ORIGINAL ARTICLE

Obstructive Sleep Apnea in Bronchial Asthma Patients: Assessment of Prevalence and Risk Factors

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Abstract

Background: Sleep-related breathing disorders are group of respiratory disease among them obstructive sleep apnea (OSA) is highly prevalent and seen among those having recognized risk factors. Recent studies have shown that asthma and OSA contribute bi directional relationship where each disorder adversely influences the other one. This study was planned to assess OSA among bronchial asthma patients.

Methodology: This study was conducted at Sleep lab of our department among adult patients of bronchial asthma after institutional ethical committee approval. Eligible and willing to participate patients were subjected to clinical assessment protocol that included history, clinical examination, measurement of Sleep Score, BMI, neck circumference etc followed by overnight Level 1 polysomnography.

Results: 50 patients with age range 30 to 68 years constituted the study population with mean age of 48.16 years. 70% patients were female with male female ratio of 1:2.3. The prevalence of OSA in asthma patients was 46%. 12% patients had mild OSA, 14% had moderate while 20% were having severe OSA. Mean BMI in our study was 27.87 Kg/m^2. OSA patients were associated with more BMI compared to patients without OSA (42% vs. 30%) (p value 0.04). Asthma patients who were smokers had more OSA symptoms compared to non-smokers (p value 0.002). Asthma patients with OSA were also associated with higher neck circumference and more snoring at night time as compared to non OSA population. Uncontrolled asthma was seen in 18 patients and 16 of them were having OSA (p=0.001). Most common co morbid illness in patients with OSA was GERD (78.26%) followed by allergic rhinitis (56%). Most of these patients (82%) were not having associated major local anatomical defect.

Conclusions: OSA is not uncommon in asthma patients. Careful assessment of sleep related symptoms and demographic parameters of asthma patients are essential to suspect diagnosis of OSA. Additional factors like smoking, obesity, GERD and allergic rhinitis are important contributing factor for higher risk of OSA among asthma patients. Early diagnosis of OSA in asthma patients by polysomnography may have a clinical benefit in the management of both diseases.

Introduction

Obstructive sleep apnea (OSA) is characterized by intermittent obstruction of the upper airway during sleep leading to early morning awakening, difficulty in maintaining sleep, hypoxemia and sleep fragmentation. Important risk factors for development of OSA are old age, obesity, smoking, anatomical factors, metabolic disorders etc.[1] Asthma is recently recognized as an independent risk factor for OSA.[2] The pathophysiology of these two conditions seems to overlap significantly, as airway obstruction, inflammation; obesity, metabolic syndrome etc. are associated with development of both these diseases. It also suggested that asthma co morbidities, like GERD, nasal polyp and medications for asthma control like oral and inhaled steroid may also contribute to development of OSA. This frequent coexistence of OSA and asthma is also referred as "Alternate Overlap syndrome" now a days.[3]

Patients with asthma who are at high risk of OSA are more likely to have worse daytime and night time asthma symptoms. Interestingly, patients who are diagnosed with OSA and treated with Continuous Positive Airway Pressure (CPAP) seem to have better asthma control.[4] There is scanty literature on association between bronchial asthma and obstructive sleep apnea from our country. This study was therefore planned to assess clinical, demographic profile and risk factors for OSA in patients having bronchial asthma at our institution.

Methods

This was a cross sectional study on adult patients presenting with signs, symptoms and history suggestive of asthma and willing to participate in the study after institutional ethical committee approval. The diagnosis of bronchial asthma was based on the Global Initiative for Asthma (GINA) guidelines.[5] The enrolled patients were assessed by detailed clinical history, clinical assessment for OSA based on day night symptoms, smoking status, Berlin Questionnaire,[6] measurement of neck circumference and Mallampatti score etc. COPD was ruled out in these patients by suggestive clinical background, radiological assessment and spirometry.

