ORIGINAL ARTICLE

Sleep quality and associated factors in Iranian inflammatory bowel disease patients

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Background: Sleep is essential in maintaining health and quality of life. Inflammatory bowel disease (IBD) patients suffer from poor sleep quality. This study aimed to investigate the prevalence of sleep disturbances in Iranian IBD patients as well as the variables which can be attributed to the quality of sleep in IBD patients. **Materials and Methods:** Seventy-one patients filled in Pittsburg Sleep Quality Index (PSQI) questionnaire and a sociodemographic questionnaire. Disease activity was assessed by Crohn's Disease (CD) Activity Index and Ulcerative Colitis (UC) Activity Index. Regression analysis was used to identify the association between sociodemographic and disease characteristics with sleep quality. **Results:** We found that 32.4% of all patients, 23.1% of patients with "in remission to mild" disease, and 66.7% of patients with "moderate" disease, had poor sleep quality. CD patients were more likely to have poor sleep quality comparing UC ones in crude (odds ratio [OR] =2.14; 95% confidence interval [CI] 1.14–4.04) and adjusted (OR = 6.19; 95% CI 1.13, 34.07) models. Patients with good quality of sleep had lower systolic blood pressure and diastolic blood pressure (P = 0.09 and 0.035 respectively). **Conclusion:** Notable percentage of IBD patients suffer from poor sleep quality even in the remission phase. Treatment of sleep disturbances, especially in CD patients, is recommended in the IBD patient-care program.

Key words: Inflammatory bowel disease, physical activity, sleep quality

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INTRODUCTION

Sleep is essential in maintaining health and quality of life. Good sleep acts as a regulation of the immune and neuroendocrine system. Impaired sleep is linked with adverse health consequences such as gastrointestinal (GI) symptoms, hypertension, cardiovascular disease, impaired glucose control, increased risk of obesity, and increased inflammation. (1-3) Sleep disturbance is also associated with other complaints such as fatigue, anxiety and depression, and more frequent physical complaints such as vasomotor and endocrine symptoms.[1,2]

The inflammatory bowel diseases (IBDs) including Crohn's disease (CD) and ulcerative colitis (UC) are chronic relapsing diseases which possibly caused by the interaction of environment, immunogenetics, and lifestyle. Impaired sleep can be one of these environmental factors through alterations in immune functions.[3,4] Previous studies reported impaired sleep in IBD patients. These patients had significantly prolonged sleep latency, frequent sleep disruption, higher consumption of sleeping medications, daytime fatigue, and poor overall sleep quality compared to healthy controls. Poor sleep quality is prevalent even in inactive IBD patients.[5] Patients in clinical remission with abnormal sleep have a high likelihood of subclinical disease activity (i.e., histologic evidence of inflammation).[3] Furthermore, sleep disturbances are associated with more disease flares.[6]

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The prevalence of sleep disturbances is 48%–72% in inactive patients and 73% to as high as 100% in patients with active disease.[3,6] Furthermore, disease activity, depression, female gender, smoking, and use of corticosteroids or narcotics have been associated with sleep disturbance in IBD patients in the previous research.[6]

Limited experience in this field exists in Iran. This study aims to assess sleep characteristics, the prevalence of sleep disturbances and its related factors in a sample of Iranian IBD patients.

MATERIALS AND METHODS

In our cross-sectional study, IBD patients were invited to participate in Poursina Hakim Gastroenterology Clinic in Isfahan, Iran. The inclusion criteria were: proved diagnosis of IBD based on British guideline[7] and capability and interest to participate. Exclusion criteria were: patients with congestive heart failure, cirrhosis, peptic ulcer disease, hypothyroidism or hyperthyroidism, cancer, sleep apnea, psychological disorders, recent hospitalization or surgery, and shift workers. Sample size calculation and the method of sampling was entirely explained in our recent article.[8]

Demographic variables consisted of age, gender, marital status, level of education, and occupation status. Anthropometric variables contained weight, height, abdominal circumference, and body mass index (BMI). Moreover, health status was defined as a health variable containing the levels of systolic blood pressure (SBP) and diastolic blood pressure (DBP), fasting blood sugar (FBS), triglyceride, low-density lipoprotein, high-density lipoprotein, cholesterol, and being anemic/nonanemic. For each variable, 0 was calculated if it was good and 1was calculated if the patients had abnormal values. This variable was classified in three groups: fairly good (patients with less than 3 points); fairly bad (patients with 4–7 points); and bad (patients with more than 8 points).

