

# Obstructive Sleep Apnea in Patients with Difficult to Treat Asthma

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## ABSTRACT

**Background:** Bronchial Asthma(BA) is quite a common chronic ailment affecting more than 334 million people worldwide. Many patients have poorly controlled asthma despite adequate treatment. Many factors are known to influence asthma control. Previously, various authors reveal the association between Obstructive sleep apnea(OSA) and BA regarding risk and popularity. The essential point of this examination was to research the occurrence of OSA in patients with difficult-to-treat asthma (DTA). **Objective:** Our objective was to determine the frequency of OSA in difficult to treat asthma patients. **Study Design:** Cross-sectional study. **Settings:** The study was conducted in the Department of Pulmonology, District Head Quarter (DHQ) Hospital, Faisalabad Pakistan. **Duration:** The time duration was 6 months starting from July 2018 to December 2018. **Methods:** 73 patients fulfilling the selection criteria were enrolled in the study from the Department of Pulmonology, DHQ Hospital, Faisalabad. Information regarding their demographic data was noted in the proforma. The frequency of obstructive sleep apnea in difficult-to-treat asthma was noted. **Results:** Mean age was 39.44±7.62 years, males were 43.8%(n=32) whereas female were 56.2% (n=41). Frequency of OSA in patients with difficult to treat asthma in our study was recorded in 56.16% (n=41) of the cases. **Conclusion:** We concluded that the frequency of OSA in difficult to treat asthmatic cases is very high. However, identification of this condition is important to reduce the cost of morbidity and quality of life, early and effective management.

**Keywords:** Bronchial asthma, Asthma, Difficult-to-treat Asthma, Obstructive Sleep Apnea, Asthmatic patients, Obstructive Syndrome, Upper Airway Resistance, OSAHS, Sleep Apnea.

## INTRODUCTION

Bronchial Asthma (BA) is a disorder of the airways of inflammatory nature which includes recurrent episodes of chest tightness, shortness of breath, wheezing, and coughing.<sup>1</sup> More than 25 million Americans have asthma. This is 7.7 percent of adults and 8.4 percent of children. Asthma has been increasing since the early 1980s in all age, sex, and racial groups.<sup>2</sup> A recent local study in Karachi enrolled adult population to know the prevalence of asthma and concluded 1.8% asthmatic cases (self-reported),<sup>3</sup> similar to India.<sup>4</sup> Globally, reported risk factors for asthma includes genetic predisposition, family history of atopy, allergic sensitization, tobacco smoke,

respiratory virus infection, diet, obese females, air pollution and occupational exposures.<sup>5,6</sup>

Multiple studies suggest that adult patients are likely to fall into one of five clusters also known as “asthma phenotypes”.<sup>7,8</sup> Different phenotypes include, non-allergic asthma, asthma with fixed airflow limitation, unfavorably susceptible asthma, late beginning asthma, and asthma with obesity.<sup>8</sup>

Many patients have uncontrolled asthma despite adequate treatment. Factors influencing BA symptoms control, such as comorbidities, adherence, environmental exposure, and inhalation technique, should be promptly

identified and adequately treated in managing severe BA.<sup>9</sup>

OSA is known as a major health problem. Commonly it is found in the middle-aged male population and contributes 6% to 17%, of the adult population.<sup>10</sup> OSA and asthma have a strong relation earlier revealed by various studies regarding their risk and prevalence. According to a cohort trial, asthma is considered as an independent etiological factor for snoring in a prospective cohort study.<sup>11</sup>

Obstructive sleep apnea (OSA) can contribute to poor control of BA symptoms. In a systemic review, the OSA prevalence in adults in Asia was reported to be 3.7% to 97.3%.<sup>12</sup> Asthma has a strong association with an increased risk of new-onset OSA.<sup>13</sup>

Overnight polysomnogram (PSG) is a standard diagnostic test while diagnosing OSA.<sup>14</sup> However, various other measures including electrooculogram, electroencephalogram, electrocardiogram, leg electromyograms and chin, finger pulse oximetry, body position, and measurements of airflow may also be helpful.

A higher rate of OSA is recorded in asthmatic patients.<sup>15</sup> The prevalence of OSA in asthmatics was found to be high, ranging from 19% to 60% in non-severe BA, reaching up to 95% in severe asthma.<sup>16</sup>

Recently studies explore the relationship of asthma and OSA in terms of epidemiology, pathophysiology or whether the treatment of one disease affects the control of other. This review will delve into the acknowledged connections and the latest diagnosis and therapies.

