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TITLE PAGE

Title: Epidemiology of Sleep Quality in Irritable Bowel Syndrome.

Short running head: Sleep quality in IBS.

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Abbreviations:	HADS	hospital anxiety and depression scale
	IBS	irritable bowel syndrome
	IBS-C	irritable bowel syndrome with constipation
	IBS-D	irritable bowel syndrome with diarrhoea
	IBS-M	irritable bowel syndrome with mixed bowel habits
	IBS-U	irritable bowel syndrome unclassified
	IBS-SSS	irritable bowel syndrome severity scoring system
	IBS-QOL	irritable bowel syndrome quality of life
	PHQ-12	patient health questionnaire-12

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What is already known on this topic.

Sleep disturbance in irritable bowel syndrome (IBS) is common but not fully understood.

Studies have examined subjective and objective sleep quality in IBS, but few have examined the characteristics of people with IBS and sleep disturbance.

What this study adds

We have confirmed a high prevalence of over 80% of poor sleep quality among people with IBS and demonstrated independent associations between poor sleep quality and older age, as well as more severe somatoform symptoms.

How this study might affect research, practice or policy

Our findings support the notion that sleep quality in IBS warrants further study, with a view to establishing whether sleep function could serve as a formal target for intervention in the management of IBS as part of holistic approach to personalised care.

ABSTRACT

Objective: Subjectively reported sleep disturbance is common in irritable bowel syndrome (IBS). Studies have examined subjective and objective sleep quality in IBS. We aimed to explore the characteristics of people with IBS according to the quality of their sleep.

Design / Method: Participants were recruited from the NIHR research register ContactME-IBS. We collected data on demographics, gastrointestinal symptoms, psychological health, and quality of life using validated questionnaires among adults with Rome IV IBS. We dichotomised the cohort according to whether they were good or poor sleepers, with poor sleepers defined by a Pittsburgh sleep index score >5 , as recommended. We compared the characteristics of the two groups and explored factors associated independently with poor sleep using logistic regression.

Results: Of 341 respondents with Rome IV IBS, 287 (84.2%) were poor sleepers. Poor sleepers were older (50.4 years vs. 44.2 years, $p=0.007$), had more severe IBS symptoms (mean total IBS severity scoring system 295.9 vs 239.7, $p<0.001$), had a longer duration of IBS (82.2% IBS for ≥ 5 years vs. 66.7%, $p=0.009$), and had higher levels of anxiety, depression, and more somatoform symptom-reporting, as well as worse IBS-specific health-related quality of life ($p<0.001$ for all analyses). After logistic regression, older age and having higher levels of somatoform symptom-reporting were independently associated with poor sleep.

Conclusion: Poor sleep in IBS is independently associated with age and somatoform symptom-reporting. Better understanding of the associations between sleep and IBS could help personalise management of IBS.

INTRODUCTION

Irritable bowel syndrome (IBS) is a common disorder of gut-brain interaction, characterised by symptoms of recurrent abdominal pain and altered bowel habit. It affects approximately 5% of the global population,¹ has a detrimental impact on work and social functioning,² and is strongly associated with an increased risk of psychological comorbidity.³ The multifactorial pathophysiology of IBS is incompletely understood, but mechanisms of mucosal and immune functions of the gut, visceral hypersensitivity, the microbiome, and central nervous system processing are all implicated.⁴ As our current understanding of the condition cannot offer a specific treatment target, management strategies focus on symptom control measures and optimising underlying lifestyle factors that may exacerbate symptoms. It is increasingly recognised that the most effective management strategies require a personalised approach, underpinned by a deeper understanding of the heterogeneous ways in which patients are affected.⁵

Subjectively reported sleep disturbance in IBS is common.⁶ Studies have demonstrated an association between poor sleep function and IBS symptom exacerbation the following day, by both subjective,^{7, 8} and objective,⁹ measures of sleep quality. Individuals with IBS have been shown to experience greater sleep fragmentation and feel less well-rested than healthy controls, with detrimental consequences for their quality of life.^{10, 11} An independent association between sleep disturbance and IBS has been observed even after controlling for psychological distress.¹²

Current evidence is by no means definitive for any causal effect between sleep disturbance and IBS symptoms but further consideration is warranted, particularly in the context of the proposed hyperalgesic effect of sleep deprivation on the gastrointestinal tract, albeit demonstrated in the context of organic disease.¹³ Melatonin offers a potential therapeutic agent candidate, with observed beneficial effects on IBS symptom severity and

IBS-related quality of life.^{14, 15} There has been limited examination of the factors associated with poor sleep quality in IBS. Developing our understanding of the role of sleep in the disease experience of the IBS community could lead to more personalised treatment. Therefore, we aimed to compare the characteristics of people with Rome IV-defined IBS, according to the subjectively reported quality of their sleep.

