Private face-to-face interviews were conducted by two trained interviewers using a checklist verified by gastroenterologists and one epidemiologist. Participants completed the checklist on demographic characteristics, age of onset of the symptoms, gender, marital status, education, diastolic blood pressure, history of diabetes, history of hypertension, permanent use of piped water, night shift work, history of thyroid diseases, depression, history of fatty liver disease, history of kidney stones, sleep time, wake-up time in the morning, and night-time sleep duration. Prior to the enrolment, informed consent was obtained from each participant.

### Statistical Analysis

Categorical variables were reported as frequency and percentage. Continuous variables were presented as mean and standard deviation (SD). In addition, *t* test and chi-square test were used. Logistic regression was also employed to analyze the association between risk factors and UC disease. Multiple regression was also performed to adjust the confounders. Odds ratios (ORs) and their respective 95% confidence intervals (CIs) were estimated. A *P* value less than 0.5 was regarded as statistically significant. All statistical analyses were performed using SPSS, version 21.0 (SPSS Inc., Chicago, IL, USA).

### Results

Demographic and behavioural characteristics of study population are shown in Table 1. Means of age at UC onset among the case and control participants were

**Table 1.** Details of Baseline Demography, Risk Factors, and Diseases

| Variable                       |              | %Total      | Case (n=27)   | Control (n=54) | P Value |
|--------------------------------|--------------|-------------|---------------|----------------|---------|
|                                |              |             | No. (%)       | No. (%)        |         |
| Gender                         | Male         | 54.3        | 17 (38.6)     | 27 (61.4)      | 0.27    |
|                                | Female       | 43.7        | 10 (27.0)     | 27 (73.0)      |         |
| Marital status                 | Single       | 8.6         | 4 (57.1)      | 3 (42.9)       | 0.16    |
|                                | Married      | 91.4        | 23 (31.3)     | 51 (68.9)      |         |
| Education                      | < Diploma    | 66.7        | 17(31.5)      | 37 (68.5)      | 0.61    |
|                                | >Diploma     | 33.3        | 10 (37)       | 17 (63)        |         |
| History of diabetes            | Yes          | 91.4        | 24 (32.4)     | 50 (67.6)      | 0.57    |
|                                | No           | 8.6         | 3 (42.9)      | 4 (57.1)       |         |
| History of hypertension        | Yes          | 88.9        | 26 (36.1)     | 46 (63.9)      | 0.13    |
|                                | No           | 11.1        | 1 (11.2)      | 8 (88.9)       |         |
| History of fatty liver disease | Yes          | 80.2        | 20 (30.8)     | 45 (69.2)      | 0.32    |
|                                | No           | 19.8        | 7 (43.8)      | 9 (56.2)       |         |
| History of thyroid diseases    | Yes          | 88.9        | 23 (31.9)     | 49 (68.1)      | 0.45    |
|                                | No           | 11.1        | 4 (44.4)      | 5 (55.6)       |         |
| History of kidney stones       | Yes          | 72.8        | 21 (35.6)     | 38(64.4)       | 0.48    |
|                                | No           | 27.2        | 6 (27.3)      | 16 (72.7)      |         |
| Depression                     | Yes          | 88.9        | 24 (33.8)     | 47 (66.2)      | 0.81    |
|                                | No           | 11.1        | 3 (30.0)      | 7 (70.0)       |         |
| Sleep time                     | Before 23:00 | 59.3        | 12 (25.0)     | 36 (75.0)      | 0.05    |
|                                | After 23:00  | 40.7        | 15 (45.5)     | 18 (54.5)      |         |
| Wake-up time in the morning    | Before 6: 00 | 52.6        | 12 (29.3)     | 29 (70.7)      | 0.76    |
|                                | After 6: 00  | 47.4        | 12 (32.4)     | 25 (67.6)      |         |
| Permanent use of piped water   | Yes          | 73.1        | 16 (28.1)     | 41 (71.9)      | 0.39    |
|                                | No           | 26.9        | 8 (38.1)      | 13 (61.9)      |         |
| Night shift work               | Yes          | 10.3        | 5 (62.5)      | 3 (37.5)       | 0.04    |
|                                | No           | 89.7        | 19 (27.1)     | 51 (72.9)      |         |
| Age at disease onset (y)       | (Mean ± SD)  | -           | 41.74 (7.91)  | 44.94 (6.67)   | <0.01   |
| Night-time sleep duration (h)  | (Mean ± SD)  | 7.14 (1.88) | 7.40 (2.35)   | 7.01 (1.60)    | 0.38    |
| Diastolic blood pressure       | (Mean ± SD)  | -           | 94.00 (13.71) | 95.20 (11.23)  | 0.66    |

41.74 years (SD: 7.16 years) and 44.94 years (SD: 6.67 years), respectively ( $P$  value  $< 0.01$ ). Majority of the study participants were male (44 vs. 37); while 32.4% of cases and 67.6% of controls were married ( $P$  value = 0.27), with less than diploma degree (31.5% for cases and 68.5% for controls,  $P$  value = 0.61).

