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Sleep quality in Crohn's disease patients

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Abstract

Therapeutic goals for chronic inflammatory bowel disease (IBD) have evolved since the STRIDE 2 consensus and now include improving quality of life in addition to controlling inflammation. One of the major components of quality of life is good sleep.

The aim of this study is to highlight the various factors that can influence sleep quality in patients with inflammatory bowel disease.

Keywords: Crohn's Disease; Sleep Quality; Disease Activity; Inflammatory Bowel Disease; Quality of Life

1. Introduction

Sleep quality is a crucial component of health and well-being, often affected in patients with Crohn's disease. This study investigates factors associated with impaired sleep in this population, focusing on disease activity and psychosocial variables.

2. Materials and Methods

We conducted a single-center cross-sectional study in the Hepatology and Gastroenterology Department "B" at Ibn Sina University Hospital over a two-month period. We included patients aged 18 years or older with a confirmed diagnosis of Crohn's disease and regular follow-up, while excluding those with psychiatric disorders, undergoing treatments affecting sleep, with pre-existing sleep disorders, or who were pregnant or breastfeeding. The data collected included demographic, clinical, and therapeutic characteristics, as well as sleep quality assessed using the Pittsburgh Sleep Quality Index (PSQI).

2.1. Statistical Study

The data were analyzed using Jamovi 2.3.9.0 software. Continuous variables are expressed as mean ± standard deviation or median with interquartile ranges. Categorical variables are presented as numbers. Comparisons between categorical variables were performed using the chi-square test or Fisher's exact test, depending on the conditions of application. Risk factors were analyzed by linear regression, with a p-value < 0.05 considered significant.

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3. Results

Of the 101 patients surveyed, we included 88 patients after applying the inclusion criteria. The average age was 44.5 ± 12.9 years, with a predominance of patients aged 40-60 years (48, or 54.5%). There was a predominance of females, with a female-to-male ratio of 1.4.

Among the participants, the majority were married (51 patients, 58%), while a significant proportion were single (26 patients, 29.5%).

Most patients lived in urban areas (73 patients, 83.0%). In terms of social status, more than half had a medium status (48 patients, 54.5%), while a minority had a high social status (9 patients, 10.2%). The majority of patients had a secondary education level (27 patients, 30.7%). However, a significant proportion had no formal education (18 patients, 20.5%).

Finally, a large proportion of participants did not smoke (80 patients, 90.9%) and did not consume alcohol (85 patients, 96.6%). These data are detailed in Table 1.

Table 1 Socio-demographic data

Characteristics	**N (%)**
Age	
Mean ± standard deviation	44,5 ± 12,9
< 40 years	32 (36.3%)
40-60 years	48 (54.5%)
> 60 years	8 (9%)
Gender	
Female	52 (59,1 %)
Male	36 (40,9 %)
Marital status	
Married	51 (58 %)
Single	26 (29.5 %)
Divorced	10 (11.4 %)
Widowed	1 (1.1%)
Habitat environment	
Urban	73 (83,0 %)
Rural	15 (17,0 %)
Social status	
Low	31 (35,2 %)
Moderate	48 (54.5%)
High	9 (10,2 %)
Level of education	
None	18 (20,5 %)
Primary	24 (27,3 %)
Secondary	27 (30,7 %)

Higher	19 (21,6 %)
Tobacco	
Smoker	8 (9,1 %)
Non-smoker	85 (96,6 %)
Alcohol consumption	
Yes	3 (3,4 %)
No	85 (96,6 %)

APLs were present in more than half of the patients (48, 54.5%), with a predominance of anal fistulas. Nineteen cases (39.6%) involved complex fistulas, while 16 cases (33.3%) involved simple fistulas, followed by ulcerated pseudorabies's (7, 14.6%).

- EDMs were present in 19 patients (21.6%), predominantly osteoarticular manifestations (12, 63.2%).
- In terms of treatment, 53 (60.2%) were on biotherapy, 35 (37.5%) on azathioprine, of which 17 (19.3%) were on combination therapy.
- Forty-four (50%) were in clinical remission and 44 (50%) had mild to moderate flare-ups.

These results are illustrated in Table 2 and figure 1.