Physical activity was classified into three groups (low, moderate, and high) based on the International Physical Activity Questionnaire short form. It is a self-administered questionnaire which assesses physical activity during seven recent days through seven questions.[9]

BP was measured twice with an interval of 10 min by the physician. New cases of hypertension diagnosed by the definition of SBP ≥140 mmHg or DBP ≥90.[10] New cases and known cases of hypertension constitute the overall percentage of the hypertension group. Blood samples were obtained to assess laboratory variables.

Quality of sleep

Pittsburgh Sleep Quality Index (PSQI) questionnaire developed by Buysee *et al*. was used for assessment of sleep quality over the last month, containing 19 items with seven components, including sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction. Every component weighted equally on a 0–3 scale. All components were summed to yield the global score which ranged from 0 to 21. Higher scores show poorer sleep quality. The global score ≥6 indicates bad sleep quality. The Persian version of PSQI was validated by Farrahi Moghaddam *et al*.[11]

Severity of disease

Ulcerative Colitis Activity Index (UCAI) was used to measure the severity of disease in UC patients. UCAI was calculated by Seo *et al*. Formula: "UCAI = (60 × number of bloody stools per day) + (13 × number of bowel movements per day) + (0.5 × erythrocyte sedimentation rate [mm/h]) − (4 × hemoglobin [g/dl]) − (15 × serum albumin [g/dl]) +200."

UCAI <150, between 150 and 220 and more than 220 were considered to be mild, moderate, and severe UC disease, respectively.[12]

Crohn's Disease Activity Index (CDAI) was used to measure disease activity in CD patients. This index had eight questions, which were filled out by a physician. CDAI ranged from 0 to 600. CDAI <150, between 150 and 220, between 220 and 450, and more than 450 were considered in remission, mild, moderate, and severe, respectively.[13]

Statistical analysis

Statistical analyses were conducted using SPSS version 18 software (IBM Corp., 2011, IBM SPSS Statistics for Windows, NY, EUA). The study utilized three sets of analysis: basic descriptive statistics, univariate analyses, and multivariate analyses.

Descriptive statistics were derived for all variables of interest in this study. Mean and standard deviation (SD) were calculated for quantitative variables, whereas frequency and percentage were generated for qualitative variables.

For univariate analyses, Chi-square test, likelihood Chi-square test (G test), and Gamma test have been used to evaluate the relationship between two categorical variables. The likelihood ratio approach had to be modified slightly for the composite null hypothesis. A composite hypothesis is a one in which the covariance is not written in terms of fixed values of a parameter θ. It is often stated by saying the parameter θ is in a specified subset of the parameter space. (H_0:θ ε Θ_0 *vs.* H_α:θ ε Θ_0^c).[14]

In multivariate analyses, the effect of IBD type on Pittsburg Sleep Quality Index (PSQI) was assessed using a binary logistic regression model to determine odds ratio (OR) and 95% confidence interval (CI). Moreover, a multiple logistic regression model with some predictors was fit using the least squares algorithm to obtain maximum likelihood estimates of the parameters.[15] This model was run in forward likelihood method, which all variables of < 0.1 in the univariate regression analyses were included as covariates to adjust for potential confounding effects. Then, the adjusted odds ratio (AORs) and 95% CIs were determined. Furthermore, ordinal logistic regression analyses were performed for subscales of PSQI with the proportion of odds model. Response variables were categorical variables that had four possible levels with a natural ordering. The first subscale of PSQI, subjective sleep quality, was grouped in four ordered categories (very good, fairly good, fairly bad, and very bad); and the rest of subscales of PSQI had four ordered classifications (no problem at all, only a very slight problem, somewhat of a problem, and a very big problem). Predictor variables were the same as those of multiple logistic regression analysis. Proportional odds assumption of the model was checked by the test of parallel lines. Statistical analyses were set at a two-tailed $P < 5\%$.

Ethical consideration

Ethical protocols were approved by the Ethics Committee of Isfahan University of Medical Sciences. The project number is 395047.

RESULTS

Overall, 71 patients with IBD participated in this study. The mean age (±SD) of all participants was 38.17 ± 11.90 years. The mean BMI was 23.50 ± 4.00 kg/m^2 for males and 25.74 ± 5.87 kg/m^2 for females. 17.4% of participants were obese and 10.1% of participants were underweight. 29.6% of patients were anemic. The smokers and those who had surgery due to IBD complications were omitted. None of our sample patients consumed biologic agents or enteral products. Our patients did not have complications such as anal fissure, fistula, or abscess.

