Original Article

Impact of overlap syndrome on severity of acute exacerbation of chronic obstructive pulmonary disease

Dipti Gothi, Shiv Sagar Gupta[1], Nishith Kumar[2], Kartik Sood[3]

Department of Pulmonary Medicine, ESI-Post Graduate Institute of Medical Sciences and Research, [3]Department of Pulmonary Medicine, National Institute of Tuberculosis and Respiratory Disease, Delhi, [1]Department of Pulmonary Medicine, Era's Lucknow Medical College, [2]Department of Pulmonary Medicine, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

ABSTRACT

Background: The severity of exacerbation in chronic obstructive pulmonary disease (COPD) due to the overlap of obstructive sleep apnea syndrome (OSAS) is not known. **Aims:** To find out the 1) severity of acute exacerbation of COPD (AECOPD) in patients with overlap syndrome compared to only COPD, 2) prevalence of overlap syndrome in AECOPD, and 3) clinical characteristics of COPD compared to overlap syndrome. **Materials and Methods:** Fifty-one patients admitted with AECOPD were classified into; Mild exacerbation: Normal arterial blood gases (ABG) treated with antibiotics, Moderate: Normal ABG treated with parenteral corticosteroids, Severe: Type 1 respiratory failure, Very severe: Type 2 respiratory failure with normal pH and Life-threatening: Type 2 respiratory failure with pH <7.35. They were evaluated for OSAS with full polysomnography after the exacerbation subsided and analysed depending on presence or absence of overlap syndrome. **Results:** The majority of only COPD cases (26/38) had mild and moderate exacerbations whereas majority of overlap patients (9/13) had severe, very severe and life-threatening exacerbations (statistically significant, $P = 0.021$). Of 51 patients, 13 had OSAS i.e. the prevalence of overlap in AECOPD was 25.5%. The mean BMI in only COPD and overlap syndrome was 20.70 ± 8.03 kg/m^2 and 31.82 ± 5.80 kg/m^2 ($P < 0.001$), respectively. Metabolic syndrome was recorded in 2/36 (5.3%) patients in only COPD and 6/13 (46.2%) patients in overlap ($P < 0.001$). **Conclusion:** Overlap syndromes are more likely have respiratory failure compared to only COPD during AECOPD. AECOPD have a high prevalence of OSAS. Overlap syndrome have significantly higher likelihood of obesity and metabolic syndrome compared to only COPD.

KEY WORDS: Acute exacerbation of COPD, metabolic syndrome, obesity, obstructive sleep apnea syndrome

Address for correspondence: Dr. Dipti Gothi, Department of Pulmonary Medicine ESI, Post-graduate Institute of Medical science and Research, Delhi, India. E-mail: diptigothi@gmail.com

INTRODUCTION

The coexistence of obstructive sleep apnea syndrome (OSAS) and chronic obstructive pulmonary disease (COPD) is termed as "overlap syndrome". Overlap syndrome has a prevalence of 10-20% reported in various studies.[1,2] Patients with overlap syndrome have several mechanical disadvantages to breathing during sleep. Apart from upper and lower airway obstruction, a reduction in respiratory drive and functional residual capacity,[3] they also have respiratory muscles fatigue. It has been shown that these patients are at a greater risk of prolonged oxygen desaturation[4,5] pulmonary hypertension compared only with COPD. It implies that overlap syndrome is important from the point of view of aggravating the effects of both the disorders.

Although many studies have shown an aggravating effect of overlap syndrome on stable COPD, but none have shown the aggravating effect on acute exacerbation of COPD (AECOPD). Also, it is known that obese patients are more likely to present with type II respiratory failure, it is not known that they may suffer from OSAS.[6] Thus, the present study was carried out with the primary aim of correlating the severity of exacerbations in patients admitted with AECOPD with or without OSAS. The secondary aims were to find out the prevalence of overlap

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.168132

syndrome in patients admitted with AECOPD and to correlate the clinical characteristics of COPD patients with and without OSAS.