Table 2 Medical treatment received

Medical treatment	Number of patients (N)	Percentage (%)
Biothérapies	53	60.2%
- Anti-TNF	44	50%
- Anti-IL-12/23	9	10.2%
Immunosuppressants	35	39.8%
- Monotherapy	18	20.5%
- Combination therapy	17	19.3%

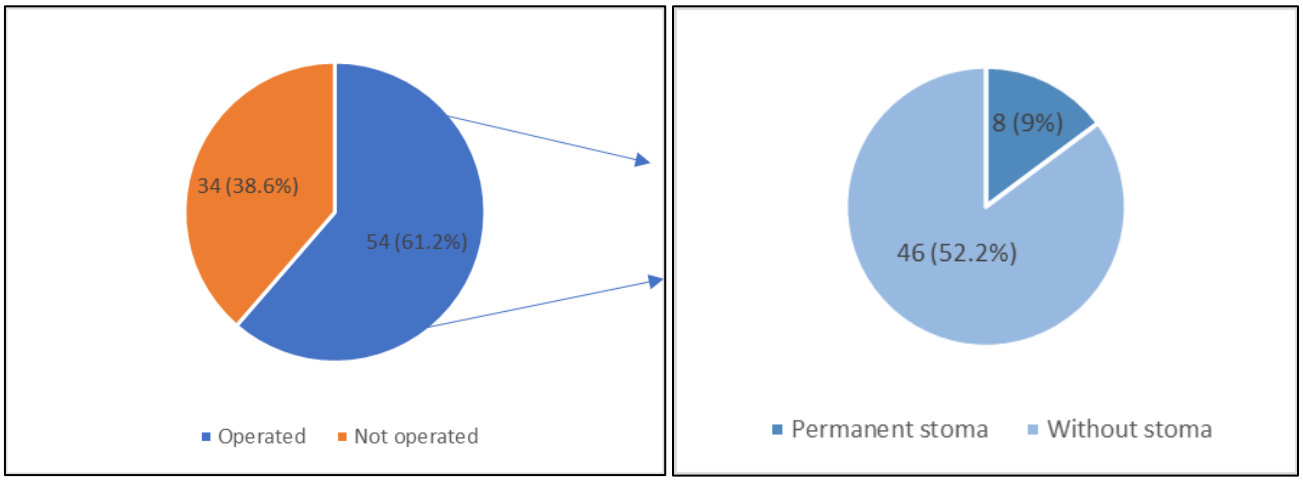

Figure 1 Surgical treatment

Sleep quality was impaired in 22 (25%) patients, with a mean PSQI score of 3.64 ± 2.5.

The mean sleep duration was 7.18 ± 1.08 hours. Fourteen patients (15.9%) suffered from nighttime pain. These data are illustrated in Graph 2 and Table 3.

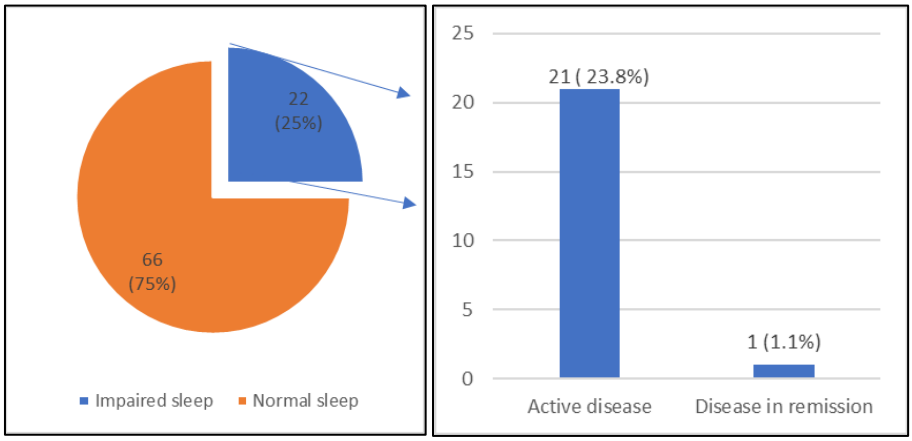

Figure 2 Sleep quality

Table 3 PSQI score results

Clinical status	Number of patients	Mean PSQI score ± standard deviation	Average sleep duration ± standard deviation (hors)	P Value
In activity	44	4.93 ± 2.62	6.7 ± 1.05	0.007
In remission	44	2.34 ± 1.52	7.6 ± 0.88	0.301

After univariate and multivariate analysis with linear regression, the only factors significantly associated with poor sleep quality were single status (p = 0.032, OR = 14.39, CI [1.255–165.0]), and the presence of an active disease (p = 0.003, OR = 45.91, CI [3.554–593.1]).

All these elements are detailed in Table 4.