About 32.4% of all patients, 23.1% of patients with "in remission to mild" disease, and 66.7% of patients with "moderate" disease, had poor sleep quality. In UC patients, 16.7% of patients with "mild" disease and 64.3% of patients with "moderate" disease had poor sleep quality. In CD patients, 31.8% of patients with "in remission to mild" disease had poor sleep quality.

As presented in Table 1, good sleepers had less SBP and DBP ($P = 0.009$ and 0.035 respectively). Furthermore, good sleepers were less hospitalized ($P = 0.029$).

According to Figure 1, good and poor sleepers had a similar bedtime, rise time, and total sleep, but they had a significant difference in sleep latency: good sleepers' sleep latency was 14 ± 13 min, while poor sleepers had 36 ± 32 min sleep latency ($P = 0.008$). There was no significant difference in sleep latency between three physical activity groups ($P = 0.054$), although as physical activity increases, sleep latency decreased.

Table 2 compared components of PSQI between UC and CD patients. It shows that there was no difference in mean values of global PSQI between patients with CD and patients with UC ($P = 0.089$).

In Table 3, multiple logistic regression analysis was performed to identify IBD type (UC and CD) independently associated with sleep quality (good and poor sleep quality). Covariates included all variables with a $P < 0.1$ in the univariate analysis as well as health status, the severity of disease, type of drug, hospitalization, and using folic acid. The results indicate that, after adjusting for confounding variables, IBD type (AOR = 6.19, 65% CI = 1.13–34.07) had a significant positive relationship with sleep quality ($P = 0.036$). Thereupon, the odds of having a good sleep quality in UC patients are 6.19 times more likely than CD patients (model $\chi^2_{(2)}$=0.107, $P < 0.001$; Nagelkerke $R^2 = 0.337$; Hosmer and Lemeshow test, $P = 0.948$). Furthermore, the sensitivity, specificity, and accuracy of the test were measured, respectively, 64.3%, 82.6%, and 78.3%.

Moreover, since the subscales of PSQI (as the dependent variables) were classified into four ordered categories, the proportional odds models were used to reflect substantial variability of subscales of PSQI frequency among the IBD types. Predictor variables were the same as the logistic regression model in Table 3. Overall, ORs in unadjusted ordinal regression models, and AORs in multiple ordinal logistic regression models indicate that IBD type (UC vs. CD) was not related to seven PSQI subscales, and total physical activity ($P > 0.05$ for all).

DISCUSSION

This is the first study concerning sleep in Iranian IBD patients. It evaluated the associations of sleep in IBD with multiple relevant parameters simultaneously, including sociodemographic, disease characteristics; the presence of anemia, BMI, FBS, lipid profile, BP, physical activity; and folic acid consumption.

Our data showed that 32.4% of all patients, 23.1% of patients with "in remission to mild" disease, and 66.7% of patients with "moderate" disease, had poor sleep quality. Sleep disturbance is also reported in various chronic inflammatory diseases such as asthma, systemic lupus erythematosus, and

Table 1: Baseline demographic and clinical variables for the total sample and the sample stratified by sleep quality (based on Pittsburg Sleep Quality Questionnaire scores), in Isfahan, Iran, 2016 (*n*=71)