MATERIALS AND METHODS

A cross-sectional observational study was undertaken after the ethic committee approval at a tertiary care institute of northern India. Treatment-naïve patients with AECOPD requiring hospitalization as per the global initiative for obstructive lung disease (GOLD) guidelines[7] from January 2011 to June 2012 were evaluated for the study. These patients were analysed in detail. Spirometry was performed after the exacerbation subsided for the confirmation of COPD. Only those patients with confirmed COPD were included in the study after taking their valid informed written consent. Patients with underlying systemic diseases like renal failure, cardiac failure and malignancy were excluded from the study. Detailed history including the cause of COPD, smoking index, duration of disease, general and systemic examination findings, routine investigations and severity of exacerbation for each patient was noted down. Additional investigations for comorbid illness and polysomnography were performed in all the cases. On the basis of presence of overlap syndrome the patients were divided into two groups, 1) without OSAS i.e., only COPD and 2) with OSAS i.e., patients having overlap syndrome and were analysed accordingly.

Diagnosis of COPD

The spirometry was performed as per the American thoracic society guidelines[8] using spirometry machine Medikro Spirostar USB M9479 (Finland). The patients were diagnosed and classified into mild, moderate, severe and very severe as per the GOLD guidelines.[7]

Severity of exacerbation

The scale for exacerbation severity was classified into following:[9]

Mild

An exacerbation with normal arterial blood gas levels treated with antibiotics but no systemic corticosteroid.

Moderate

An exacerbation with normal arterial blood gas levels treated with parenteral corticosteroids with or without an antibiotic.

Severe

Type 1 respiratory failure with hypoxemia but no carbon dioxide retention or acidosis; PaO_2 <60 mmHg and $PaCO_2$ = 35-45 mmHg.

Very severe

Type 2 respiratory failure, compensated with hypoxia, carbon dioxide retention but no acidosis; PaO_2 <60 mmHg, $PaCO_2$ >50 mmHg and pH >7.35.

Life-threatening

Type 2 respiratory failure, decompensated with acidosis and carbon dioxide retention; $PaCO_2$ >50 mmHg and pH <7.35.

Diagnosis of OSAS

An overnight in-laboratory polysomnography with Resperonics ALICE®LE-Philips Respironics system (type 1 study) was performed in all the patients a day prior to their discharge i.e., once the patient had been normalized to the level of activity prior to admission and did not require inhaled bronchodilator more frequently than 4 hourly, did not have night awakening, and had been stable for more than 24 hours. The diagnosis of OSAS was done using the clinical guidelines for the evaluation, management and long-term care of OSAS in adults recommended by the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine.[10]

Diagnosis of comorbid diseases

Diagnosis of comorbid diseases was made on the basis of findings of examination and investigations. These were height, weight, blood pressure, blood sugar fasting, lipid profile, electrocardiogram and 2-dimensional echocardiography (2D Echo). The weight categories of the patients were determined using International Classification of adult as underweight, normal weight, overweight and obese according to their body mass index (BMI).[11]

Metabolic syndrome was diagnosed using adult treatment plan-III criteria.[12] The diagnosis of diabetes was made as per the American Diabetes Association criteria[13] and hypertension was diagnosed as per the American Hypertension Association criteria.[14]

Statistical analysis

The data was analysed using Statistical Package for Social Sciences (SPSS) version 15.0. The data is represented as number, percentages and mean ± standard deviation. Chi-square test was used for proportions while parametric assessment was done using Analysis of Variance (ANOVA) and Student's "*t*" test. The confidence level of the study was kept at 95%, hence a "*P*" value less than 0.05 indicates a statistically significant association.

RESULTS

Among patients hospitalized for AECOPD, a total of 51 patients who satisfied the inclusion criteria were enrolled and evaluated for the presence of overlap syndrome. Out of a total of 51 patients, 38 (74.5%) did not have OSAS i.e., they had only COPD, while 13 (25.5%) had COPD with OSAS i.e., overlap syndrome. Table 1 and Chart 1 show the comparison of severity of exacerbation between only COPD and overlap. The majority of only COPD cases had mild and moderate exacerbations whereas majority of cases in overlap had severe, very severe and life-threatening exacerbations. Statistically, the difference

between two groups was significant (P = 0.021). Also, with the increasing severity of exacerbation, the mean apnea hypopnea index (AHI) increased [Chart 2, Table 2]. The average saturation on admission and during polysomnography was also significantly worse in overlap group compared to only COPD group [Table 2].