Table 4 Multivariate analysis of the various factors

	OR	IC=95%	P value
Habitat environment	0.769	[0.036-16.02]	0.866
Marital status			
Single	12.57	[1.025-1.025]	**0.048**
Married	0.963	[0.118-7.803]	0.972
Level of education			
None	0.108	[0.003-3.695]	0.218
Higher	0.844	[0.136-5.210]	0.855
Activity	33.07	[2.643-413.8]	**0.007**
APL	3.316	[0.475-23.14]	0.226
EDM	2.932	[0.542-15.84]	0.211
Night pain	4.400	[0.529-36.57]	0.170
Location	1.968	[0.250-15.46]	0.520
Treatment			
Immunosuppressants	0.602	[0.046-7.847]	0.699
Anti-IL 12-23	0.892	[0.077-10.23]	0.927

4. Discussion

IBD, including Crohn's disease, is often associated with sleep disorders due to its inflammatory and psychological impact [1,3]. Sleep, which is essential for immune regulation and general well-being [2], can be disrupted by inflammation, nighttime pain, and certain extra-digestive manifestations [5]. Psychosocial factors, such as stress or marital status, can also influence this impairment [6]. However, assessment tools such as the PSQI are based on subjective perceptions, which can sometimes limit the interpretation of results [7].

The aim of this discussion is to analyze the factors influencing sleep quality in patients with CD, comparing our results with those in the literature.

To better understand the impact of IBD on sleep, it is essential to examine the pathophysiological mechanisms that regulate sleep and its interaction with inflammation.

Quality sleep is characterized by structured cycles alternating between slow-wave sleep (SWS) and rapid eye movement (REM) sleep, which play a key role in regeneration and immune modulation. Sleep deprivation or fragmentation increases pro-inflammatory cytokines, exacerbating inflammation and disrupting tissue repair [2]. Stress, pain, and chronic inflammation exacerbate these disturbances by activating inflammatory and neuroendocrine pathways [5,8]. In an experimental study on animal models, Tang et al. [9] showed that sleep deprivation significantly aggravated intestinal inflammation and delayed mucosal repair.

The interactions between sleep and inflammation are not specific to IBD. In fact, other chronic inflammatory diseases share similar mechanisms, with significant repercussions on sleep quality. These include lupus, multiple sclerosis, and rheumatoid arthritis, which have a notable impact on quality of life [10]. A study of 50 patients with lupus showed that disease activity and pain were major determinants of impaired sleep quality ($p < 0.001$) [11]. Although these results are statistically significant, the sample size was small and could introduce selection bias [11]. In addition, certain confounding factors such as treatments or psychiatric disorders were not taken into account.

In our study, however, nighttime pain was not significantly associated with poor sleep quality, which could suggest different pathophysiological mechanisms in CD, where intestinal inflammation plays a more central role than pain.

As such, it is worth asking whether these observations, which concern systemic diseases, can be transposed to IBD, where inflammation is mainly localized in the digestive tract. Sleep disorders are indeed common in IBD, even during periods of remission.

In a prospective study including 16 patients with IBD in remission, Keefer et al. [12] assessed sleep quality using the PSQI and polysomnography. The objective was to examine whether patients in clinical remission continued to experience sleep disorders compared to healthy controls. The results showed that 62% of patients in remission reported impaired sleep quality, despite the absence of severe digestive symptoms.

Remission in this study was defined according to clinical and biological criteria, with a CDAI < 150 for CD and a UCAI < 3 for UC. However, no endoscopic criteria were used to confirm the absence of mucosal inflammation, which is a notable limitation of the study. It is possible that some patients had undetected subclinical inflammation, which may partly explain the persistent sleep disturbances.

The study also highlights that the sleep disturbances observed could be influenced by psychosocial factors, such as anxiety or chronic fatigue, rather than by active inflammation itself. However, the subjective assessment of sleep using the PSQI, without complementary objective measures such as actigraphy, limits the scope of these conclusions.

Similarly, our results show that patients with active CD had significantly higher PSQI scores than those in remission, highlighting the direct impact of clinical inflammation on sleep quality.

The results of our study also highlighted the impact of marital status on sleep quality. Indeed, single status showed a significant association with poor sleep quality (OR = 14.39, $p = 0.032$). This observation is consistent with a well-documented body of literature, in which social isolation is recognized as a major risk factor for sleep disorders [6]. Lack of emotional support can also amplify negative perceptions of the disease and emotional distress, contributing to impaired sleep quality. According to Maunder et al. [1], psychosocial stress, reinforced by social isolation, activates the hypothalamic-pituitary-adrenal axis, increasing cortisol levels and disrupting immune regulation. This phenomenon could create a vicious cycle in which isolation and stress amplify inflammation, thereby aggravating the symptoms of

the disease. This activation is mediated by an increase in pro-inflammatory cytokines, such as IL-6 and TNF-α, which disrupt immune regulation and impact psychological well-being [3].

