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# Prevalence, Impact and Influencing Factors of Sleep Disturbances in Inflammatory Bowel Disease: A Review of Literature

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## Abstract

Inflammatory Bowel Disease (IBD), comprising Crohn’s disease (CD) and ulcerative colitis (UC), is a chronic inflammatory condition that can be induced and exacerbated by environmental factors such as sleep disorders. Sleep disturbances are increasingly recognized as both a symptom and risk factor for poor outcomes in IBD, influencing disease progression through immune system dysregulation. This literature review assesses the prevalence and risk factors for sleep disorders among IBD patients. Studies included span from 2011 to 2024, with sample sizes ranging from 34 to 10,634 participants.

The prevalence of poor sleep quality is notably high, ranging from 32.2% to 82%, with active disease being a significant predictor. For instance, 77% of patients with active IBD and 49% in remission reported poor sleep quality, with similar findings across several studies. Depression, anxiety, and restless legs syndrome were identified as psychological and clinical risk factors. Moreover, elevated inflammatory markers such as C-reactive protein and certain adipokine profiles were associated with poor sleep quality. Socio-cultural factors, including gender, age, and work-related shifts, also influenced sleep disturbances in IBD patients. While biological therapies like anti-TNF showed improvements in sleep, no significant differences were noted between other treatment modalities.

The findings underscore the complex interplay between sleep quality, disease activity, and psychological well-being in IBD patients, highlighting sleep disturbances as a critical factor in disease management. Further research is needed to explore the impact of treatment interventions on sleep and to develop holistic care strategies for IBD patients.

## Keywords

Inflammatory bowel disease, sleep quality, relations, risk factors, prevalence.

## Background

Inflammatory bowel disease (IBD) is a set of recurrent chronic illnesses that mostly affect Crohn's disease (CD) and ulcerative colitis (UC) patients. It is distinguished by a progressive course and the possibility of developing complications, such as extra-intestinal manifestations (EIMs) [1, 2].

Several environmental factors, including smoking, sleep disorders, and depression have been implicated in the development of IBD [3-5]. IBD can cause symptoms like diarrhea and abdominal pain. It is also associated with extra-intestinal manifestations, including joint pain and skin rashes [6, 7].

Sleep is a critical biological function that is receiving increasing attention for its role in overall health. Abnormal sleep has been linked to negative health outcomes, including cardiovascular disease [8], metabolic syndrome [9], as well as increased risk of death [10]. Additionally, it has been associated with significant economic costs due to decreased productivity and increased healthcare utilization [11]. Furthermore, research has shown that sleep plays a role in regulating several gastrointestinal functions, such as gastrointestinal motility and secretion [12]. Disrupted sleep has been linked to higher levels of inflammatory cytokines, such as IL-6 and TNF-α, which are implicated in the development of

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inflammatory bowel disease [13-15]. Poor sleep has also been studied in chronic inflammatory diseases [16], it was found to be prevalent in conditions like rheumatoid arthritis [17] as well as multiple sclerosis [18].

Sleep disorders are common in patients with IBD, with reported rates ranging from 32.2% to 82% [19-24]. Studies have also shown that sleep disorders can impact the progression and relapse of IBD by affecting the immune system [21,23,25]. However, during active IBD, symptoms such as abdominal pain and diarrhea can disrupt sleep and worsen the situation, creating a cycle that perpetuates itself [22, 26]. Additionally, anxiety and depression are also reported to be common among IBD patients, playing an important role in the occurrence and development of sleep disorders [25, 27-30]. Sleep quality may also be a prognostic factor in IBD, as associations have been observed between sleep and an increased likelihood of hospitalization and risk of relapse. The current literature review aimed to assess the prevalence as well as risk factors of sleep disorders among IBD patients.

**Current literature evidence**

The majority of studies used to illustrate this article were cross-sectional and single-centered studies. Publication dates ranged from 2011 to 2024. Most studies were conducted in the USA (14 studies), Poland (4 studies), China (3 studies), and Iran (2 studies). Other regions were also included such as Turkey, Greece, and Japan. The sample size at the different studies ranged from 34 up to 10,634 participants with confirmed IBD diagnosis. The disease duration among IBD cases ranged from 3 up to 15 years with an age ranged from 25 to 47 years. The proportion of male participants ranged from 27% to 58%. The mostly used tool for assessing sleep quality at different studies was The Pittsburgh Sleep Quality Index (PSQI) (30 studies) (46). Other scales such as the Reported Outcomes Measurement Information Systems Sleep Disturbance (PROMIS-SD), The PROMIS-SD questionnaire, and the Basic Nordic Sleep Questionnaire (BNSQ) were also used [19, 22-60].

