

# Association of irritable bowel syndrome and sleep apnea in patients referred to sleep laboratory

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**Background:** Irritable bowel syndrome (IBS) is assumed as one of the most frequent gastrointestinal disorders, which decreases the patient's quality of life. IBS pathogenesis, however, is not clearly defined. It seems that sleep apnea induces or escalates IBS clinical symptoms. This study aims at evaluating of IBS prevalence in patients, who are afflicted or are not afflicted with sleep apnea. **Materials and Methods:** This was a case-control study, which was implemented in a sleep laboratory located in Isfahan, Iran. We recruited 200 patients being more than 15 years from 2014 to 2015. Based on the apnea-hypopnea index (AHI), we recruited 100 patients in each of two groups: negative sleep apnea (NSA) (AHI  $\leq 4$ ) and positive sleep apnea (PSA) (AHI  $> 4$ ). IBS was diagnosed through a Rome III diagnostic questionnaire. **Results:** Overall, the prevalence of IBS among patients referred to sleep laboratory was 17.6%. Indeed, IBS prevalence in NSA and PSA groups were 8.2% and 27.1%, respectively. Furthermore, odds ratio of IBS in PSA group versus NSA was 3.92 (95% confidence interval = 1.58–9.77,  $P = 0.003$ ). Our results showed that the prevalence of IBS did not differ significantly between various severity of sleep apnea ( $P = 0.452$ ). **Conclusion:** This study showed that there was a positive association between sleep apnea and IBS.

**Key words:** Irritable bowel syndrome, polysomnography, prevalence, sleep apnea syndrome

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## INTRODUCTION

Irritable bowel syndrome (IBS) is assumed as one of the most frequent chronic gastrointestinal disorders, which is commonly diagnosed according to its clinical symptoms and absence of organic causes. Epidemiological studies authenticate that IBS is prevalent among 7%–21% of the world population. To elaborate, the lowest and the highest prevalence of IBS is estimated in the USA and Southern Asia, respectively.<sup>[1,2]</sup>

This disease significantly decreases the patient's quality of life and occupational efficiency. For example, more than 31 million individuals annually attend in outpatient clinics in the USA, and it seems that the direct and indirect expenditure of disease treatment reaches up to \$20 billion.<sup>[2]</sup>

Although IBS pathogenesis is not clearly defined, some environmental factors such as early life stressor, antibiotic usage, food intolerance, enteric infections, and physiological stressors may contribute to the disease incidence. On the other hand, altered pain perception, dysregulation of brain-gut axis, dysbiosis, increased intestinal permeability, as well as visceral hypersensitivity, and increased gut mucosal activation could be assumed as individual causes leading to IBS.<sup>[2]</sup>

Nevertheless, neither of those justifies all of the clinical signs and symptoms.

Furthermore, some articles documented that autonomic system could be clearly involved in IBS pathogenesis. For example, a systematic review article, which evaluated 196 case-control studies, authenticated that dominant sympathetic nervous system correlates with IBS incidence.<sup>[3]</sup> In 2009, Manabe *et al.* compared the autonomic system activity in patients afflicted by

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IBS with healthy individuals. This study documented that, by comparison with healthy individuals, reduced parasympathetic nervous system function, as well as enhanced sympathetic nervous system activity, was found in IBS patients. In fact, sympathetic activation leads to the perception of intestinal distention. This perception would be appeared as abdominal pain and bloating symptoms, which were frequently reported in IBS patients.<sup>[4]</sup>

Sleep apnea, a prevalent sleep disorder, has been considered as a potential cause, which yields to acute and sustained activation of the sympathetic nervous system.<sup>[5,6]</sup> In accordance with the epidemiological studies, which was implemented from 1993 to 2013, the prevalence of sleep apnea in males and females were 22% and 17%, respectively. Furthermore, these studies documented that the disease prevalence escalated with time.<sup>[7]</sup>

Different evidence show that the patients who frequently experienced sleep apnea would be afflicted by hypoxia and hypercapnia, which result in increased sympathetic nervous system activity. Furthermore, this enhancement conventionally lasts in waking.<sup>[8]</sup>

Overall, it sounds plausible that sleep apnea leads to increased sympathetic nervous system activity which induces or escalates IBS clinical symptoms. This study aims at evaluating of IBS prevalence in patients, who are afflicted or are not afflicted with sleep apnea.

## MATERIALS AND METHODS

This was a case-control study, which was implemented in Bamdad sleep laboratory, Isfahan, Iran. The study protocol was approved by the Ethical Committee of Isfahan University of Medical Sciences, Isfahan, Iran (Project Number: 394273). We recruited patients referred to Bamdad sleep laboratory from 2014 to 2015. The convenience sampling method was applied in the present study. Inclusion criteria encompassed all of the patients ranging from 15 to 60 years while they were referred to a sleep laboratory for apnea assessment. Exclusion criteria were irregular menstruation, chronic constipation, and known organic bowel disease. We provided all of the patients with the oral description, and informed consent was obtained from them.