MATERIALS AND METHODS

Participants and Setting

We recruited participants from a database of registrants with ContactMe-IBS, a UK national registry managed by County Durham and Darlington NHS Foundation. The registry contains more than 4,200 members with IBS who are interested in participating in research.¹⁶ ContactME-IBS members are recruited via advertisement in primary care, hospital clinics, pharmacies, and on social media. They complete an online questionnaire regarding their bowel symptoms and provide contact details. 2268 (53%) members have seen a primary care physician with their IBS, and 1455 (34%) a gastroenterologist. The remainder are individuals who meet criteria for IBS based on reporting typical symptoms.

We performed a cross-sectional questionnaire survey of individuals recruited from ContactME-IBS. This was a follow-up study in which individuals who had previously responded to a baseline questionnaire were invited to provide additional data. Recruitment was via electronic mailshot in July 2022, with a reminder email sent to non-responders in August 2022. Responses were stored in an online database. The only exclusion criteria was an inability to understand written English. The chance to win a £100 gift card was offered to those who completed the questionnaire. The University of Leeds research ethics committee approved the initial study in March 2021 (MREC 20-051), with an amendment for this follow-up study in April 2022. (MREC 20-051, Amendment 1). We have previously reported data from this cohort.^{2, 17-21}

Data Collection and Synthesis

Demographic and Symptom Data

We collected demographic data, including age, sex, lifestyle factors such as tobacco and alcohol consumption, ethnicity, marital status, and educational level. We defined the presence of IBS using the Rome IV questionnaire,²² assigning presence of Rome IV-defined IBS according to the scoring algorithm proposed for its use.²³ We categorised IBS subtype using the proportion of time stools were abnormal according to the Bristol stool form scale. All participants also identified their most troublesome symptom from a list of five possibilities: abdominal pain; constipation; diarrhoea, abdominal bloating or distension; or urgency. We also asked participants whether their IBS started after an acute enteric infection.

Sleep quality

We assessed sleep quality using the Pittsburgh Sleep Quality Index (PSQI).²⁴ This is a validated questionnaire containing 19 self-rated questions regarding sleep quality in the preceding 1 month. The component questions pertain to subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. There are an additional five questions that can be rated by an observing bedpartner or roommate if one is available, but these are for clinical information only and are not included in the scoring system. Responses to the self-rated questions contribute to a global score on a scale of 0 to 21. A global PSQI score of >5 defines a 'poor sleeper', with a diagnostic sensitivity of 89.6% and specificity of 86.5%.²⁴ The PSQI was not included in the March 2021 baseline questionnaire and was only administered in this follow-up study. Assessing sleep quality in IBS was not the main rationale for the follow-up

study, nor was sleep mentioned in the participant information leaflet or other participant-facing materials.

IBS Symptom Severity

We assessed IBS symptom severity via the IBS severity scoring system (IBS-SSS),²⁵ which measures presence, severity, and frequency of abdominal pain, presence and severity of abdominal distension, satisfaction with bowel habit, and degree to which IBS symptoms are affecting, or interfering with, the individual's life. The IBS-SSS carries a maximum score of 500 points, with <75 indicating remission of symptoms, 75-174 mild symptoms, 175-299 moderate symptoms, and 300-500 severe symptoms.

Mood and Somatic Symptoms

We used the hospital anxiety and depression scale (HADS) to collect symptoms of anxiety and depression. The total HADS score ranges from 0 to 21 for either anxiety or depression.²⁶ We collected somatic symptom data using the patient health questionnaire-12 (PHQ-12),²⁷ derived from the validated PHQ-15.²⁸ The total PHQ-12 score ranges from 0 to 24. For each of these tools, a score of 0 indicates the lowest burden of symptoms.

IBS-specific Health-related Quality of Life

We used the irritable bowel syndrome quality of life (IBS-QOL), a validated IBS-specific questionnaire, to measure health-related quality of life in individuals with IBS.^{29, 30} The IBS-QOL consists of 34 items, each ranked on a 5-point Likert scale ranging from 0 to 4, with a total possible score of 0 to 136. Lower scores indicate better quality of life. The 34 items include questions regarding dysphoria, interference with activity, body image, health worry, food avoidance, social reactions, sexual activity, and relationships. The score was

converted to 0-to-100-point scale, as recommended, where 0 indicates the worst quality of life and 100 indicates the best quality of life.