**Prevalence of Poor Sleep among IBD Patients**

The prevalence of sleep problems among patients with IBD is consistently high across various studies. The study of Hashash and colleagues found that 57.5% of IBD patients experienced a high fatigue burden, with 64.4% of Crohn's disease (CD) patients and 46.2% of ulcerative colitis (UC) patients affected [33]. Similarly, 44.1% of IBD patients reported sleep disturbances, emphasizing the widespread occurrence of these issues [35]. The Manitoba IBD Cohort Study further supported these findings, with 77% of patients with active IBD and 49% with inactive disease reporting poor sleep quality [24] Another study noted that 78% of IBD patients with active disease experienced poor sleep, compared to 35% of those in remission [41]. Moreover, 54% of IBD patients were reported to have poor sleep quality in the study of Ballou and colleagues [43], while a separate cohort indicated a much higher rate; 82% of IBD patients experienced poor sleep, irrespective of their use of immunomodulator or biologic therapy [45].

**Clinical Risk Factors of Poor Sleep among IBD patients**

Takahara and colleagues' study among Japanese concluded that out of 80 outpatients with IBD, the prevalence of Restless Legs Syndrome (RLS) was 20%. Patients with RLS demonstrated significantly poorer sleep quality compared to those without RLS (PSQI > 5; 62.5% vs. 34.4%, $P < 0.05$) [34]. Furthermore, another Japanese study highlighted that sleep disturbances were common in IBD patients, affecting 44.1% of the cohort, and were a significant risk factor for disease flare (OR 3.09, 95% CI 1.47–6.43) [35]. Moreover, Frigstad and colleagues conducted a multicenter study with 405 IBD patients in 2018, their study revealed that no significant association was found between vitamin D deficiency and fatigue or sleep disturbance [44].

Habibi and colleagues compared Crohn's disease (CD) to ulcerative colitis (UC) among Iranian IBD patients; after investigating 71 patients, CD patients were significantly more likely to report poor sleep quality compared to UC patients, with an odds ratio (OR) of 6.19 (95% CI 1.13, 34.07) [51].

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Furthermore, in comprehensive assessments, factors such as abdominal pain, joint pain, the presence of extraintestinal manifestations and inflammatory markers like C-reactive protein (CRP) were reported to predict sleep efficiency among patients with active disease in several studies [54, 57].

Additionally, the relationship between sleep disturbances and specific adipokine profiles was explored in the study of Sobolewska-Włodarczyk and colleagues in 2020, revealing that higher serum resistin levels and lower levels of serum adiponectin and leptin ($p = 0.0458$, .0215, .0201, respectively) to be significantly associated with poor sleep quality [52]. This indicates a potential biochemical pathway linking sleep disturbances and disease activity in IBD patients.

Harvey-Bradshaw Index and the Subtle Cognitive Impairment test (SCIT) were performed in the study of van Langenberg and colleagues, the primary measure of response time (SCIT-RT) among 49 CD patients and 31 controls, serum CRP, abdominal pain, plasma hemoglobin and concurrent fatigue were each independently associated with slower SCIT-RT in CD (each $p < 0.05$), with a trend for poorer sleep quality ($p = 0.06$), yet conversely, higher fecal calprotectin titers were associated with faster SCIT-RT ($p < 0.01$) [36]. Additionally, another cohort study involving 131 subjects revealed that poor sleep was more prevalent in those with higher CRP levels (70% vs. 39%, $P = 0.009$), indicating a potential relationship between inflammation and sleep disturbances independent of nighttime symptoms [23].

Lastly, Bucci and colleagues investigated the prevalence of sleep bruxism among IBD patients and its correlation to other dental disorders, a relationship between bruxism and sleep disturbances was noted in CD patients, with a significant positive correlation between bruxism and pathological sleep (PSQI > 5) [47].

