## <u>original research</u>

# Distribution of LPRD in OSAHS Patients: Is There a Correlation?

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## ABSTRACT

**Objective** • Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) and Laryngopharyngeal Reflux Disease (LPRD) are interrelated medical conditions affecting the respiratory system. This article aimed to investigate the potential correlation between the two.

**Methods** • This cross-sectional study was carried out on a total of 52 participants diagnosed with both OSAHS and LPRD. Clinical data of baseline demographics of year, sex, BMI, including clinical indicators such as AHI (Apnea Hypopnea Index), OSAHS severity grading, RFS (Reflux Finding Score), RSI (Reflux Symptom Index), and 24-hour pH level were collected. Statistical analysis was then conducted to evaluate the correlation between OSAHS and LPRD.

**Results** • Among the 52 patients, the the average age was  $43.3\pm11.6$  years with a mean  $24.7\pm2.9$  kg/m<sup>2</sup> BMI level. The mean duration of OSAHS was  $4.1\pm1.7$  years with mean  $38.7\pm12$  AHI scores and 30.8% mild OSAHS, 51.9% moderate OSAHS, and 17.3% severe OSAHS. Mean LPRD

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## INTRODUCTION

Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) is one of the most prevalent sleep disorders, affecting a large number of individuals all around the world.<sup>1</sup> It can significantly impair both physical and mental health.<sup>2</sup> In OSAHS pathology, recurrent cycles of partial or complete airway obstruction can result in breath pause, frequent awakenings, and disruption of regular sleep patterns for several times during sleep.<sup>3</sup>

duration was 3.2±1.5 years with a mean 15.9±4.9 RFS score, mean 28.0±6.8 RSI score, and mean 3.9±0.8 24-hour pH level. There was a strong positive correlation between AHI scores and both the RFS score (r>0.9, P < .01) and RSI score (r>0.9, P < .01). While a strong negative correlation between AHI scores and 24-hour pH level was observed (r < -0.8, P< .01). And there was a strong positive correlation between OSAHS severity levels and both the RSF score (r>0.8, P <.01) and RSI score (r>0.79, P < .01). While a significant negative correlation between OSAHS severity and 24-hour pH level was detected (r < -0.7, P < .01).

**Conclusions** • The findings of this cross-sectional study demonstrate a strong positive correlation between the severity of OSAHS, as indicated by AHI scores, and the severity of LPRD, as measured by RFS and RSI scores. A negative correlation was also observed between AHI scores and 24-hour pH level, indicating a connection between these two medical conditions. (*Altern Ther Health Med.* [E-pub ahead of print.])

Therefore, the symptoms experienced by individuals with OSAHS are various and they often suffer from symptoms like loud snoring, breath cessation, morning headaches, dry mouth or sore throat, as well as daytime sleepiness and fatigue.<sup>3</sup> Furthermore, untreated OSAHS can also be extended to a potential cause of multiple system disturbances like cardiovascular diseases, metabolic disorders, cognitive and memory impairment, and even decreased quality of life.4,5 Among current treatment options, continuous positive airway pressure (CPAP) therapy has been proven to be very efficient in maintaining airway open during sleep.<sup>6</sup> Additionally, lifestyle modifications like losing weight or doing sports have also demonstrated potential in managing OSAHS, especially in individuals with obesity.<sup>7</sup> In some severe cases, surgeries to reshape airway structures may be considered the final option.8 As for OSAHS diagnosis, polysomnography (PSG) currently remains the gold standard in clinical practice.9

Since OSAHS is a complicated disease caused by multiple mechanisms, identifying the related risk factors is essential in

understanding and managing OSAHS effectively. Risk factors like obesity, hypertension, family history, and sex have been reported to increase the susceptibility to OSAHS.<sup>10,11</sup> Recently, some researchers have found that laryngopharyngeal reflux disease(LPRD) may contribute to OSAHS due to the anatomical and physiological connections between the upper airway and gastrointestinal system.<sup>12</sup>

LPRD is a medical condition that refers to the backflow of stomach acid into the larynx and pharynx, thus resulting in irritation and inflammation in the upper airway.<sup>13</sup> Individuals with LPRD can experience symptoms such as chronic cough, voice changes, throat clearance, and swallowing difficulty.<sup>14</sup> The diagnosis of LPRD typically involves a thorough examination via laryngoscope to observe throat structures for signs of inflammation or irritation, and pH monitoring or score evaluation can also be conducted to help diagnosis.<sup>15,16</sup>