The Body mass index (BMI) was calculated by measurement of height

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Table 1: Severity of OSA in asthma patients

OSA	Male	Female	Total
Mild	4	2	6
Moderate	3	4	7
Severe	4	6	10

Table 3: Comparison of clinical symptoms in asthma patients with or without OSA

Clinical symptoms	No OSA (n= 27)	OSA (n=23)	p value
Daytime Symptoms			
Morning headache	16	19	0.137
Morning dry mouth	6	8	0.503
Fatigue	23	21	0.82
decrease concentration	10	13	0.274
Excessive day time sleepiness	8	11	0.304
Night symptoms			
Snoring	18	21	0.08
Witness apnea	11	15	0.149
Disturb sleep	19	15	0.932
Nocturnal thrust	6	8	0.503
Nocturnal diuresis	16	15	0.888
Nocturnal sweating	12	19	0.013

Table 4: Comparison of co-morbidities in asthma patients with or without OSA

Co-morbid illness	No OSA (n= 27)	OSA (n=23)	p value
Hypertension	5	11	0.056
Diabetes Mellitus	3	5	0.526
Hypothyroid	4	5	0.79
Allergic Rhinitis	8	13	0.103
GERD	12	18	0.032

in meter and weight in kilogram using following formula:

$$\frac{\text{Weight (Kg)}}{\text{Height (m2)}}$$

A BMI of 18.5 to 24.9 was considered normal, 25 to 29.9 overweight, and 30 to 34.9 as obesity.

All eligible and willing to participate patients were subjected to overnight polysomnography (Level 1) at sleep lab of our department using Alice PDX diagnostic system as per standard protocol.

Apnea- hypopnea Index (AHI) was calculated with following formula:

$$\text{AHI} = \frac{\text{Total no. of Apneas + total no. of Hypopneas}}{\text{Total sleep time (in hours)}}$$

Based on the AHI, the OSA was classified as following:

Mild OSA: AHI ≥5/hr and <15/hr

Table 2: Demographic and anthropometric profile of Asthma patients with or without OSA

Parameters	No OSA (n=27)	OSA (n=23)	Total (n=50)	p value
Mean age	45.74	50.82	48.16	0.573
Male: female ratio	4:23	11:12	15:35	0.26
Smoker	1	10	11	0.002
Mean BMI	27.10	28.11	27.87	0.04
Mean neck circumference in cm	34.48	36.30	35.14	0.192

Moderate OSA: AHI ≥15/hr and ≤30/hr

Severe OSA: AHI >30/hr

Patients of Bronchial Asthma having OSA of different severity were further scanned in the light of demographic features, associated co-morbid illness, Berlin Questionnaire, BMI etc.

Statistical analysis

The data were entered using Microsoft Excel sheet. Descriptive statistics frequencies and percentages were calculated. Data of different groups were compared by using Chi square test and p value <0.05 was considered as statistically significant.

Results

In the present study, 50 patients of Bronchial asthma constituted the study population. Most of the patients (40/50, 80%) were between the age group 30-60 years. 13 patients were between 30-40 years, 14 patients were 41-50 years, 13 patients were 51-60 years and 10 patients were >60 years of age. The mean age of patients was 48.16 years. There were 15 male (30%) and 35 female (70%) patients with male: female ratio of 1: 2.3.

23 patients (11 male and 12 female) were found to have OSA making a prevalence of 46% among asthma patients. 27 patients (54%) (4 male and 23 female) were not found to have OSA. Table 1 shows severity of OSA in asthma patients.

11 male patients were smoker (22%) while 4 male patients were non-smokers (8%). All female patients were non-smokers (70%). Asthma patients who were smokers had more OSA symptoms compared to non-smokers (p value .002). Most of the patients (54%) were having neck circumference of 35-40 cm with mean value of 35.14 cm. Most of the patients (44%) were over-weight while 28% were obese with mean BMI value of 27.87kg/m^2. OSA patients were associated more BMI compared to non OSA patients and this was statistically significant (p value 0 .04).

Table 2 shows demographic and anthropometric variables among asthma patients with or without OSA.

Most common day time symptom was fatigue seen in 44 cases (88%) followed by morning headache (35 cases, 70%), decreased concentration (46%) and excessive daytime sleepiness (38%). Most common night symptom was snoring seen in 39 patients (76%) followed by disturb sleep (70%), night thrust (70%), symptom of Gastro Esophageal Reflux Disease (GERD) (68%), night diuresis (56%), witness apnea (52%), night sweating (18%) etc. Although day and night time symptoms showed no significant difference between these two groups, the snoring was more common in OSA group (p value 0.08) (Table 3).

