

Clinical Profile of Overlap Syndrome at a Tertiary Care Center in Western India

Gautam Sarawade¹, Neenu Najeeb², Vitthalrao Mohan Chintalwar³, Ketaki Utpat⁴, Unnati Desai⁵, Magizh Samuel⁶, Rahul Bagul⁷, Hem Shah⁸

Received on: 31 July 2023; Accepted on: 20 August 2023; Published on: 06 October 2023

ABSTRACT

Background: Overlap syndrome refers to the coexistence of chronic respiratory disease and obstructive sleep apnea syndrome (OSAS) in the same patient. Untreated OSAS results in complications like cardiovascular disease, metabolic disorder, and cognitive impairment. Patients with overlap syndrome have a greater risk of morbidity and mortality compared with OSAS alone. Recognition of overlap syndrome is significant as the survival of patients with untreated overlap syndrome is significantly inferior to treated patients.

Methodology: A prospective observational study of 90 patients with symptoms of OSAS was conducted in our tertiary care center with ethical approval. All patients underwent overnight polysomnography (PSG). Coexisting respiratory diseases were noted.

Results: All 90 patients included in the study were diagnosed with OSAS, which was confirmed by overnight PSG. About 31% had mild, 23% had moderate, and 46% had severe OSAS. The mean age was 53.81 years, and the majority of the participants were male (64%). The majority (67%) had overlap with chronic obstructive pulmonary disease, 27% with interstitial lung disease (ILD), and 6% with bronchial asthma (BA). About 55% had hypertension, 33% had diabetes mellitus (DM), and 18.88% had hypothyroidism, 20% had hypertension and DM, 11.11% had hypertension and hypothyroidism, 4.4% had DM and hypothyroidism as non-respiratory comorbidities.

Conclusion: Overlap syndrome in our tertiary center in India shows predilection toward the male sex, obesity, and frequent association with non-respiratory comorbidities such as hypertension, DM, and hypothyroidism. Chronic obstructive pulmonary disease and obstructive sleep apnea (OSA) overlap is more common than ILD and BA. Early detection and treatment of OSA among patients with respiratory disease can aid in better patient management and overall improvement in the quality of life.

Keywords: Obstructive sleep apnea syndrome, Overlap syndrome, Sleep score.

Indian Journal of Sleep Medicine (2023): 10.5005/jp-journals-10069-0115

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by periodic narrowing and obstruction of the pharyngeal airway during sleep. It is a chronic sleep-related breathing disorder that is commonly seen. Diagnostic criteria of OSAS include excessive daytime somnolence or any two of the following symptoms of snoring, witnessed apneas, unrefreshing sleep, daytime fatigue, poor concentration, and sleep study showing apnea-hypopnea index (AHI) > 5.¹ If not treated, OSAS patients can develop cardiovascular complications, metabolic disorders, cognitive impairment, and depression. Significant morbidity and mortality are observed in patients with OSAS and chronic obstructive pulmonary disease (COPD), which also constitute the major burden of patients visiting pulmonologists. The two diseases are known to coexist. This entity was termed by Flenley as the “overlap syndrome.”² Patients of interstitial lung disease (ILD), obliterative bronchiolitis, and bronchial asthma (BA) having symptoms and signs of OSAS can also be included under overlap syndrome. Prevalence of overlap syndrome is 4.5–7.5% according to studies done by Shawon et al.³ Flenley found that patients who had COPD with OSAS had a greater amount of nocturnal hypoxemia and hypercapnia than patients with COPD or OSAS alone. Patients with overlap syndrome are also associated with daytime oxygen desaturation and lower quality of life.

The most common diseases in pulmonology are OSAS and COPD. Patients with overlap syndrome exhibit more nocturnal hypoxemia than those with either disease alone.^{4,5} The combination

^{1–8}Department of Pulmonary Medicine, TNMC and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India

Corresponding Author: Unnati Desai, Department of Pulmonary Medicine, TNMC and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India, Phone: +91 2223027643, +91 9869627955, e-mail: unnati_desai82@yahoo.co.in