Patients underwent overnight polysomnography monitoring comprised electrocardiography, electrooculography, electromyography, and electroencephalography. The results of polysomnography were reported by apnea-hypopnea index (AHI). This index was defined as follow: all of the apneas and hypopneas occurring within an hour of sleep. In fact, airflow halt for 10 s or more was considered as apnea and hypopnea was defined as a minimum 30% decrease in

airflow making at least 2% reduction of oxygen saturation for 10 s or more.<sup>[9]</sup> The patients are considered as negative sleep apnea (NSA) if their AHI is  $\leq 4$ . In contrast, AHI in positive sleep apnea (PSA) is  $>4$ .

Consistently, 100 patients were recruited in each of the PSA and NSA groups. Patients with PSA were categorized as mild sleep apnea (5–14), moderate sleep apnea (15–29), and severe sleep apnea ( $\geq 30$ ).<sup>[10]</sup>

In addition, demographic data (which included age, sex, and race) as well as information regarding weight, height, and history of being a smoker were recorded. Afterward, IBS was diagnosed through a Rome III diagnostic questionnaire. This was a self-reported questionnaire, which included eight questions regarding the most convenient clinical signs and symptoms of IBS. Based on Rome III, IBS patients were afflicted by recurrent abdominal discomfort or pain lasted at least 3 days in a month during the past 3 months while these patients met two or more of the following criteria: (i) pain relief with defecation, (ii) association between onset of pain and alteration in frequency of defecation, and (iii) association between onset of pain and alteration in form of the feces. Furthermore, patients' symptoms should initiate for at least 6 months before diagnosis. The questionnaire validity and reliability were approved in previous studies.<sup>[11]</sup>

Importantly, the absence of other gastrointestinal problems was confirmed by clinical examination of the participants implemented by a gastroenterologist. In this context, paraclinical assessment of the patients was carried out when it was needed.

### Statistical analysis

All statistical analysis was conducted using SPSS version 18 (SPSS Inc., Chicago, IL, USA). Demographic data were shown through the application of descriptive statistics. Quantitative variables were reported as means and standard deviations while quantitative statistics were presented as a percentage. We used independent samples *t*-test and Mann-Whitney U-test to compare age and body mass index (BMI) variables between two groups, respectively. IBS prevalence was compared between the two groups through Pearson Chi-square test. We applied binary logistic regression to compare the risk of IBS between the two groups while age, sex, and BMI were adjusted. We set the level of statistical significance at  $P < 0.05$ .

## RESULTS

Out of 200 included participants, three ones were excluded due to irregular menstruation (two) and known organic bowel disorders (one) which all of them were assign to NSA

group. Therefore, we finally undertook this study among 197 participants. Some characteristics of the patients are shown overall and according to their sleep apnea category in Table 1.

By comparison with NSA group, the male frequency was significantly higher in PSA group ( $P = 0.006$ ). Furthermore, patients of PSA group were significantly older and more obese than their NSA counterparts (in both of the mentioned variables:  $P < 0.001$ ).

Overall, the prevalence of IBS among patients referred to sleep laboratory was 17.6% ( $n = 34$ ). Most of the PSA patients afflicted with severe and moderate sleep apnea (56.6% [ $n = 56$ ] and 27.3% [ $n = 27$ ] respectively) while a minority of the PSA patients were assigned in mild sleep apnea (16.2% [ $n = 16$ ]).

In comparison with NSA group, the prevalence of IBS was significantly higher in PSA (odds ratio [OR] = 4.13, 95% confidence interval [CI] = 1.76–9.68,  $P = 0.001$ ). Indeed, IBS prevalence in NSA and PSA groups were 8.2% ( $n = 8$ ) and 27.1% ( $n = 26$ ), respectively ( $P = 0.001$ ) [Table 2].

Our results showed that 40% ( $n = 6$ ) of the mild sleep apnea cases were afflicted by IBS. IBS prevalence in severe and moderate sleep apnea were 26.4% ( $n = 14$ ) and 22.2% ( $n = 6$ ), respectively. However, there was not any association between IBS prevalence and AHI levels ( $P = 0.452$ ) [Table 3].

For all subjects studied, regardless of whether they were in the NSA or PSA group, the prevalence of male IBS was higher than female IBS (25% [ $n = 26$ ] vs. 9.2% [ $n = 8$ ] [ $P = 0.004$ ]). IBS prevalence in males and females afflicted by sleep apnea was 36.1% ( $n = 22$ ) and 11.4% ( $n = 4$ ), respectively ( $P = 0.009$ ). IBS prevalence in male patients allocated to NSA group was higher than female (9.3% [ $n = 4$ ] vs. 7.7% [ $n = 4$ ] [ $P = 0.779$ ]).