The relationship between OSAHS and LPRD is complex and has not fully clarified so far. Researchers have proposed several pieces of evidence to reveal their potential relationship.<sup>17</sup> On one hand, the upper airway and gastrointestinal system share anatomical and physiological connections.<sup>18</sup> Acid reflux from the stomach can reach the upper airway, potentially aggravating airway inflammation and narrowing in individuals with OSAHS.<sup>19</sup> On the other hand, the vibrations that occur during loud snoring and breath disturbances in OSAHS patients can push stomach acid back up into the laryngopharyngeal area, thus aggravating LPRD in reverse.<sup>20</sup> Moreover, it's also essential to notice that both OSAHS and LPRD share some common risk factors, such as obesity and lifestyle habits like smoking or alcohol consumption.<sup>21,22</sup>

While the exact relationship between these two medical conditions still remains complex. Therefore, in this article, we will explore the association based on the data collected from clinical patients in order to be more comprehensive in both symptoms and improve therapeutic effects for diagnosed individuals in clinical practice.

## PATIENTS AND METHODS

#### Participants

This cross-sectional research was carried out in Zhuhai Hospital of Integrated Traditional Chinese & Western Medicine from 6/2022 to 6/2023, in accordance with the tenets of the Declaration of Helsinki. Ethical approval was achieved by the Institutional Review Board of Zhuhai Hospital of Integrated Traditional Chinese & Western Medicine. A total of 52 patients diagnosed with both OSAHS and LPRD were enrolled in this study, and they should provide written informed consent before participating.

## Methods

Demographic information like years, sex, body mass index (BMI), and duration of OSAHS and LPRD were already recorded in patients' medical records.

OSAHS was assessed using the Apnea Hypopnea Index (AHI) and severity classification criteria. AHI (Apnea Hypopnea Index) score was calculated using polysomnography (PSG),

which included tests to measure airflow and oximetry during sleep. The subjects were classified as having mild OSAHS with AHI scores between 5 and 15, moderate OSAHS with scores between 16 and 30, and severe OSAHS with scores above 30.

LPRD was assessed using Reflux Symptom Index (RSI), Reflux Finding Score (RFS) and 24-hour pH level. 24-hour pH level was monitored and evaluated via a single-use, two-channel, triple sensor antimony pH catheter, and a measurement system was used to record the pH level. In RSI (Reflux Symptom Index) evaluation, subjects would report whether they had symptoms like voice problems, throat clearance, swallowing difficulty, choking, and so on. Each RSI symptom was scored from 0 (no complaint) to 5 (severe complaint). If the final score was more than 13, then the subject was considered to have LPRD. And in RFS(Reflux Finding Score) evaluation, specialists would use a microscope to check pathologic changes like laryngeal or subglottic edema, erythema or hyperemia, tissue granulation, posterior commissure hypertrophy and so on. The subjects were considered to have LPRD if the RFS total score was more than 7.

#### Statistical analysis

All statistical analyses were performed by using the Statistical Package for Social Sciences (SPSS) software version 26 (IBM Corporation, Armonk, NY, USA). Data were presented as mean  $\pm$  standard deviation (SD) for continuous variables and frequencies (percentages) for categorical variables. The correlations between OSAHS indicators and LPRD indicators were examined using Pearson's correlation analysis if the data were distributed normally and Spearman's rank correlation analysis if the data were not distributed normally. *P* < .05 was considered to be statistically significant.