The awareness of the determinants of asthma control may help to achieve better disease control. However, while treatment adequacy, treatment adherence, and patient's perception of their own asthma control have been studied, other determinants for asthma control have not been assessed as thoroughly. The essential point of this examination was to explore the predominance of OSA in patients with difficult-to-treat asthma (DTA).

## METHODS

In this cross-sectional study, we enrolled a total of 73 cases, the sample size calculation was done on the following: Prevalence = 74.5%<sup>10</sup>, Confidence level = 95%, and Absolute precision was 10%. The sample population was adults of either gender between 18-65 years of age and those with difficult to treat asthma with Body Mass Index between 18-25 kg/m<sup>2</sup>, we excluded the cases not willing to participate in the study and diagnosed cases of bronchiectasis, pulmonary tuberculosis and chronic obstructive pulmonary disease.

In our study, obstructive sleep apnea was diagnosed using Centers for Medicare & Medicaid Services criteria for diagnosis and treatment of obstructive sleep apnea

A diagnosis for OSA is established if any of the following criteria are met:

1. Apnea-Hypopnea Index (AHI) > 15 events/hour, or
2. AHI  $\geq$  5 and  $\leq$  14 events/hour with established symptoms of excessive daytime sleepiness (EDS); insomnia; mood disorders; impaired cognition; or documented ischemic heart disease, hypertension or history of stroke

The AHI is defined as the frequency of hypopnea and apnea per hour. AHI was calculated by the Level III polysomnography study.

Bronchial asthma was diagnosed on the basis of the history of shortness of breath, recurrent wheezing, cough, and the demonstration of reversibility of bronchial airways obstruction as characterized by an average of more than 12% minimum increase in FEV1 after 15 minutes with inhalation of 400  $\mu$ g salbutamol.

The criteria for difficult to treat asthma were those cases whose symptoms could not be controlled or partially controlled by using a combination of high-dose inhaled corticosteroids (>800 mcg budesonide per day or >500 mcg fluticasone per day), long-acting  $\beta$ 2 agonists (salmeterol 100 mcg daily) and long-acting muscarinic agent 18 mcg per day) for 2 months.

Uncontrolled or partially controlled asthma was labeled if the following criteria are fulfilled:

### Asthma Symptom Control:

In the last 4 weeks, has the patient had:

- Day time BA symptoms > 2 episodes/week? Yes/No
- Any nocturnal waking due to BA? Yes/No
- Rescue use for symptoms > 2 times/week? Yes/No
- Activity limitation due to BA symptoms? Yes/No

### Level of asthma symptom control:

- Well-controlled: None of above
- Partially controlled: 1-2 of above
- Uncontrolled: 3-4 of these

Approval from the ERC committee was obtained. The cases enrolled in the study from the outpatient department of pulmonology ward DHQ Hospital Faisalabad. Informed consent was taken from them before enrolling in the study. Information regarding their demographic data was noted in the proforma. All the patients underwent full history taking, full clinical examination, spirom-

entry and polysomnography. For polysomnography patient was admitted to the ward for one day & sleep study was done overnight by ALICE NIGHTONE sleep study machine. Apnea-hypopnea index was measured by a sleep study device. All information collected was entered on a proforma.

The data was entered for analysis in SPSS-. Where numerical variable i.e. age was computed and presented as mean  $\pm$  standard deviation. Qualitative variables like gender, duration of asthma, OSA was presented in the form of frequency and percentages.

## RESULTS

Out of 73 cases, 43.84% (n=32) cases were between 18-30 years of age and 56.16% (n=41) cases were between 31-65 years of age. The mean age was 39.44 $\pm$ 7.62 years. Males were 43.8% (n=32) whereas female were 56.2% (n=41)

Frequency of OSA in patients with difficult to treat asthma in our study was recorded in 56.16% (n=41) of the cases, whereas 43.84% (n=32) had no findings of this morbidity. There was no significant relationship between OSA and age or gender. (Table II, III).

**Table 1: Characteristics of study population**

	Parameter	n (percentage)
Age Categories	18-30	32(43.8%)
	31-65	41(56.2%)
Gender Distribution	Male	32 (43.8%)
	Female	41 (56.2%)
Obstructive Sleep Apnea	Yes	42 (57.5%)
	No	31(42.5%)

**Table 2: Stratification of obstructive sleep apnea with respect to age**

		Obstructive Sleep Apnea		Total
		Yes	No	
Age Categories	18-30	17	15	32
	31-65	24	17	41
Total		41	32	73
Chi Square		0.214		
P-Value		0.644		

**Table 3: Stratification of obstructive sleep apnea with respect to gender**

		Obstructive Sleep Apnea		Total
		Yes	No	
Gender	Male	14	18	32
	Female	27	14	41
Total		41	32	73
Chi-Square Value		3.567		
P-Value		0.059		

## DISCUSSION

OSA cases are having a higher risk of adverse clinical outcomes including quality of life, daytime alertness, cardiovascular morbidity and mortality.