Variable		Total sample	Sample stratified by sleep quality		*P*
			Good (*n*=46)	Poor (*n*=22)	
Age (years)	Mean±SD	38.2±11.9	38.4±11.6	38.4±13.5	0.996[b]
Gender	Males, *n* (%)	25 (36.8)	17 (37.0)	8 (36.4)	0.962[c]
Marital status	Single, *n* (%)	17 (25.8)	10 (22.7)	7 (31.8)	0.426[c]
	Married, *n* (%)	49 (74.2)	34 (77.3)	15 (68.2)	
Level of education	Middle school and less, *n* (%)	18 (26.9)	10 (22.2)	9 (36.4)	0.442[c]
	High school, *n* (%)	19 (28.4)	13 (28.9)	6 (27.3)	
	College and more, *n* (%)	30 (44.8)	22 (48.9)	8 (36.4)	
Occupation status	Unemployed, *n* (%)	37 (54.4)	25 (54.3)	12 (54.5)	0.988[c]
	Employed, *n* (%)	31 (45.6)	21 (45.7)	10 (45.5)	
BMI (kg/m^2)	Mean±SD	24.96±5.38	25.46±5.75	24.28±4.86	0.359[b]
	Under-weight, *n* (%)	7 (10.6)	4 (8.7)	3 (15.0)	0.081[d]
	Normal, *n* (%)	31 (47.0)	26 (56.5)	5 (25.0)	
	Over-weight, *n* (%)	17 (25.8)	11 (23.9)	6 (30.0)	
	Obese, *n* (%)	11 (16.7)	5 (10.9)	6 (30.0)	
Weight (kg)	Mean±SD	68.24±13.78	67.68±14.22	67.90±12.60	0.953[b]
Height (cm)	Mean±SD	165.82±10.40	167.01±10.06	164.43±11.30	0.360[b]
Abdominal[#] (cm)	Mean±SD	90.02±14.95	89.18±14.63	89.61±15.41	0.918[b]
SBP (mmHg)	Mean±SD	116.82±16.05	112.69±15.56	126.15±23.94	0.009*[,b]
DBP (mmHg)	Mean±SD	78.13±13.29	75.76±13.02	83.47±13.31	0.035*[,b]
FBS (mg/dl)	Mean±SD	89.46±14.23	89.18±14.95	91.16±13.33	0.648[b]
	No diabetes, *n* (%)	45 (81.8)	32 (82.1)	13 (81.3)	0.934[f]
	Pre-diabetic, *n* (%)	7 (12.7)	5 (12.8)	2 (12.5)	
	Diabetic, *n* (%)	3 (5.5)	2 (5.1)	1 (6.3)	
TG (mg/dl)	Mean±SD	110.29±50.79	116.07±52.90	97.13±47.51	0.235[b]
	Good, *n* (%)	41 (78.8)	14 (93.3)	27 (73.0)	0.101[d]
LDL (mg/dl)	Mean±SD	77.22±53.87	78.23±51.00	69.95±61.10	0.560[b]
	Good, *n* (%)	24 (47.1)	6 (40.0)	18 (50.0)	0376[c]
HDL (mg/dl)	Mean±SD	50.11±14.63	49.85±16.44	48.87±10.51	0.832[b]
	Good, *n* (%)	39 (76.5)	12 (80.0)	27 (75.0)	0.503[d]
Chol (mg/dl)	Mean±SD	165.49±43.69	166.20±42.71	164.07±47.21	0.884[b]
	Good, *n* (%)	33 (78.6)	11 (78.6)	22 (78.6)	0.645[d]
Anemia	Anemic, *n* (%)	19 (27.9)	13 (28.3)	6 (27.3)	0.346[c]
Hypertension	Yes, *n* (%)	14 (21.9)	8 (17.8)	6 (31.6)	0.222[c]
Drug type	Not use, *n* (%)	1 (1.5)	0 (0.0)	1 (4.5)	0.260[d]
	5-ASA, *n* (%)	13 (19.7)	2 (9.1)	11 (23.9)	
	5-ASA and corticosteroid, *n* (%)	4 (6.1)	2 (9.1)	2 (4.3)	
	5-ASA and immunomodulator, *n* (%)	33 (50.0)	9 (40.9)	24 (52.2)	
	5-ASA and corticosteroid and immunomodulator, *n* (%)	16 (24.2)	8 (36.4)	8 (17.4)	
Antibiotic	Not use, *n* (%)	54 (79.4)	16 (72.7)	38 (82.6)	0.346[c]
Folic acid	Not use, *n* (%)	22 (32.4)	5 (22.7)	17 (37.0)	0.241[c]
Duration of disease (years)	Mean±SD	8.2±5.5	7.6±4.6	7.6±4.6	0.338[b]
	<5 years, *n* (%)	21 (30.9)	14 (30.4)	7 (31.8)	0.908[f]
	>5 years, *n* (%)	47 (69.1)	32 (69.6)	15 (68.2)	
Hospitalization (*n*)	Mean±SD	2±4	1±4	3±4	0.230[b]
	Yes, *n* (%)	25 (39.7)	14 (31.1)	11 (61.1)	0.029*[,d]
IBD type	CD, *n* (%)	24 (35.3)	16 (34.8)	8 (36.4)	0.898[c]
	UC, *n* (%)	44 (64.7)	30 (65.2)	14 (63.9)	1.000[f]
CDAI	In remission, *n* (%)	21 (31.3)	15 (33.3)	6 (27.3)	
	Mild, *n* (%)	1 (1.5)	0 (0.0)	1 (4.5)	

Contd...