## RESULTS

The demographic characteristics of all the participants were shown in Table 1. A total of 52 individuals (25 males, 48.1% and 27 females, 51.9%), with age ranging from 22 to 64 years (mean 43.3 $\pm$ 11.6) were enrolled in this study. The mean BMI ranged from 19.3 to 30.0 kg/m<sup>2</sup> (mean 24.7 $\pm$ 2.9). Regarding OSAHS, disease duration ranged from 1.5 to 7 years (mean 4.1 $\pm$ 1.7). AHI scores ranged from 18 to 62 (mean

Table 1. Demographic characteristics of the participants

Variables	n=52	
Age(years)	43.3±11.6(22-64)	
Gender		
Male	25(48.08%)	
Female	27(51.92%)	
BMI(kg/m <sup>2</sup> )	24.7±2.9(19.3-30.0)	
OSAHS duration(years)	4.1±1.7(1.5-7.0)	
AHI(times/h)	38.7±12.0(18-62)	
OSAHS severity		
Mild	16(30.8%)	
Moderate	27(51.9%)	
Severe	9(17.3%)	
Maxium obstructive apnea time(s)	31.5±7.8(18-50)	
LPRD duration(years)	3.2±1.5(1-6)	
RFS score	15.9±4.9(7-24)	
RSI score	28.0±6.8(18-40)	
24-hour pH level	3.9±0.8(2.0-5.2)	

Abbreviations: n, Number; BMI, body mass index; AHI, apnea hypopnea index; RFS, reflux finding score; RSI. reflux symptom index.

38.7 $\pm$ 12), and maximum obstructive apnea time ranged from 18 to 50 seconds (mean 31.5 $\pm$ 7.8). In OSAHS severity classification, 16 patients (30.8%) had mild OSAHS, 27 patients had moderate OSAHS (51.9%), and 9 patients (17.3%) had severe OSAHS. Regarding LPRD, disease duration ranged from 1 to 6 years (mean 3.2 $\pm$ 1.5). According to pHmetry data, 24-hour pH levels ranged from 2.0 to 5.2 (mean 3.9 $\pm$ 0.8). RFS score ranged from 7 to 24 (mean 15.9 $\pm$ 4.9), and RSI score ranged from 18 to 40 (mean 28.0 $\pm$ 6.8).

Table 2 shows the correlations between AHI scores and RSI scores, RFS score, and 24-hour pH levels. Based on Spearman's correlation analysis, there was a strong positive correlation between AHI scores and both the RFS score(r>0.9, P < .01) and RSI score(r>0.9, P < .01). Furthermore, the correlation analysis demonstrated a strong negative correlation between AHI scores and 24-hour pH level (r < -0.8, P < .01).

Table 3 demonstrates the correlations between OSAHS severity and RSI score, RFS score, and 24-hour pH level. Based on the Spearman's correlation analysis, the results revealed a strong positive correlation between OSAHS severity levels (graded as mild, moderate, and severe) and both the RSF score(r>0.8, P < .01) and RSI score(r>0.79, P < .01). In contrast, the analysis indicated a significant negative correlation between the severity of OSAHS and the 24-hour pH level (r < -0.7, P < .01).

## DISCUSSION

OSAHS and LPRD are prevalent medical conditions that can severely impact an individual's quality of life if left untreated. Recent findings have found some potential correlation between each other, while the accurate mechanism still remains unknown. Therefore, in this study, we carried out an analysis on a total of 52 participants diagnosed with both OSAHS and LPRD. Clinical data of baseline demographics of year, sex, BMI, including clinical indicators such as AHI (Apnea Hypopnea Index), OSAHS grading, RFS (Reflux Finding Score), RSI (Reflux Symptom Index), and 24-hour pH level, were collected. And Statistical analysis was then conducted to evaluate the correlation between OSAHS and LPRD.

Among the 52 patients, the average age was  $43.3\pm11.6$  years with mean  $24.7\pm2.9$  kg/m<sup>2</sup> BMI level. The mean duration of OSAHS was  $4.1\pm1.7$  years with mean  $38.7\pm12$  AHI scores and 30.8% mild OSAHS, 51.9% moderate OSAHS and 17.3% severe OSAHS. Mean LPRD duration was  $3.2\pm1.5$  years with a mean  $15.9\pm4.9$  RFS score, mean  $28.0\pm6.8$  RSI score, and mean  $3.9\pm0.8$  24-hour pH level.