How to cite this article: Sarawade G, Najeeb N, Chintalwar VM, et al. Clinical Profile of Overlap Syndrome at a Tertiary Care Center in Western India. *Indian J Sleep Med* 2023;18(2):25–28.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

of OSAS and COPD has important implications for diagnosis, treatment, and outcome. Patients with either COPD or OSAS alone have a lesser risk of morbidity and mortality as compared with overlap syndrome.^{6–8} To diagnose OSAS in patients with respiratory diseases such as COPD, ILD, and BA, it is necessary to identify the relevant clinical features and use screening questionnaires such as Epworth sleepiness score (ESS) and SACS, which is useful in identifying patients for overnight study. Simple and easy pretest probability scores (ESS and SACS) were used and they also had high sensitivity. The gold standard test for diagnosis of OSAS is overnight polysomnography (PSG).⁹ In patients with COPD, BA, and ILD

Table 1: Demographic details

Age-group (years)	Number of patients	Percentage (%)
30–40	7	8
41–50	31	34
51–60	35	39
61–70	12	13
>70	5	6
Gender	Number	Percentage (%)
Men	58	64
Women	32	36

identification of OSAS are important because if overlap syndrome is not recognized, it will remain untreated. Treatment of overlap syndrome with continuous positive airway pressure (CPAP) during sleep is an important part of treatment as it will decrease morbidity and mortality and will improve the quality of sleep.¹⁰

METHODOLOGY

A prospective observational study of 90 patients was conducted at our tertiary care center in the Department of Pulmonary Medicine for duration of 2 years. Institutional Ethics Committee permission was obtained before the initiation of the study (ECARP/2019/117). After taking the written informed consent, patients more than 18 years of age having OSAS symptoms were included and patients who were not willing to give consent were excluded from the study. Participants were evaluated with a detailed history of symptoms like loud snoring, witnessed apneas, nocturnal choking, nocturia, excessive daytime sleepiness, early morning headache, irritability, memory lapses, cough, dyspnea, clinically with systemic and general examination. Anthropometric measures like body mass index (BMI), cricomenal distance, neck circumference, and Mallampati grading (MPG) were taken. Pretest probability scores like ESS and SACS were calculated. Complete hemogram, fasting blood and postprandial blood sugar, lipid profile, thyroid function test, chest X-ray, high-resolution computed tomography (HRCT) thorax, spirometry, and two-dimensional echocardiography (2DECHO) were performed in all patients. All patients underwent overnight PSG. coexisting respiratory diseases are also noted.

RESULTS

A total of 90 patients were included in our study. All 90 were diagnosed with OSAS confirmed by overnight PSG. About 53.81 years was the mean age of participants. Among the 90 patients, the youngest patient studied was 32 years old, and the oldest was 78 years old. Patients aged 51–60 years formed the major group 35 (39%), and the least number of patients were from the age-group more than 70 years comprising 5 (6%). Seven (8%) patients were from the age-group of 30–40 years. Patients aged 41–50 years were 31 (34%), and patients aged 61–70 years were 12 (13%). Out of total 90 patients with overlap syndrome, 58 (64%) were male and 32 (36%) were female (Table 1). The mean height was 159.65 cm with a standard deviation (SD) of 10.19. The mean weight was 83.40 kg with SD of 24.72. The mean BMI was 32.95 kg/m² with a SD of 8.34. The mean neck circumference was 39.66 cm with a SD of 4.75.

The majority of patients [43 (48%)] had MPG II, and the least number of patients [7 (8%)] had MPG I. Patients with MPG III were 30 (33%) and MPG IV were 10 (11%) (Table 2). Among 90 patients, an overlap of obstructive sleep apnea (OSA) with COPD was seen

Table 2: Mallampati grade

Mallampati grade (MPG)	Number	Percentage (%)
MPG I	7	8
MPG II	43	48
MPG III	30	33
MPG IV	10	11

Table 3: Disease profile

Disease	No. of patients	Percentage (%)
Chronic obstructive pulmonary disease	61	67
Interstitial lung disease	24	27
Bronchial asthma	5	6

Table 4: Spirometry

Spirometry	Mean	SD
Forced expiratory volume in 1 sec by forced vital capacity (FEV1/FVC) ratio	69.64	12.3
FEV1	58.52	10.4
FVC	61.73	12.5

in majority of patients [61 (67%)], whereas only 5 (6%) patients had an overlap of OSA with BA and 24 (27%) patients had an overlap of OSA with ILD (Table 3). The majority of patients [69 (77%)] had a cricomenal distance of less than 1.5 cm whereas only 21 (23%) had a cricomenal distance more than 1.5 cm. Among the total cases, 50 (55%) had hypertension, 30 (33%) had diabetes mellitus (DM), and 17 (18.88%) had hypothyroidism as non-respiratory comorbidities. A total of 18 (20%) patients had both hypertension and DM whereas 10 (11.11%) patients had hypertension and hypothyroidism, and only 4 (4.4%) patients had DM and hypothyroidism.