The normal diastolic blood pressures were 94.0 mmHg and 95.2 mmHg for the case and control participants, respectively ( $P$  value = 0.66); 91.4% had a history of diabetes (32.4% for cases and 67.6% for controls,  $P$  value = 0.66), 88.9% had a history of hypertension (36.1% for cases and 73.9% for controls,  $P$  value = 0.13), 80.2% had a history of fatty liver disease (30.8 for cases and 69.2% for controls,  $P$  value = 0.32), 88.0% had a history of thyroid disease (31.9% for cases and 68.1% for controls,  $P$  value = 0.45), 72.8% had a history of kidney stones (35.6% for cases and 64.4% for controls,  $P$  value = 0.48),

and 88.9% had experience of depression (33.8% for cases and 66.3% for controls,  $P$  value = 0.13).

The sleep time for 40.7% of participants was after 23 o'clock (45.5 % for cases and 54.5% for controls,  $P$  value = 0.05) and wake-up time in the morning for 47.4% of them was after 6 o'clock (32.4% for cases and 67.6% for controls,  $P$  value = 0.76). The mean sleep duration was  $7.14 \pm 1.88$  hours per night, with a mean of  $7.01 \pm 1.60$  for the control subjects and  $7.40 \pm 2.35$  hours of sleep per night for UC subjects. Overall, there were no significant differences between the two groups in terms of the risk factors.

Univariate and Multiple Analysis of Risk Factors for UC Demographic characteristics of the study participants and related risk factors are shown in Table 2. Based on the univariate analysis, there was no significant correlation between UC and any of the factors of gender, marital

**Table 2.** Risk factors Associated With Ulcerative Colitis in the Study Participants

| Variable                       |                            | %     | Univariate OR (95% CI) | $P$ Value | Adjusted OR (95% CI) | $P$ Value |
|--------------------------------|----------------------------|-------|------------------------|-----------|----------------------|-----------|
| Gender                         | Male                       | 54.32 | Ref                    |           | -                    |           |
|                                | Female                     | 45.68 | 1.70 (0.66-4.37)       | 0.27      | -                    |           |
| Marital status                 | Single                     | 8.64  | Ref                    |           | Ref                  | Ref       |
|                                | Married                    | 91.36 | 0.33 (0.07-1.63)       | 0.17      | 0.68 (0.11-4.24)     | 0.68      |
| Education                      | Less than a diploma degree | 66.66 | Ref                    |           | Ref                  |           |
|                                | Diploma degree and higher  | 33.34 | 1.28 (0.46-3.37)       | 0.67      | -                    |           |
| History of diabetes            | No                         | 8.64  | Ref                    | 0.57      | -                    |           |
|                                | Yes                        | 91.36 | 0.13 (0.13-3.08)       |           | -                    |           |
| History of hypertension        | No                         | 88.88 | Ref                    |           | Ref                  |           |
|                                | Yes                        | 11.12 | 4.52 (0.53-38.19)      | 0.16      | 3.13 (0.34-28.48)    | 0.30      |
| Permanent use of piped water   | Yes                        | 74.00 | Ref                    |           | -                    |           |
|                                | No                         | 26.00 | 1.57 (0.55-4.52)       | 0.39      | -                    |           |
| Night shift work               | No                         | 86.41 | Ref                    |           | Ref                  |           |
|                                | Yes                        | 13.59 | 4.47 (0.97-20.56)      | 0.05      | 3.82 (0.71-20.55)    | 0.11      |
| History of thyroid diseases    | No                         | 11.11 | Ref                    |           | -                    |           |
|                                | Yes                        | 88.89 | 0.58 (0.14-2.39)       | 0.45      | -                    |           |
| Depression                     | No                         | 12.34 | Ref                    |           | -                    |           |
|                                | Yes                        | 87.66 | 1.19 (0.28-5.02)       | 0.81      | -                    |           |
| History of fatty liver disease | No                         | 19.75 | Ref                    |           | -                    |           |
|                                | Yes                        | 80.25 | 0.57 (0.18-1.75)       | 0.32      | -                    |           |
| History of kidney stones       | No                         | 72.83 | Ref                    |           | -                    |           |
|                                | Yes                        | 27.17 | 1.47 (0.50-4.33)       | 0.48      | -                    |           |
| Sleep time                     | Before 23:00               | 59.25 | Ref                    |           | Ref                  |           |
|                                | After 23:00                | 40.75 | 2.50 (0.97-6.44)       | 0.58      | 2.10 (0.72-6.06)     | 0.16      |
| Wake-up time in the morning    | Before 6:00                | 50.61 | Ref                    |           | -                    |           |
|                                | After 6:00                 | 49.39 | 1.16(0.44-3.03)        | 0.72      | -                    |           |
| Age at disease onset (y)       |                            |       | 0.92 (0.85-1.00)       | 0.06      | 0.93 (0.85-1.01)     | 0.11      |
| Night-time sleep duration      | (Mean $\pm$ SD)            |       | 1.11 (0.87-1.43)       | 0.38      | -                    |           |
| Systolic blood pressure        | (Mean $\pm$ SD)            |       | 0.99 (0.95-1.03)       | 0.65      | -                    |           |