Table 1: Contd...

Variable		Total sample	Sample stratified by sleep quality		*P*
			Good (*n*=46)	Poor (*n*=22)	
	Moderate, *n* (%)	1 (1.5)	0 (0.0)	1 (4.5)	
	Severe, *n* (%)	1 (1.5)	0 (0.0)	1 (4.5)	
UCAI	Mild, *n* (%)	30 (44.1)	25 (54.3)	5 (22.7)	0.105[f]
	Moderate, *n* (%)	14 (20.6)	5 (10.9)	9 (40.9)	
Health status[$]	Fairly good, *n* (%)	5 (7.4)	1 (2.2)	4 (18.2)	0.341[f]
	Fairly bad, *n* (%)	15 (22.1)	12 (28.1)	3 (13.6)	
	Bad, *n* (%)	48 (70.6)	33 (71.7)	15 (68.2)	
Physical activity[£]	Low (*n*=38)	38 (56.7)	26 (57.8)	12 (54.5)	0.727[f]
	Moderate (*n*=16)	16 (23.9)	11 (24.4)	5 (22.7)	
	High (*n*=13)	13 (19.4)	8 (17.8)	5 (22.7)	

[$]Health status: Refers to the levels of FBS, TG, LDL, HDL, Chol, blood pressure, and anemic or not, that fairly good: Patients with <3 points; fairly bad: Patients with 4–7 points; and bad: Patients with >8 points. [#]Abdominal circumference; [£]Based on IPAQ scores; [b]*P* value by independent samples *t*-test; [c]*P* value by Pearson Chi-square test; [d]*P* value by likelihood ratio test; [f]P value by gamma test; *Statistically significant at the level of 5%. PSQI=Pittsburgh Sleep Quality Index (good sleep quality: global PSQI score <6.0, and poor sleep quality: Global PSQI score≥6.0). SBP=Systolic blood pressure; DBP=Diastolic blood pressure; FBS=Fasting blood sugar; TG=Triglyceride; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; Chol=Cholesterol; IBD=Inflammatory bowel disease; CD=Crohn's disease; UC=Ulcerative colitis; CDAI=Crohn's Disease Activity Index; UCAI=Ulcerative Colitis Activity Index; IPAQ=International Physical Activity Questionnaire