However, our study did not find a significant correlation between age, gender, or other demographic variables and sleep quality. This finding contrasts with some previous studies, which found associations between these factors and sleep disorders in IBD. [5].

Furthermore, studies have shown a strong correlation between depression, anxiety, and poor sleep quality, as suggested by Brass et al. [10], who found that depression predicted poor sleep quality in patients with multiple sclerosis. This relationship could be linked to a vicious cycle in which Crohn's disease promotes depressive disorders, which increase inflammation and worsen the disease, thereby disrupting sleep [1,2]. In our study, patients being treated for known depression or anxiety disorders were excluded in order to limit bias in the assessment of sleep quality. This approach, while necessary to focus on factors specific to Crohn's disease, is a limitation because it prevents a comprehensive analysis of the interactions between psychological disorders and sleep quality. The inclusion of these parameters in future research would be essential to explore these complex mechanisms.

Furthermore, the impact of sociocultural context on sleep habits and the perception of sleep disorders is well documented [6]. Studies conducted in Asia, for example, report lower average PSQI scores in patients with Crohn's disease (CD) compared to European cohorts, probably due to cultural differences, dietary habits, or different access to healthcare [15]. In our study, we analyzed socioeconomic status via living environment, which partly reflects access to healthcare. However, no statistically significant relationship was observed between this factor and sleep quality.

Disease activity was found to be the most influential factor on sleep quality in our study, with a high OR (45.91, $p = 0.003$). This result highlights the central role of clinical inflammation in sleep disturbances in patients with CD.

These results are consistent with the work of Sochal et al. [4], who identified a positive correlation between HBI and PSQI scores ($r = 0.390$, $p = 0.001$). Their study showed that patients in clinical flare-ups had significantly impaired sleep quality, characterized by prolonged latency, frequent nighttime awakenings, and higher PSQI scores.

Several hypotheses support this relationship between disease activity and sleep disorders: the presence of pro-inflammatory cytokines [16], abdominal pain and discomfort [14], and altered circadian rhythms via modulation of the hypothalamic-pituitary-adrenal axis, leading to increased cortisol levels, which can disrupt deep and REM sleep phases [13].

In our study, patients in clinical remission had significantly lower PSQI scores than those with active disease, corroborating the observations of Keefer et al. [12]. However, sleep disturbances persist in some patients in remission, probably due to subclinical inflammation or unmeasured psychosocial factors such as stress or anxiety.

However, unlike other studies [3], no significant association was found between nighttime pain and sleep quality, despite their theoretical link to sleep disturbances. This could suggest that nighttime abdominal pain, although a common symptom in Crohn's disease patients, is not solely responsible for sleep disturbances in this population.

At the same time, extraintestinal manifestations (EIMs), such as arthralgia, uveitis, and erythema nodosum, are frequently associated with impaired quality of life, including sleep [5]. For example, Ballesio et al. [5] reported that chronic pain related to arthralgia contributes significantly to sleep disturbances, although its precise role in IBD requires further study to better understand its impact.

Similarly, with regard to anorectal lesions (ARLs), Spinelli et al. [17] noted that they are a significant source of discomfort in patients with Crohn's disease. Although their direct impact on sleep is not always measured, the associated pain and discomfort could indirectly disrupt sleep cycles. However, in our study, no statistically significant association was found between the presence of EDM or APL and sleep quality. These results highlight the complexity of the interactions between clinical symptoms and sleep disorders.

Finally, although biological treatments, such as anti-TNF agents, are known for their ability to control inflammation, no significant link was observed between their use and sleep quality in our study. This could be explained by the fact that patients treated with anti-TNF agents in our cohort were often those with a more severe form of the disease, with complications or insufficient disease control. Thus, these factors could neutralize the potentially beneficial effects of these treatments on sleep quality.

5. Conclusion

Our study highlighted the main factors influencing sleep quality in patients with Crohn's disease. Active disease was associated with higher PSQI scores, highlighting the predominant role of inflammation in disrupting sleep cycles, while single status, as a potential marker of social isolation and psychosocial stress, was also identified as a factor detrimental to sleep quality.

No significant association was found with age, gender, living environment, nighttime pain, or biological treatments.

These results highlight the complexity of the interactions between clinical, psychosocial, and biological factors in Crohn's disease. They also underscore the importance of considering sleep quality in the overall management of these patients, incorporating strategies that target not only inflammation but also psychosocial and behavioral dimensions. Finally, these observations encourage future studies that incorporate objective assessment tools and explore parameters that have not yet been studied in depth, such as the gut microbiota, lifestyle habits, and psychological comorbidities.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Statement of informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

Author contributions

All authors have contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

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