Crude OR of IBS in PSA group versus NSA was 4.14 (95% CI = 1.76–9.69,  $P = 0.001$ ). This OR was changed to 3.92 (95% CI = 1.58–9.77,  $P = 0.003$ ) when age, sex, and BMI variables were adjusted through logistic regression analysis.

## DISCUSSION

The results of the present study showed that there is a positive association between sleep apnea and IBS.

Our study as well as similar ones, which was implemented in Puerto Rico showed that sleep apnea was more prevalent in males and obese people. Furthermore, comparison with

**Table 1: General characteristics of the patients referred to the sleep laboratory overall and according to their sleep apnea category**

Variable	Group			P
	Overall (n=197)	PSA (n=100)	NSA (n=97)	
Age, mean±SD	45.24±12.05	51.97±10.15	38.15±9.6	<0.001
Gender, n (%)				
Male	108 (55.4)	65 (65)	43 (45.3)	0.006
Female	87 (44.6)	35 (35)	52 (54.7)	
BMI group				
<18.5	1	0	2.2	<0.001
18.5–24.99	17.9	0	37	
25–29.99	44.7	41.8	47.8	
≥30	36.4	58.2	13	

SD = Standard deviation; BMI = Body mass index; NSA = Negative sleep apnea; PSA = Positive sleep apnea

**Table 2: Irritable bowel syndrome prevalence in positive sleep apnea group versus negative sleep apnea group**

IBS	Sleep apnea		P
	Yes, n (%)	No, n (%)	
Yes	26 (27.1)	8 (8.2)	0.001
No	70 (72.9)	89 (91.8)	

IBS = Irritable bowel syndrome

**Table 3: Irritable bowel syndrome prevalence according to the severity of sleep apnea in patients referred to sleep laboratory**

IBS	Severity of sleep apnea			P
	Mild, n (%)	Moderate, n (%)	Sever, n (%)	
Yes	6 (40)	6 (22.2)	14 (26.4)	0.452
No	9 (60)	21 (77.8)	39 (73.6)	

IBS = Irritable bowel syndrome

NSA group, the mean age of the participants allocated in PSA was higher.<sup>[12]</sup>

Surprisingly, our study documented that, in comparison with females, IBS was more prevalent in males, but, by contrast, previous studies showed that the prevalence of IBS was higher among female participants.<sup>[13]</sup> This discrepancy between the present and former studies could be attributed to our study population differing with the corresponding ones.

There are rarely published data regarding the association of IBS and sleep apnea. Nevertheless, in a study, which was implemented at the Sleep Center of Drexel University (Philadelphia, USA) on patients being 18–85 years, the researchers authenticated that obstructive sleep apnea (OSA) associated with a wide range of the gastrointestinal symptoms. Their study, which was undertaken through Rome questionnaire, indicated that IBS was the most common cause of lower gastrointestinal symptoms.<sup>[14]</sup> Gold *et al.* compared AHI in lean women

afflicted by IBS and healthy female population. They showed that the AHI was higher in the former group though it was not significant.<sup>[15]</sup> It seems that small sample size of the latest above-mentioned study ( $n = 24$ , 12/each group) could be accountable for results differing from ours. Furthermore, IBS patients, who were recruited by Avram *et al.*, were lean; hence, selection bias may be affected their results.

It sounds plausible that sympathetic nerve dominance could potentially associate IBS and sleep apnea. To elaborate, hypoxia induces activation of sympathetic nervous system, which provides critical levels of oxygen being indispensable for physiological function.<sup>[8]</sup>

It is well documented that activation of the sympathetic nervous system continuously and disproportionately occurs in patients afflicted with OSA. Causes, which may contribute to over-activation of sympathetic nervous system in OSA patients are as follows.<sup>[16]</sup>

The results of our study indicated that, in comparison with severe and moderate sleep apnea cohort, IBS prevalence was rather higher in mild sleep apnea group; nevertheless, this difference was not significant. Avram *et al.* evaluated the association of sleep disorder breathing with the functional somatic syndrome. They showed that the prevalence of IBS, headache and sleep onset of insomnia was high in upper airway resistance syndrome (UARS) patients, whose AHI was <10/h. This prevalence, however, decreased when the severity of sleep disorder breathing escalated. It seems that, by comparison with healthy individuals, the prevalence of alpha-delta sleep is higher in UARS patients. Hence, deterioration of sleep quality may contribute to the dysfunction of autonomic nervous system.<sup>[17]</sup>

## CONCLUSION

Overall, this study showed that there was a positive association between sleep apnea and IBS.

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### Conflicts of interest

There are no conflicts of interest.

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