Statistical Analysis

All respondents who met Rome IV criteria for IBS were included in the analysis. We dichotomised participants according to whether they were a good sleeper or a poor sleeper, according to their PSQI score, and compared the characteristics of the two groups.

Categorical demographic variables such as sex, marital status, alcohol and tobacco use, and level of educational attainment, as well as disease-related characteristics, such as IBS subtype and IBS symptom severity, were compared using a χ^2 test. Continuous data such as age, HADS scores, PHQ-12 scores, and IBS-QOL scores were compared between groups using an independent samples *t*-test. Statistical significance was defined using a *p* value <0.01. We performed logistic regression to explore factors that were independently associated with poor sleep quality, with the results reported using odds ratios (OR) with 95% confidence intervals (CIs). All analyses were performed using SPSS for Windows (version 30.0 SPSS, Chicago, IL).

RESULTS

Of 1278 individuals responding to the baseline questionnaire, 604 (47.3%) completed the follow-up questionnaire (mean age 50.6 years (range 19-85 years), 85% female). Of these, 341 (56.5%) met Rome IV criteria for IBS (mean age 49.4 years (range 20 to 82 years), 300 (88.0%) female, and 330 (96.8%) white) and were included in the study. Among the 341 participants, the median PSQI score was 10 (interquartile range 7 to 13). In total, 287 (84.2%) were poor sleepers in the preceding 1 month, according to a global PSQI score >5 .

Among poor sleepers, 88.5% were female, compared with 85.2% of good sleepers ($p=0.492$). Poor sleepers were, on average, older (mean age 50.4 years vs. 44.2 years, $p=0.007$). There were no other statistically significant differences in demographic data between good and poor sleepers (Table 1), although there was a trend towards a greater proportion of good sleepers having attained a higher level of education ($p=0.014$)

In total, 61 (17.8%) respondents had IBS-C, 145 (42.5%) IBS-D, and 133 (39.0%) IBS-M. Among poor sleepers, IBS-D was most prevalent (42.9%), followed by IBS-M (39.7%), and then IBS-C (16.7%). Regarding disease factors, there were no statistically significant differences between good and poor sleepers according to their IBS subtype or most troublesome symptom, but poor sleepers had more severe IBS symptoms (mean total IBS-SSS 295.9 vs 239.7, $p<0.001$). A significantly higher proportion of poor sleepers had a duration of IBS of ≥ 5 years (82.2% vs. 66.7%, $p=0.009$). There were no statistically significant differences in the proportion reporting IBS following an acute enteric infection.

Poor sleepers had significantly higher HADS-anxiety scores (10.7 vs. 7.1, $p<0.001$) and HADS-depression scores (8.23 vs. 3.85, $p<0.001$). Levels of somatoform symptom-reporting differed significantly between the two groups, with poor sleepers having higher PHQ-12 scores (10.9 vs. 6.4, $p<0.001$). Poor sleepers reported significantly lower levels of IBS-related quality of life, according to the IBS-QOL ($p<0.001$).

We performed logistic regression analysis with the variables that were significantly associated with poor sleep on univariate analysis entered in the model. Poor sleepers were more likely to be older (OR per year = 1.06; 95% CI 1.03-1.09) and to have higher levels of somatoform symptom-reporting according to their PHQ-12 score (OR per point on the PHQ-12 = 1.37; 95% CI 1.20-1.57). Overall, the logistic regression model explained 43% of the variance of the data.

DISCUSSION

This cross-sectional survey examined the prevalence of, and associations with, poor sleep among individuals with Rome IV IBS. More than 80% of participants were poor sleepers, as defined by a PSQI score of >5 . On univariate analysis, poor sleepers were older, had more severe IBS symptoms, had a longer duration of IBS, had higher HADS-anxiety HADS-depression, and somatoform symptom-reporting scores, and had worse IBS-specific health-related quality of life scores. After logistic regression, older age and higher somatoform symptom-reporting scores were independently associated with being a poor sleeper.

Our study has several limitations. We did not have access to participants' medical records, and we were therefore unable to objectively exclude conditions that may mimic IBS, such as inflammatory bowel disease or coeliac disease. However, over 80% of the cohort had been diagnosed with IBS for ≥ 5 years and, given that guidelines recommended screening for these conditions in suspected IBS, it is likely that participants did truly have IBS. Nor did we have access to information about current medications or knowledge of lifestyle factors, such as diet or caffeine intake, which may affect sleep. We were also unable to screen for specific sleep disorders, such as obstructive sleep apnoea, or exclude the presence of functional chronic pain syndromes, such as fibromyalgia, which may confound associations between IBS and subjective sleep disturbance.³¹ In addition, we did not have data on body mass index, which could have helped to identify those who may have been more likely to have sleep disorders such as sleep apnoea. The generalisability of our findings is limited by the disproportionately high representation of females, although IBS is recognised to be more common in women, and those of white ethnicity. This overrepresentation could reflect a propensity of females and those of white ethnicity to register with the ContactME-IBS database from which we recruited, but any underlying explanations for this are beyond the

scope of our study. Finally, as the number of good sleepers in the study population was small, we were probably underpowered to detect significant differences between those with good sleep and those with poor sleep.