On spirometry, the mean forced expiratory volume in 1 second by forced vital capacity (FEV1/FVC) ratio was 69.64 with SD of 12.3, mean FEV1 was 58.52 with SD of 10.4, and mean FVC was 61.73 with SD of 12.5 (Table 4). The mean 6-minute walk distance (6MWD) was 300.88 meters with a SD of 72.36. Mean serum cholesterol was 161 with a SD of 36.72, the mean triglyceride level was 149.35 with a SD of 71.04, mean high-density lipoprotein (HDL) level was 47.17 with a SD of 11.62. Pulmonary artery systolic pressure (PASP) was measured by the tricuspid regurgitation jet method on 2DECHO. About 33 cases (36.6%) had mild pulmonary hypertension (PH), 55 (61.1%) had moderate PH, and 2 (2.2%) had severe PH in our study.

Out of total 90 patients, 31% (28) had mild, 23% (21) had moderate, and 46% (41) had severe OSAS (Table 5). In mild OSAS patients mean PASP was 40.17 with a SD of 5.68, in moderate OSAS mean PASP was 43.8 with a SD of 6.87, in severe OSAS mean PASP was 44.26 with a SD of 7.46, and overall mean PASP was 42.88 with a SD of 6.99. The mean SACS was 44.68 with a SD of 5.6, mean ESS was 12.8 with a SD of 5.17. In the sleep study, the mean AHI obtained was 32.82 with a SD of 24.43, mean minimum oxygen saturation (SpO₂) of 72.35 with a SD of 13, whereas the mean average SpO₂ was 90.85 with a SD of 5.9 (Table 5).

DISCUSSION

Obstructive sleep apnea syndrome is a known prevalent comorbidity for respiratory diseases such as COPD, BA, and ILD. The coexistence

Table 5: Sleep scores, polysomnography, and severity of obstructive sleep apnea syndrome

<i>Sleep scores</i>	<i>Mean</i>	<i>SD</i>
Sleep apnea clinical score	44.68	5.6
Epworth sleepiness score	12.8	5.17
<i>Polysomnography</i>	<i>Mean</i>	<i>SD</i>
Apnea-hypopnea index	32.82	24.43
MIN oxygen saturation (SpO ₂)	72.35	13.0
AVG SpO ₂	90.85	5.9
<i>Severity of OSAS</i>	<i>Number</i>	<i>Percentage (%)</i>
Mild obstructive sleep apnea syndrome (OSAS)	28	31
Moderate OSAS	21	23
Severe OSAS	41	46

of OSAS and chronic respiratory disease is seen in overlap syndrome. In OSAS patients, the respiratory effort is present during sleep but there is repetitive episodes of upper airway collapse, which result in significant reduction or cessation in the airflow. Criteria for diagnosis of OSAS includes excessive daytime somnolence or any two of the following symptoms: snoring, witnessed apneas, unrefreshing sleep, daytime fatigue, poor concentration, and sleep study showing AHI > 5.¹ Overlap syndrome may lead to a rise in morbidity as well as mortality as compared with a single disorder. Obstructive sleep apnea syndrome and other respiratory disorders may show differences in severity and can present with various clinical phenotypes. So, it is important to have a personalized management plan. Early diagnosis and management can result in significant improvement in sleep, quality of life, and overall disease outcome. Obstructive sleep apnea syndrome is one of the major public health problems that often go under noticed. There is an increase in the prevalence of OSAS with time. It is an independent risk factor for metabolic and cardiovascular diseases which often leads to a greater increase in management cost. Hence, physicians should be aware of clinical manifestations of OSAS and symptoms like excessive daytime sleepiness, witnessed apneas, loss of concentration, and neurocognitive deficiency, eventually leading to a low quality of life. Obstructive sleep apnea syndrome and other respiratory disorders like COPD and ILD are independent risk factors for various cardiovascular diseases. These respiratory diseases and OSAS have additive effects on each other so this risk is increased in overlap syndrome patients. Pulmonary hypertension is also seen frequently in overlap syndrome patients. When these disorders coexist, there is an increase in cumulative morbidity and mortality. Diagnosis of OSAS in patients with COPD, BA, and ILD is important as a line of management is different for overlap syndrome than these respiratory diseases alone. If overlap syndrome patients are not treated with nocturnal positive airway pressure therapy, then there is a decrease in the chance of survival of the patient. Treatment of overlap syndrome includes prevention of upper airway collapse with CPAP or other noninvasive positive pressure ventilation and oxygen supplementation if there is nocturnal desaturation.⁷ Prevalence of overlap syndrome from studies done by Shawon et al.³ is 4.5–7.5%, whereas it is 3.1% by other studies of Mansell et al.¹¹