status, education, diastolic blood pressure, history of diabetes, history of hypertension, permanent use of piped water, night shift work, history of thyroid diseases, depression, history of fatty liver disease, history of kidney stones, and sleep time and wake-up time in the morning. As can be seen in the univariate analysis, age at disease onset had a protective effect on UC (OR=0.92, 95% CI: 0.85-1.00). The variables of marital status, history of hypertension, night shift work, and sleep time (Table 2) with a *P* value less than 0.2 in univariate analysis were entered into the multiple regression analysis, though no significant correlations were found between them and UC.

## Discussion

Exploring UC risk factors would be a great opportunity to advance our understanding of disease pathogenesis by investigating this aspect when the disease is newly emerging. The present study showed that there were no significant correlations between UC and gender, marital status, education, diastolic blood pressure, history of diabetes, history of hypertension, permanent use of piped water, night shift work, history of thyroid diseases, depression, history of fatty liver disease, history of kidney stones, sleep time, wake-up time in the morning, and night-time sleep duration.

Moreover, no significant differences were observed between UC patients and control subjects in terms of education and marital status in this study. Likewise, no significance difference was found in some previous studies between UC cases and control subjects regarding education and marital status.<sup>11,12</sup> Furthermore, there was no difference in gender distribution between cases and controls in the present study; this result agreed with that of a study by Ng et al.<sup>13</sup> The association between interrupted sleep and IBD might be bidirectional, such that whilst poor sleep quality might exacerbate IBD, increased disease activity in turn might disrupt the sleep. Both reduced and prolonged duration of sleep were associated with increased risk of UC.<sup>14</sup> Several observational studies have found an increased prevalence of sleep disruption in IBD.<sup>14-16</sup> However, according to the results of the present study, there was no significant correlation between UC and sleep duration; this result consisted with that of the study of Ananthakrishnan et al.<sup>17</sup> Thus, it is possible that sleep quality as an environmental variable does not truly impact the UC. Further studies are warranted to evaluate the impact of sleep quality on the disease outcomes in patients with UC. Additionally, in this study there was no significant difference in terms of history of thyroid disease between the cases and controls. This result corroborated that of Bianchi et al.<sup>18</sup> in that there was no difference between UC patients and control subjects, although enlargement of the thyroid gland occurred more often in CD patients compared to the control subjects. Similarly, the study of Neubauer et al<sup>19</sup> reported that enlargement of

the thyroid gland was observed more commonly in UC patients than in control individuals. Furthermore, the study of Tsai et al<sup>20</sup> demonstrated a higher proportion of prior hyperthyroidism among UC patients compared to the control subjects.

Many studies have documented that UC is a multifactorial disease.<sup>21,22</sup> For example, a previous study mentions that genetic expressions, immune responses, environmental factors, and patient lifestyle might play major roles in the incidence of UC.<sup>21,23</sup> Thus, further studies are necessary to better understand the other risk factors and environmental determinants of UC.

## Limitations

We are aware that a number of limitations might have influenced the obtained results. A main plausible error of the study is that it was a retrospective study, relying on recall of participants' events and ingestions. There is a potential recall bias on some variables such as sleep time, wake-up time in the morning, and night-time sleep duration.

The second limitation of this study is the small number of cases. Therefore, the association found between risk factors and prevalence of UC needs to be tested in larger samples. The low sample size may reduce the statistical power to demonstrate a difference.

## Ethical Approval

The study protocol was approved by the Ethics Committee of Shahrekord University of Medical Science (Code of Ethics: IR.SKUMS.RE.1396.239).

## Conflict of Interest Disclosures

The authors declare no conflicts of interest.

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