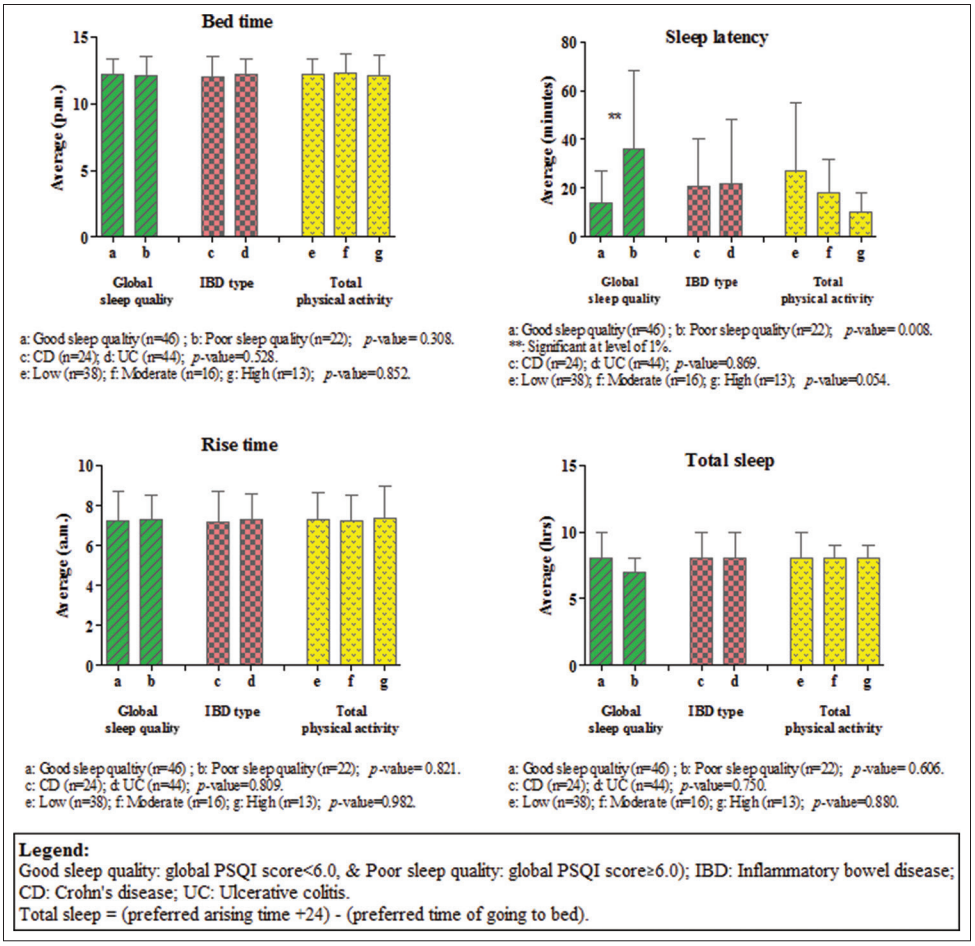

Figure 1: Comparison between groups in global sleep quality (based on Pittsburg Sleep Quality Questionnaire scores), inflammatory bowel disease type, and physical activity (based on International Physical Activity Questionnaire scores), in Isfahan, Iran, 2016 (*n* = 71)

rheumatoid arthritis.[16-19] In our recent work, we found that poor sleep is associated with lower health quality of life.[8] There are few studies investigating sleep in IBD patients; the largest one reported that 73% of patients with active disease and 48% of patients who are in remission have poor sleep quality.[6] Mentioned statistics are near to results we found in our study. Our lower prevalence may be due to not having enough patients with severe disease in the sample or sample's different characteristics or different measures used to determine patients with poor sleep quality.

Table 2: Global sleep quality and seven Pittsburgh Sleep Quality Index subscales in the total sample and the sample stratified by inflammatory bowel disease type, in Isfahan, Iran, 2016 (*n*=71)

	Total sample	IBD type		*P*
		UC (*n*=46)	CD (*n*=22)	
Global sleep quality, *n* (%)				
Good	46 (67.6)	30 (68.2)	16 (66.7)	0.898[a]
Poor	22 (32.4)	14 (31.8)	8 (33.3)	
PSQI sub-scale				
Subjective sleep quality 4, *n* (%)				
Very good	24 (33.8)	16 (34.8)	8 (32.0)	0.725[b]
Fairly good	36 (50.7)	22 (47.8)	14 (56.0)	
Fairly bad	6 (8.5)	5 (10.9)	1 (4.0)	
Very bad	5 (7.0)	3 (6.5)	2 (8.0)	
Sleep latency, *n* (%)				
No problem at all	17 (34.6)	10 (22.2)	7 (29.2)	0.927[b]
Only a very slight problem	24 (34.8)	16 (35.6)	8 (33.3)	
Somewhat of a problem	21 (30.4)	14 (31.1)	7 (29.2)	
A very big problem	7 (10.1)	5 (11.1)	2 (8.3)	
Sleep duration, *n* (%)				
No problem at all	26 (37.7)	19 (42.2)	7 (29.2)	0.533[b]
Only a very slight problem	32 (46.4)	18 (40.0)	14 (58.3)	
Somewhat of a problem	3 (4.3)	2 (4.4)	1 (4.2)	
A very big problem	8 (11.6)	6 (13.3)	2 (8.3)	
Habitual sleep efficiency, *n* (%)				
No problem at all	53 (77.9)	33 (75.0)	20 (83.3)	0.323[b]
Only a very slight problem	7 (10.3)	4 (9.1)	3 (12.5)	
Somewhat of a problem	3 (4.4)	3 (6.8)	0 (0.0)	
A very big problem	5 (7.4)	4 (9.1)	1 (4.2)	
Sleep disturbance, *n* (%)				
No problem at all	5 (7.0)	2 (4.3)	3 (12.0)	0.366[b]
Only a very slight problem	38 (53.5)	27 (58.7)	11 (44.0)	
Somewhat of a problem	25 (35.2)	16 (34.8)	9 (36.0)	
A very big problem	3 (4.2)	1 (2.2)	2 (8.0)	
Use of sleeping medication, *n* (%)				
No problem at all	25 (35.7)	15 (33.3)	10 (40.0)	0.520[b]
Only a very slight problem	17 (24.3)	12 (26.7)	5 (20.0)	
Somewhat of a problem	10 (14.3)	8 (17.8)	2 (8.0)	
A very big problem	18 (2.7)	10 (22.2)	8 (32.0)	
Daytime dysfunction, *n* (%)				
No problem at all	20 (28.2)	11 (23.9)	9 (28.2)	0.649[b]
Only a very slight problem	28 (39.4)	19 (41.3)	9 (36.0)	
Somewhat of a problem	14 (19.7)	9 (19.6)	5 (20.0)	
A very big problem	9 (12.7)	7 (15.2)	2 (8.0)	