Our response rate of 47.3% is in line with other longitudinal follow-up studies conducted over a similar timeframe,^{32, 33} but lower than response rates of 60% to 74% observed in other questionnaire-based studies of sleep and disorders of gut-brain interaction.^{12, 34} We also acknowledge the potential for selection bias, as it is possible that those with more severe IBS symptoms may have been more likely to respond. Indeed, less than 15% of participants had mild IBS, and the prevalence of poor sleepers was high at over 80%, when compared with the prevalence reported in other studies. A 2018 meta-analysis of 36 studies established a pooled prevalence of sleep disturbance of approximately 40% among individuals with IBS across Asia, North America, and Europe.³⁵ Other population-based studies have observed a prevalence of sleep disturbance in IBS ranging from 30% in a study of 2269 participants conducted in Minnesota in 2004,³⁴ to 47% in a study of 651 adults and adolescents conducted in Saudi Arabia 2023.³⁶ Another study reported a higher prevalence of 74%, but this was among only 23 participants, who were referred by a gastroenterologist for participation in the study.⁸

Our use of the validated PSQI to identify poor sleepers is a strength of the study. This is the most widely used measure of subjective sleep quality in IBS-related sleep studies and can be utilised easily in large cohorts, compared with more objective measures, such as polysomnography and actigraphy, which are limited by the need for specialised equipment.⁶ However, to our knowledge, it has not been validated for use in IBS, specifically. We have confirmed findings from other studies that poor sleep is associated with greater somatoform symptom-reporting,¹¹ although we could not determine the direction of these effects due to the cross-sectional design of the study. Unlike other studies, we did not show an association

between poor sleep and more severe IBS symptoms.⁶ Subjectively reported sleep disturbance has been consistently associated with gastrointestinal symptoms in IBS, whereas studies employing objective measures have yielded more variable results.⁶ This may be because objective assessment measures sleep patterns and sleep quality directly, whereas subjective sleep questionnaires are at risk of recall bias, and participant's assessment of their sleep quality is subjective, meaning that those with more severe IBS symptoms may be more likely to report poorer sleep, possibly due to the disturbance of sleep by their gastrointestinal symptoms. However, a sleep diary study among women with IBS suggests that it is sleep disturbance that influences IBS symptoms, with those reporting poor sleep quality experiencing an exacerbation of gastrointestinal symptoms the following day, with no change in effect when psychological distress or stress were controlled for.⁷ The observation that poor sleep drives symptoms, rather than *vice versa*, is partially supported by another study employing both subjective and objective sleep measures.⁹ Investigators found that self-reported reduced sleep quality predicted worse abdominal pain, anxiety, and fatigue the next day in patients with IBS and reduced sleep efficiency. Objective measure of sleep quality by actigraphy also showed a positive trend with worse abdominal pain the next day, but this was not significant. However, the inverse was not true; worse IBS symptoms did not predict subsequent sleep disturbance. In the study, self-rated sleep quality scores and objective measures of sleep quality were significantly correlated with each other, but this relationship was deemed to be of low magnitude.⁹

Sleep disturbance is a recognised feature of common mental disorders, such as depression and anxiety.^{37, 38} These conditions are prevalent in IBS,³ and could confound the association between sleep quality and IBS symptoms. We found poor sleepers to have significantly higher anxiety and depression scores on univariate analysis, replicating the positive associations between greater psychological distress and poor sleep in IBS seen by

others.^{7, 39, 40} However, the direction of this effect is less clear. Our logistic regression analysis found no independent association between anxiety and depression and poor sleep. A population-based study of 1322 Australians found more severe subjective sleep disturbance to be a significant predictor for meeting diagnostic criteria for IBS, even after controlling for age, sex, and psychological distress.¹² Another study also concluded that the poorer sleep quality observed in patients with IBS, confirmed both subjectively and objectively, was not due to differences in their baseline levels of anxiety or depression.¹⁰ Conversely, in a prospective case-control study, patients with IBS slept more hours per day compared with healthy controls, but had more waking episodes and felt less well-rested.¹¹ Waking episodes were correlated with worse abdominal pain and poorer quality of life, and it was concluded that sleep disturbance was partially mediated by mood. Nonetheless, there are questions related to the potential for misperception in sleep studies, and the robustness of non-invasive sleep measures, such as the wrist-worn movement sensors used in actigraphy, which may misreport wakeful stillness as sleep.⁴¹ The inconsistent findings regarding the associations between IBS, sleep, and psychological factors warrant further study. It may be that, as alluded to above, IBS symptom severity is driving poor sleep, poor psychological health, and somatoform symptom-reporting.