As there is a strong association of adverse clinical outcomes in OSA, we intend to investigate and record the predominance of OSA in the patients with difficult-to-treat asthma (DTA). We recorded OSA in patients with difficult to treat asthma in our study was recorded in 56.16% (n=41) of the cases, Selma Firat Guven and colleagues<sup>17</sup> evaluated the prevalence of OSA in a difficult-to-treat asthma (DTA) population and recorded 74% of the cases with OSA. These findings are slightly higher than our study.

Julien *et al.* compared 3 groups: severe asthmatics, moderate asthmatics, and non-asthmatic controls. They reported OSA rates of 88% in severe asthmatics, 58% in moderate asthmatics, and 31% in the control group.<sup>18</sup> However we did not categorize the severity of asthma in our cases.

Another trial by Yigla *et al.* used PSG to study 22 patients with DTA. They found a 95.5% prevalence of OSA in the study group.<sup>19</sup> It also shows a higher rate of OSA than recorded in our study. However, asthma is a common disease and affects patients of all ages and both genders. Unfortunately, there are still some asthmatics whose symptoms are poorly controlled despite aggressive therapy.<sup>20</sup> Once the diagnosis of asthma is confirmed and adherence to the treatment plan with appropriate inhaler technique is assessed, it is important to thoroughly examine other factors or comorbidities that can contribute to poor asthma control. OSA is one contributing factor, particularly in patients with nocturnal symptoms. A high prevalence of OSA, ranging from 50% to 96%, has been reported by both questionnaires and PSG in patients with severe asthma.<sup>21</sup>

Another study<sup>22</sup> concluded that coexisting asthma and OSA are associated with poorer sleep quality and more profound nocturnal hypoxemia than either of the conditions alone. The results are similar to earlier findings related to OSA and chronic obstructive pulmonary disease, but they have not previously been described for asthma.

Another study performed by Dixit Ramkant<sup>13</sup> evaluated the adult population for the association of OSA and asthma control level. OSA is largely overlooked in the patients having uncontrolled asthma. The patients with poor asthma control despite optimal recommended management need to be screened for possible OSA so as to reduce treatment cost, morbidity, and improved quality of life in such patients.

The result of our study supported by the above-mentioned studies clarified the association between OSA and uncontrolled bronchial asthma.

It is pertinent to mention that OSA may cause adverse effects in asthma-related outcomes. The accumulative evidence suggests that OSA cases are strongly associated with the poor control of asthma, more frequent exacerbations in asthma and nocturnal symptoms.<sup>23</sup> Interestingly, patients who are diagnosed with OSA and treated with continuous positive airway pressure (CPAP) appear to have better asthma control as shown by morning peak expiratory flow rates and personal satisfaction. It seems that CPAP has beneficial effects on mechanical and neuromechanical properties of lower airways apart from ameliorating gastroesophageal reflux and local as well as systemic inflammation. CPAP also restores sleep and further helps to control asthma.<sup>24</sup>

## CONCLUSION

We concluded that the frequency of OSA in difficult to treat asthmatic cases is very high. However, identification of this condition is important to reduce the cost of morbidity and quality of life, early and effective management.

## LIMITATIONS

The applicability of the findings of present study is limited due to relatively small sample size and restricted to only single institute. All the tests were performed during the daytime, indicating that variations in respiratory functions between day and night and between sitting and lying positions were not given any significance. The frequency of OSA and asthma together and identification of patients who will receive benefit from therapeutic intervention can be established by conducting prospective case studies.

## SUGGESTIONS / RECOMMENDATIONS

The screening for OSA should be performed routinely due to high frequency and adverse effects of OSA in asthmatics. The clinicians should recognize the link between asthma and OSA, early detect and diagnose, and treat OSA patients with asthma to regress airway remodeling rate and deterioration in lung functions.

The casual relationship between OSA and asthma has yet to be elucidated because the underlying pathophysiological mechanisms and co-morbidities due to both the conditions overlap each other. More research work is required to evaluate the influence of extensive treatment of OSA on the clinical outcomes of management of asthma.

## CONFLICT OF INTEREST / DISCLOSURE

Our study has no conflict of interest that would cause any troublesome situation.

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