[a]*P* value by Pearson Chi-square test, [b]*P* value by likelihood ratio test. PSQI=Pittsburgh Sleep Quality Index (good sleep quality: Global PSQI score<6.0, and poor sleep quality: global PSQI score≥6.0). IBD=Inflammatory bowel disease; CD=Crohn's disease; UC=Ulcerative colitis

CD patients were more likely to have a bad sleep quality comparing UC patients in both crude (OR = 2.14) and adjusted (OR = 6.19) regression models. One hypothesis is that subclinical inflammation in these patients may disturb the sleep-wake cycle. The patients in remission who suffer disturbed sleep have a high likelihood of subclinical inflammation.[3] The CD patients who were in remission and had poor sleep quality had two-fold possibility of experiencing a flare-up in 6-month follow-up compared to those with good sleep quality.[6] Sleep is altered during infection and sickness. Furthermore, immune signaling molecules (such as the cytokine interleukin 1 [IL-1]) play a role in the regulation of normal sleep.[20] Tumor necrosis factor-alpha, IL-1, and IL-6 are major cytokines in normal sleep physiology.[21] One of the contributing factors in the pathogenesis of IBD is the inappropriate response of the immune system; therefore, the disturbed immune system may lead to impaired sleep.

Having CD was one of the predictors of disturbed sleep in a cohort study (OR = 1.35).[6] More severe symptoms such as bowel movements can disturb sleep continuity, but due

Table 3: Results of binary and ordinal regression models of inflammatory bowel disease type (ulcerative colitis vs. Crohn's disease) associated with global sleep quality, Pittsburgh Sleep Quality Index subscales, and total physical activity in Isfahan, Iran (*n*=71)

Dependent variable	β	OR (95% CI)	*P*	β	AOR† (95% CI)	*P*
Global sleep quality (good vs. poor sleep quality)[a]	0.76	2.14 (1.14–4.04)	0.019*	1.82	6.19 (1.13–34.07)	0.036*
PSQI subscales						
Subjective sleep quality (vs. very good)[b]	−0.02	0.98 (0.39–2.47)	0.963	0.32	1.37 (0.44–4.23)	0.585
Sleep latency (vs. no problem at all)[c]	−0.28	0.76 (0.31–1.87)	0.548	0.53	1.69 (0.56–5.09)	0.350
Sleep duration (vs. no problem at all)[c]	0.26	1.30 (0.51–3.30)	0.588	0.53	1.70 (0.52–5.50)	0.379
Habitual sleep efficiency (vs. no problem at all)[c]	−0.58	0.56 (0.16–2.01)	0.374	-0.25	0.78 (0.15–3.93)	0.759
Sleep disturbances (vs. no problem at all)[c]	0.15	1.00 (0.46–2.98)	0.751	0.34	1.41 (0.43–4.55)	0.570
Use of sleeping medication (vs. no problem at all)[c]	−0.003	1.00 (0.41–2.41)	0.995	0.67	1.95 (0.61–6.20)	0.257
Daytime dysfunction (vs. no problem at all)[c]	−0.49	0.62 (0.25–1.51)	0.287	-0.61	0.54 (0.18–1.60)	0.268
Total physical activity (vs. high)	0.04	1.04 (0.40–2.70)	0.944	1.72	5.60 (0.84–37.27)	0.075