On assessment of patients by Berlin Questionnaire high score was observed in 69% patients with OSA compared to 14.8% patients in non OSA patients. Low score was observed in 85% patients in non OSA group compared to 30% of OSA group. This difference was statistically significant (p value <0.001). The overall sensitivity of B.Q was 69.5% with a specificity of 85%, Positive predictive value of 80% and negative predictive value of 76.6% (p value <0.001).

Most common co morbidity in OSA group was GERD (78.26%) with statistically significant association (p value 0.03), followed by allergic rhinitis (56.52%) and hypertension (47.83%). Five patients each (21.73%) in OSA group were having Diabetes mellitus and hypothyroidism. In non OSA group also similar trend was seen in frequency of co morbid illness although their number was less but statistically not significant (Table 4).

Only 10 patients showed some kind of minor anatomical defect like adenoid hypertrophy (3 patients), deviated nasal septum (5 patients) or nasal polyp (2 patients). Only 9 asthma patients with OSA showed this type of defects compared to only 1 patient in non OSA group, however, this difference was statistically not significant (p value 0.07). 80% patients in our study have

Table 5: Comparison of level of asthma control in patients with or without OSA

OSA status	Well controlled (n=13)	Partial controlled (n=19)	Uncontrolled (n=18)	p value
Asthma with OSA	1	6	16	
Asthma without OSA	12	13	2	
Prevalence of OSA	7.69%	31.57%	88.88%	0.001

no anatomical defect.

Mallampatti score was measured based on examination of oral cavity on visualization of various structures and classified accordingly. Grade 1 Mallampatti score was seen in 44% of patients of asthma not having OSA. On the other hand 86% of patients having bronchial asthma with OSA had Mallampatti score 2 or 3. However, association of Mallampatti score with OSA was statistically not significant (p value 0.08).

As per GINA, asthma was well controlled in 13(26%), partially controlled in 19(38%) and uncontrolled in 18(36%) patients. Table 5 shows distribution of asthma patients having OSA and without OSA with their level of asthma control. Uncontrolled asthma was more common in patients having OSA than those without OSA (p value 0.001).

Discussion

23 patients (46%) of bronchial asthma were having OSA confirmed by level 1 polysomnography in the present study. A wide variation in prevalence of Obstructive sleep apnea ranging from 27% to 74% has been found in different studies among asthma patients worldwide.[2,7-9] This could possibility due to difference in sample size and selection criteria of study patients. To best of our knowledge we could not found Indian literature on prevalence of OSA among asthma patients evaluated by level 1 polysomnography.

Mean age of asthma patients having OSA was 50.82 years while in non OSA group it was 45.74 year. Mean age in OSA group was 52.1±5.9 compared to non OSA group (47.3±9.21 years) in a study by Zidan et al.[3] Another studies by Byun et al[10] and Guven et al[7] also found higher mean age in OSA group. These studies suggest that OSA is more common in middle age group among asthma patients.

Asthma is a female predominance disease. In present study 52.17% female patients were having associated OSA. The female predominance of asthma patients having OSA is also observed by other worker i.e. 59.2% by Madama et al[11] and 66.66% by Zidan et al.[3]

Smoking and obesity are strong predictor of OSA in general as well as in asthma patients. 90.91% smoker asthmatics were also having OSA in present study. Byun et al[10] observed 60.4% smoker having OSA among asthma patients. Several possible factors for development of OSA in smokers include upper airway inflammation, stimulant effects of nicotine on upper airway muscles and increased production of mucus.[12]

In present study, we screen asthma patients for OSA by Berlin Questionnaire and 59.5% patients suspected by Berlin Questionnaire score were found to have OSA on polysomnography. This figure is superior to 39.5% observed by Auckley et al.[13]

Mean BMI in asthma patients with OSA was 28.11 in our study. Zidan et al[3] and Julien et al[8] also observed a higher BMI i.e. 29.2±3.28 and 27.8±1.1 kg/m^2 respectively among asthma patients having associated OSA. Obesity causes collapsibility of upper air way due to excess fat deposition which contributes to more risk of OSA. Excess weight gain in asthma patients may also occur due to limited ability to exercise, sleep deprivation with increased insulin resistance or the use of oral steroids.[14]