This cross-sectional study's results provided valuable insights into the potential correlation between OSAHS and LPRD. The strong positive correlation observed between the severity of OSAHS, as indicated by AHI scores, and the severity of LPRD, as measured by both the RFS and RSI scores, suggested a potential interplay between these two medical conditions. As OSAHS became more severe, it appeared to be associated with a greater chance of experiencing LPRD symptoms. 
 Table 2. Correlation between AHI and RFS, RSI, 24H pH

 level

AHI	RFS	RSI	24h pH level
r	0.9	0.938	-0.801
P value	<.01	<.01	<.01

**Abbreviations**: AHI, apnea hypopnea index; RFS, reflux finding score; RSI, reflux symptom index.

**Table 3.** Correlation between OSAHS severity and RFS, RSI,24H pH level

OSAHS severity	RFS	RSI	24h pH level
r	0.826	0.79	-0.738
P value	<.01	<.01	<.01

Abbreviations: RFS, reflux finding score; RSI, reflux symptom index.

The observed strong negative correlation between AHI scores and 24-hour pH level indicated a potential link between OSAHS severity and the presence of acid reflux in the upper airway. The reduction in pH levels as OSAHS worsened suggested a higher prevalence of acid in the larynx and pharynx, implying that OSAHS severity might influence the occurrence of acid reflux. This finding was consistent with previous research that explored the relationship between sleep apnea and acid reflux.<sup>23,24</sup> Our results indicated that the mechanical changes and pressure fluctuations in the upper airway during apnea episodes may facilitate the flow of gastric contents back into the laryngopharynx.<sup>25,26</sup>

Furthermore, the study demonstrated a strong positive correlation between OSAHS severity (mild, moderate, severe) and both the RFS and RSI scores. This finding indicated that as OSAHS became more severe, the severity of LPRD symptoms tended to increase at the same time. These results were consistent with the previous hypothesis that the severity of OSAHS may be a potential contributing factor to the development and exacerbation of LPRD.<sup>27,28</sup> As OSAHS progressed, the increased collapsibility of the upper airway could facilitate acid reflux and worsen LPRD symptoms to some extent.

The potential association between OSAHS and LPRD was supported by the findings observed in this study, suggesting that these two medical conditions might act as a risk factor for each other. The coexistence of OSAHS and LPRD in the same patient raised the question of shared pathophysiological mechanisms. It was reasonable that the inflammation and irritation caused by repeated episodes of acid reflux may lead to increased pharyngeal collapsibility, thus contributing to the development or aggravation of OSAHS.<sup>29</sup> Conversely, OSAHS-related upper airway obstruction may promote the aspiration of gastric contents back into the larynx and pharynx, thus contributing to the onset or exacerbation of LPRD.<sup>30</sup>

While it was also important to acknowledge some limitations of this study. The cross-sectional design did not delve deeper into analyzing and exploring the causal relationship between OSAHS and LPRD, and longitudinal studies or randomized controlled trials would be highly beneficial. Moreover, the relatively small sample size and data collected from medical records of this study may limit the generalizability of these findings. Therefore a larger and multicenter study that involves more participants from different demographics and geographic regions would enhance the generalizability and persuasiveness of these findings. Additionally, this study focused on adult patients, and the findings may not directly apply to pediatric populations. Further research should explore the potential correlation between OSAHS and LPRD in children to comprehensively understand the relationship across different age groups.

Despite these limitations mentioned above, the findings discovered from this study exhibited clinical significance and implications for patient diagnosis and treatment. Furthermore, collaboration between sleep-related specialists and gastroenterologists could facilitate a comprehensive assessment and treatment plan for patients diagnosed with both medical conditions. At the same time, healthcare providers or experts should consider addressing both OSAHS and LPRD simultaneously, as successful management of one condition may positively impact the other.

#### CONCLUSION

In conclusion, this study has highlighted the significant correlation between OSAHS and LPRD. The findings suggest that the higher the severity of OSAHS, the higher the frequency and severity of LPRD symptoms and a decrease in the 24-hour pH level. These results contribute to our understanding of the complex interplay between OSAHS and LPRD, emphasizing the importance of comprehensive evaluation and management strategies for patients with both medical conditions in clinical practice.

#### ETHICAL COMPLIANCE

The ethics committee of Zhuhai Hospital of Integrated Traditional Chinese & Western Medicine approved this study. Signed written informed consent were obtained from the patients and/or guardians.

#### CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

#### AUTHOR CONTRIBUTIONS

GC and FX designed the study and performed the experiments, RZ and HL collected the data, GW and RW analyzed the data, GC prepared the manuscript. All authors read and approved the final manuscript.

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