**Disease Activity Risk Factor**

In the Manitoba IBD Cohort Study of 318 participants, 72% of those with active disease were experiencing poor sleep ($P < 0.001$). Additionally, logistic regression analysis revealed that elevated fatigue was directly associated with active disease (OR 4.2, 95% CI 2.2-7.8) [24].

Furthermore, the study of Ali and colleagues recruited 3,173 IBD patients, finding revealed that among those in remission, impaired sleep was linked to a two-fold increase in the risk of active disease at six months (adjusted OR 2.00; 95% CI, 1.45-2.76) [25]. another study of 41 patients indicated that abnormal Pittsburgh Sleep Quality Index (PSQI) scores were present in 100% of those with active disease, but only 72% in those with inactive disease (odds ratio = 2.8, $P = 0.007$) [26].

in a cohort of 90 IBD patients, 45.56% experienced poor sleep quality, with those lacking mucosal healing displaying significantly higher Pittsburgh Sleep Quality Index (PSQI) scores ($P<0.001$), and this was statistically linked to poor sleep quality ($P<0.05$) specifically in CD patients [40]. Similarly, a prospective observational study involving 65 patients found that 78% of those with clinical exacerbations reported poor sleep, compared to only 35% in remission ($P = 0.002$; OR 6.5, 95% CI: 1.8 - 23.6) [41]. Lastly, one study reported that patients with active IBD had significantly poorer sleep quality than those in remission, with 69.2% out of 65 patients with clinically active disease reporting poor sleep compared to only 7.7% with inactive disease ($p = 0.0023$) [52].

**Socio-cultural Risk Factors of Poor Sleep among IBD patients**

The cultural context influencing the quality of sleep in IBD patients was highlighted in several reports in literature. For instance, Zeng and colleagues conducted a large multi-center study in 2023, out of 2,478 IBD patients recruited in their study, 60.17% reported poor sleep quality, particularly among older patients ($p = 0.003$) [59]. Moreover, in a study involving 47 UC patients, poor sleep quality was strongly associated with female gender [42]. Furthermore, eveningness chronotype was reported to be more prevalent in IBD patients compared to healthy controls, with a significant proportion of patients (12.2% in CD and 18.4% in UC) exhibiting

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evening preferences ($p < 0.001$) [56]. This may suggest cultural habits influencing sleep patterns among these patients.

The study of Zhang and colleagues in 2024 conducted a multivariate analysis after recruiting IBD patients, their study revealed that older age (OR, 1.070; 95% CI: 1.035–1.105, P = 0.000), smoking (OR, 2.698; 95% CI: 1.089–6.685, P = 0.032) were risk factors for sleep disorders in IBD patients. On the other hand, higher body mass index (OR, 0.879; 95% CI: 0.790–0.977, P = 0.017) was identified as a protective factor in their study [60].

Additionally, work-related factors such as rotating night shifts was identified as a predictor of poor sleep quality (OR 6.116; 95% CI: 1.312-28.514) in the study of Calvo and colleagues [58].
Furthermore, 2,478 IBD patients were enrolled in the study of Zeng and colleagues to investigate their sleep quality using the Pittsburgh sleep quality index (PSQI. According to multivariable logistic regression, age ($p = 0.014$), Patient Health Questionnaire-9 (PHQ-9) score ($p < 0.001$), systemic ($p < 0.001$) and emotional performance ($p = 0.015$) were risk factors of the presence of poor sleep quality [59].

**Psychological Risk Factors of Poor Sleep among IBD patients**

Depression and anxiety have been consistently linked to poor sleep quality in IBD patients. In one study, mood levels, as assessed by the Beck Depression Inventory, were identified as significant factors affecting sleep quality [53]. Furthermore, in another cohort study, a positive correlation between both anxiety and depression scores and the Pittsburgh Sleep Quality Index (PSQI) score was reported (Spearman correlation: $r = 0.31$ for anxiety and $r = 0.38$ for depression) [28].

Moreover, in the Manitoba IBD Cohort Study, psychological distress was found to correlate with elevated fatigue and poor sleep quality, another study also concluded the same relationship. These conclusions emphasize the need for a holistic approach to managing IBD that includes mental health considerations [24,54].
Additionally, in a cohort of patients assessed for fatigue, sleep quality and depression, those with IBD reported significantly worse health-related quality of life compared to healthy controls, emphasizing the psychological burden of sleep disorders in this population [32, 42, 60]. Nevertheless, contrasting results emerged from the study of Kani and colleagues in 2020, they reported significant lower anxiety and depression levels in IBD patients compared to healthy controls (HCs) [49].