Most common day time symptom in OSA group was fatigue (91.30%) followed by morning headache and decreased concentration. Most common night symptom in OSA group was snoring (91.30%). These findings are consistent with other studies in the literature.[3,4,11,15]

GERD was most common co morbid illness among OSA patients in our study with 78.26% prevalence. Zidan et al[3] found 56% of asthmatic patients with OSA having GERD symptoms. Green et al[16] and Valipour et al[17] reported GERD in 62% and 58% patients respectively. This situation may be due to increased trans diaphragmatic pressure and decreased intra thoracic pressure occurring during the apneic episodes. Proximal migration of gastric acid and prolonged clearance of acid during sleep further causes upper airway dysfunction and tendency to collapse during sleep.[18]

Allergic rhinitis not only causes poor asthma control but is also an associated risk factor for OSA. In a large population based study by Braido et al[19] in 2014, over 1941 patients were evaluated for risk of OSA in asthma patients with or without allergic rhinitis. 47.3% patients with asthma alone were having OSA while 55.9% asthma patients with allergic rhinitis had associated OSA. Zidan et al,[3] Guven et al[7] and Shen et al[20] also found similar results. Allergic rhinitis causes nasal as well as upper airway obstruction in asthma patients, that in turn increases the negative pressure at upper airway during inspiration, ultimately increasing the risk of OSA.[14]

Effect of anatomical factors over incidence of OSA is not clearly defined. There is paucity of data about anatomical defect and its effect on OSA. In current study only 18% OSA patients were having some kind of anatomical defect. Isono et al[21] found adenoid hypertrophy in 57% patients, abnormal hard palate in 29% patients and enlarged palatine tonsil in 14% asthma patients having OSA. Teodorescu and co workers[22] in 2012 found nasal polyps in 15% patient of bronchial asthma. Upper airway inflammation and rhinitis in asthma patients facilitates deviated nasal septum and polyp formation that may block normal air flow and fluid drainage which in turn causes more obstruction at upper airway especially during sleep[23] and may contributes to higher occurrence of OSA in such patients.

Mallampatti score could be an important screening tool for OSA and essential part of pre-test physical examination. However, its role in predicting severity of OSA remains doubtful and needs further study. A cross sectional study by Hukins et al[24] over 953 patients concluded that there was no statistically significant correlation between AHI and Mallampatti score. Our study also could not found a significant correlation between OSA and higher Mallampatti score especially at score 3 and 4 in asthma patients.

There are several studies that links obstructive sleep apnea (OSA) with the level of asthma control and shows that OSA is associated with poor asthma control.[3] Repeated upper airway obstruction results in increased intra thoracic pressure, frequent arousal, sleep fragmentation and intermittent hypoxemia that contributes to activation of inflammatory process both at upper as well as lower respiratory tract. Poor asthma controlled was also observed more commonly in asthma patients having OSA in our study.

There are few limitations in this study. Firstly the study participants were selected from hospital settings who were willing to participate. Secondly there were only few young asthmatic patients. More so, we adopted convenient sampling where all the asthma patients of different age group from community did not have equal chance of selection, therefore findings of this study can't be generalized. Large sample sizes with multicentre data's are needed to estimate an actual burden of OSA among asthma patients and explore further details in this association that largely remains under recognized at present.

Despite these limitations our study first time highlights the OSA as important co morbidity in patients of bronchial asthma and its risk factor from our country. We conclude with a remark that careful assessment of sleep related symptoms and demographic parameters of asthma patients is important to sensitize the clinician towards the diagnosis of possible OSA. Additional factors i.e. smoking, obesity, GERD and allergic rhinitis are important contributing factor to suspect higher risk of OSA among asthma patients. In present study, there was no difference in symptoms of excessive day time sleepiness and snoring in the two groups, therefore, the critical symptoms of OSA may not be sufficient to predict the diagnosis of OSA in routine clinical practice. Polysomnography is therefore an important tool for confirming OSA in asthma patients especially among those with poor symptom control despite optimal medical management.

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