We found older age to be independently associated with poor sleep in Rome IV IBS, and this has also been reported in other studies.⁴² The relevance of this association is uncertain as sleep disturbance is common in the older population.⁴³ However, a population-based study of 2269 participants in Minnesota found that IBS was significantly more common among individuals with self-reported sleep disturbance, even after adjusting for age, sex, and somatoform symptom-reporting.³⁴ Our age-related results contrast with the only other study we are aware of to have examined sleep disturbance specifically among individuals with Rome IV-defined IBS.³⁶ This study, conducted in Saudi Arabia, reported a

lower prevalence of poor sleep quality of 46% using the same PSQI definition, and found that younger participants were more likely to have poor sleep. However, this might reflect differences in the study populations, particularly the much younger demographic of their cohort, with a median age of 28 years, compared with our study.

In summary, in this study people with Rome IV IBS reported a high burden of sleep disturbance with significant consequences for their health-related quality of life. Poor sleep was associated with older age and higher levels of somatoform symptom-reporting. Although current evidence regarding sleep disturbance in IBS is inconsistent, sleep quality should be explored as a target for treatment. Melatonin has shown potential as a therapeutic option, improving overall IBS symptom severity, abdominal pain severity, and IBS-specific health-related quality of life.^{14, 15} Controlled, prospective studies of sleep disturbance in IBS, using standardised protocols for subjective and objective measures of sleep quality, could improve our understanding of the importance of sleep in the management of IBS, as part of an holistic and personalised approach to care.

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CONFLICTS OF INTEREST/STUDY SUPPORT

Guarantor of the article: MSC is guarantor.

Specific author contributions: MSC, VCG, CEN, CJB, and ACF conceived and drafted the study. VCG and CEN collected all data. MSC and VCG analysed and interpreted the data.

MSC, CJB, and ACF drafted the manuscript. All authors have approved the final draft of the manuscript.

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Table 1. Characteristics of 341 Individuals with Rome IV Irritable Bowel Syndrome According to Sleep Quality.

	Good sleeper (n = 54)	Poor sleeper (n = 287)	P value*
Female (%)	46 (85.2)	254 (88.5)	0.492
Mean age (SD)	44.2 (15.2)	50.4 (14.3)	0.007
White ethnicity (%)	50 (92.6)	280 (97.6)	0.058
Married (%)	43 (79.6)	185 (64.5)	0.030
Smoker (%)	3 (5.6)	24 (8.4)	0.483
Alcohol user (%)	39 (72.2)	162 (56.4)	0.031
University or postgraduate level of education (%)	32 (59.3)	118 (41.1)	0.014
IBS subtype (%)			
IBS-C	13 (24.1)	48 (16.7)	0.438
IBS-D	22 (40.7)	123 (42.9)	
IBS-M	19 (35.2)	114 (39.7)	
Most troublesome symptom (%)			
Abdominal pain	15 (27.8)	66 (23)	0.192
Constipation	6 (11.1)	29 (10.1)	
Diarrhoea	4 (7.4)	55 (19.2)	
Bloating or distension	12 (22.2)	74 (25.8)	
Urgency	17 (31.5)	63 (22)	
Mean total IBS-SSS (SD)	239.7 (98.2)	295.9 (101.1)	<0.001
IBS-SSS severity (%)			
Mild	11 (21.6)	38 (13.4)	0.064
Moderate	23 (45.1)	103 (36.3)	
Severe	17 (33.3)	143 (50.4)	
IBS after acute infection (%)	111 (20.4)	37 (12.9)	0.147
IBS diagnosed for 5 years or more (%)	36 (66.7)	236 (82.2)	0.009
Mean PHQ-12 score (SD)	6.4 (3.4)	10.9 (4.2)	<0.001

Mean HADS-anxiety score (SD)	7.1 (4.2)	10.7 (4.5)	<0.001
Mean HADS-depression score (SD)	3.85 (2.7)	8.23 (4.5)	<0.001
Mean IBS-QOL (SD)	66.78 (21.07)	46.57 (23.37)	<0.001

**P* value for Pearson χ^2 for comparison of categorical data. independent samples *t*-test for continuous data.

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