Furthermore, in a systematic review aimed to assess the prevalence of anxiety and depression in IBD patients, a total of 171 studies, comprising 158,371 adult participants were analyzed. The pooled prevalence for anxiety disorders was 20.5%, while symptoms of anxiety were more common at 35.1%. Moreover, anxiety was significantly higher (75.6%) among patients with active disease compared to those in remission. For depression, the pooled prevalence was 15.2%, with depressive symptoms at 21.6%. Depressive symptoms were more frequent in Crohn's disease (25.3%) and during active disease (40.7%) compared to remission [30].

**Impact of IBD Treatment on sleep**

Stevens and colleagues conducted a study to investigate Vedolizumab therapy association to sleep quality among 160 IBD patients, finding revealed that patients undertaken biologic therapy showed a significant improvement in sleep quality over six weeks, indicating the beneficial effects of treatment on sleep ($P = 0.002$) [29]. Nevertheless, Lee and colleagues investigated the effect of Immunomodulator and biologic agents on sleep quality among 56 IBD patients, findings indicated no significant differences between those taking immunomodulators or biologic agents and those not on such therapies [45].

Bazin and colleagues conducted a study to illustrate the association between sleep quality and the activity of IBD, findings indicated that using wrist actigraphy is associated with lower sleep efficiency

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in patients with active CD compared to those in remission [48].

In a study recruited 160 IBD patients with (49 under anti-TNF therapy and 111 under Vedolizumab therapy), no significant difference was detected between these drugs in regard to improvement in sleep, depression and anxiety, another study also indicated that no significant differences between the use of steroids as well as body mass index among IBD patients and abnormal sleep [26, 29].

## Prospects for Future Development

Future research and clinical interventions should focus on refining the understanding of sleep disturbances in patients with IBD and their bidirectional relationship with disease activity. Clinically, integrating routine sleep quality assessments into the management of IBD could offer a more comprehensive approach to treatment, recognizing sleep disturbances as a modifiable risk factor for disease exacerbation. Large-scale longitudinal studies are needed to elucidate the causal pathways between sleep dysfunction, inflammation, and disease relapse, as well as the potential role of specific biomarkers, such as adipokines, in predicting sleep disturbances.

Moreover, Artificial intelligence (AI) holds significant potential to advance both research and clinical care in this field. AI-driven predictive models can help identify patients at higher risk for sleep disorders based on real-time health data, including wearable devices and electronic health records (EHRs). For example, machine learning algorithms have been recently (2023) investigated in cardiology to predict sleep apnea using physiological data like heart rate variability [61]. Similarly, AI can assist in the development of personalized treatment plans for IBD patients by analyzing patterns in sleep quality, disease activity as well as treatment response.

Furthermore, AI alongside virtual health approaches could offer continuous patient support by monitoring sleep quality and providing behavioral interventions like cognitive-behavioral therapy for insomnia (CBT-I) remotely [62]. Such technologies have been successfully implemented in managing mental health, as seen with AI tools like Woebot, which uses natural language processing to deliver cognitive behavioral therapy interventions for depression and anxiety [63].

## Study Limitations

The methodologies employed across these studies varied, with sample sizes ranging from 41 up to 10,634 participants, moreover, diverse assessment tools were adopted such as the Pittsburgh Sleep Quality Index, PROMIS measures, and disease activity indices like the Harvey-Bradshaw Index. Notably, the observational nature of many studies raises considerations regarding the generalizability of findings across different IBD populations and the potential for bias in self-reported measures. Furthermore, despite the fact that all cited studies are relevant to current study objectives, several related studies in other subscribed-only platforms or grey literature may have been missed. Lastly, current study did not undergo meta-analysis of prevalence of poor sleep among IBD patients or its associated risk factors, such analysis will act as a cornerstone for containment policies or therapeutic strategies.

## Conclusion

The current review showed that poor sleep quality risk factors among IBD patients are active disease, elevated inflammation, depression, anxiety, restless legs syndrome as well as others. The burden of sleep disturbances is significant across various patient demographics. Additional research is required in this area to consider implementing sleep-targeted interventions in an IBD population.

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