[a]Global sleep quality was assessed with the PSQI good sleep quality: PSQI score <6.0 and poor sleep quality: PSQI score ≥6.0; analysis was performed by binary logistic regression analysis; [b]Using ordinal logistic regression analysis. The dependent variable had four ordered categories (very bad, fairly bad, fairly good, and very good). The reference category was assumed as the "very good" in the analysis; [c]Using ordinal logistic regression analysis. The dependent variable had four ordered categories (no problem at all, only a very slight problem, somewhat of a problem, and a very big problem). The reference category was assumed the "no problem at all" in the analysis, [d]Total physical activity was assessed with the international physical activity (IPAC) questionnaire. The variable was classified as low, moderate, and high. The analysis was performed by binary logistic regression analysis and high IPAQ was considered as the referenced category, †Adjusted for potential confounders such as health status, severity of disease, type of drug, hospitalization, and using folic acid, *Significant at level of 5%. IBD=Inflammatory bowel disease; PSQI=Pittsburg Sleep Quality Index; β=Regression coefficient using Wald statistic; OR=Odds ratio; AOR=Adjusted OR; CI=Confidence interval

to considering disease severity in the adjusted analysis, subclinical inflammation may describe more chance of sleep disturbance in CD patients because of pan GI inflammation, transmural inflammation, and more extra-GI symptoms in CD. Psychosocial dysfunction, depression, and anxiety were more common in CD patients rather than UC ones.[9,22,23] Thus, worse sleep quality in CD may be due to psychological issues.

Good and bad sleepers had a similar bedtime and rise time, but they were different in sleep latency time (P = 0.008). Although it was not statistically significant (P = 0.054) while increasing in physical activity degree, sleep latency time decreases. Previous researches indicate that higher habitual physical activity was associated with better sleep quality in elderly people.[21] intervention of increasing physical activity improved sleep in nursing home residents.[23] Therefore, this may consider the conclusion that physical activity may have a role in decreasing sleep latency and thus improving sleep quality.

We also found that bad sleepers have higher SBP and DBP. The design of our study is not capable of differentiating that higher BP resulted in lower quality of sleep or poor sleep quality caused higher BP. It is reported that elderly people whose time in bed (TIB) was >8 h and <6 h/day, SBP was significantly higher than the group whose TIB was 6–8 h.[24] The global PSQI score and its subscales were associated with hypertension and higher BP.[25,26]

Some researches indicate that female gender is a risk factor of sleep disturbance in general population[27] as well as in IBD patients,[6] while some believe that women have better sleep quality, longer sleep times, shorter sleep latency, and higher sleep efficacy,[17] although we did not find any significant association between gender and sleep quality.

Adults with insomnia consumed significantly lesser quantities of folic acid compared to good sleepers.[10] Restless leg syndrome is one of the complaints which prevents from falling sleep, women with restless leg syndrome during pregnancy had lesser levels of folate, preconception, and at each trimester compared with those without restless leg complaints. Furthermore, these patients had significantly more delayed time to sleep onset and depressed mood. Rather than indicators of iron-deficiency anemia, reduced serum folate was associated with the occurrence of restless leg syndrome,[16] although we did not observe any significant association between folic acid consumption and sleep quality.

We also compared sleep quality between anemic and nonanemic IBD patients. About 29.6% of our sample was anemic. No significant difference was found. The associations between sleep and anemia in IBD patients have not been focused enough in available published articles. Murat *et al*. reported that patients with iron-deficiency anemia have poorer sleep quality compared to the control group irrespective of psychological symptoms.[18] Correction of anemia with recombinant erythropoietin reduced sleep arousals and fragmentations and improved sleep quality, daytime alertness, and restorative sleep in end-stage renal disease patients.[19]

Strengths and limitations

As the first study about Iranian IBD patients' sleep, we examined different aspects, which may affect sleep quality in these patients, such as socio-demographic variables,

clinical status, treatment strategy, folic acid consumption (as a supplement), disease history, the presence of anemia, and BMI. We note the limitations of this study, including cross-sectional design, not investigating psychological factors such as depression and anxiety and exclusive use of subjective sleep measures. These subjective measures are not able to diagnose the patients in the primary stages of sleep disturbance. Further prospective studies are warranted to evaluate the relationship between BP and sleep quality. Exploring the associations of types of anemia and blood folic acid level with IBD patients' sleep is recommended.

CONCLUSION

High prevalence of IBD patients, especially CD patients suffer from poor sleep quality even the ones in remission status. Sleep disturbance is associated with IBD type and higher BP. Regular evaluation of sleep quality in patients' care program and pharmacological and nonpharmacological treatment of sleep disturbances and disease activity is recommended.

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Conflicts of interest

There are no conflicts of interest.

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