In our prospective study, we included 90 patients with different respiratory diseases along with symptoms of OSA. Out of the 90, the majority were above 50 years of age (57%). This is in concordance with studies done by Senaratna et al.¹² Mean age of cases is 59.9 ± 9.6 years in the studies done by Nair et al.¹³ Most of

our study group were men (64%) and 36% were women, which is similar to the study done by Young et al.¹⁴ Among overlap patients, the majority had COPD–OSA overlap (67%). This coincided with the results from the study done by Narasimhan et al.¹⁵ Interstitial lung disease–OSA overlap was second most common consisting of 27% which was in concordance with a study by Utpat et al.¹⁶ Bronchial asthma–OSAS overlap patients were least common, 6% in our study. Fifty patients (61%) were found to be obese in our study, which is in concordance with other studies by Soler et al.,¹⁷ Gunduz et al.,¹⁸ and Wu et al.¹⁹ Majority of patients [43 (48%)] had only MPG II. Also, 77% of patients had a cricomenal distance of less than 1.5 cm. Overlap syndrome patients may not present with all the clinical features of OSA. From the sleep studies conducted, the mean AHI obtained was 32.82, mean minimum SpO₂ of 72.35, whereas the mean average SpO₂ was 90.85.

The majority of patients had severe OSAS (46%), 23% had moderate OSAS, and 31% patients had mild OSAS. The most common comorbidity seen in our study was hypertension (55%) followed by DM being the second most common (11%). This was similar to studies done by Voulgaris et al.²⁰ Pulmonary hypertension was found in all 90 patients we studied. This was in concordance with studies done in overlap patients by Chaouat et al.²¹ About 36.6% cases in our study had mild PH, 61.1% had moderate PH, and 22.2% had severe PH. On spirometry, obstructive pattern was found to be more common than restrictive pattern as majority of overlap patients were having COPD as a coexisting respiratory disease. This is similar to studies by Chaouat et al.,²¹ which shows mild-to-moderate obstructive abnormality in spirometry in most patients of overlap syndrome. The mean FEV1/FVC ratio was 69.64, the mean FEV1 was 58.52, and the mean FVC was 61.73. The mean 6MWD was 300.88 meters with a SD of 72.36. The mean SACS in our study was 44.68, and the mean ESS was 12.8. Epworth sleepiness score and sleep apnea clinical score were found to be useful in the assessment of overlap syndrome patients in our study, which coincided with a study by Faria et al.²²

In a tertiary care center in India, overlap syndrome is common in male and obese individuals and is associated with non-respiratory diseases like hypertension, DM, and hypothyroidism. Chronic obstructive pulmonary disease–OSAS overlap was more common than ILD–OSAS overlap, whereas BA OSAS overlap was found to be the least common among respiratory diseases. Pretest probability sleep scores, SACS and ESS along with PSG, spirometry, and HRCT thorax were found to be useful in early diagnosis of patients with overlap syndrome. Pretest probability scores, SACS and ESS, if routinely and correctly used, can help predict the likelihood of OSAS in respiratory disease patients. Early detection and treatment of OSAS among respiratory disease patients will help in better patient management, lesser exacerbations, and overall improvement in quality of life. The limitation of the study is that it represents the experience of just one hospital. Our study data may be helpful in increasing awareness about overlap syndrome and its long-term consequences among doctors and patients.

ORCID

Unnati Desai  <https://orcid.org/0000-0002-7647-0469>

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