The prevalence of overlap syndrome in patients admitted with COPD exacerbation was 25.5%. There were 45 men and six women. There were 34/38 and 11/13 men in only COPD and overlap group respectively. Male: female ratio between only COPD and overlap was statistically insignificant (P = 0.220). The age of the patients was between 40 and 71 years. The mean age of patients in only COPD was 59.18 ± 8.56 years (range 40-71 years) whereas the mean age of patients in overlap was 58.38 ± 2.90 years (range 52-63 years). The difference in age between the two groups was significant statistically (P = 0.005). The agewise distribution is given in Table 3.

Table 1: Comparison between two groups with respect to severity of exacerbations

Severity of exacerbation	Total	Only COPD (n=38)		Overlap (n=13)	
		No.	%	No.	%
Mild	13	13	34.2	0	0.0
Moderate	17	13	34.2	4	30.8
Severe	11	8	21.1	3	23.1
Very severe	6	3	7.9	3	23.1
Life-threatening	4	1	2.6	3	23.1

χ^2=11.560 (df=4), P=0.021. COPD: Chronic obstructive pulmonary disease

Table 2: Distribution of cases in two groups according to polysomnography, spirometry blood sugar and lipid parameters

Parameter	Only COPD (n=38)		Overlap (n=13)		Significance	
	Mean	SD	Mean	SD	"t"	"P"
Saturation on admission	91.16	6.89	83.08	6.56	3.694	0.001
AHI*	4.11	3.50	31.85	16.03	10.165	<0.001
Overnight average saturation	95.63	3.72	86.62	7.58	5.666	<0.001
FEV_1**	39.24	13.06	39.62	10.04	−0.094	0.925
FEV_1/FVC***	54.68	5.08	56.32	9.24	−0.801	0.427
Fasting blood sugar (mg/dl)	95.58	16.35	128.08	21.06	−5.741	<0.001
S. cholesterol (mg/dl)	147.29	22.39	188.23	18.62	−5.919	<0.001
LDL (mg/dl)****	96.75	23.96	124.41	15.45	−3.880	<0.001
VLDL (mg/dl)*****	24.02	7.17	25.89	8.18	−0.784	0.437
HDL (mg/dl)******	41.13	2.83	41.32	2.41	−0.209	0.835

*AHI: Apnea hypopnea index, **FEV_1: Forced expiratory volume in one second, ***FVC: Forced vital capacity, ****LDL: Low-density lipoprotein, *****VLDL: Very low-density lipoprotein, ******HDL: High-density lipoprotein, COPD: Chronic obstructive pulmonary disease

The spirometry comparison is given in Tables 2 and 4. The mean forced expiratory volume in one-second (FEV_1) % predicted was 39.24 ± 13.06% in only COPD and 39.62 ± 10.04% in overlap. FEV_1/forced vital capacity (FVC) in only COPD was 54.68 ± 5.08% and in overlap was 56.32 ± 9.24%. The difference between the two groups was statistically insignificant. The majority of the patients in both the groups were in stage III and IV. Overall there was more number of patients in only COPD group. Hence, the number of patients with COPD stage I and II was higher in only COPD (21.1%) as compared to overlap (7.7%) but the difference was not found to be significant statistically (P = 0.473). Thus, there was no difference between the two groups in spirometry. 2D Echo could be done in only 19 cases, 14 of only COPD and five from overlap. Nine out of fourteen patients (64.3%) with only COPD and four out of five patients (80%) with overlap had cor pulmonale. Since, a complete data of 2-D Echo was not available, the findings were not evaluated statistically.

Majority of subjects in only COPD were underweight or normal weight whereas majority of subjects in overlap were obese. Mean BMI in only COPD was 20.70 ± 8.03 kg/m^2 and that in overlap was 31.82 ± 5.80 kg/m^2. The mean waist circumference in only COPD was 58.21 ± 20.07 cm and in overlap was 96.62 ± 17.61 cm. Both mean BMI and waist circumference in overlap were significantly higher as compared to only COPD (P < 0.001). The distribution of patients according to weight category has been shown in Table 5 and Chart 3.

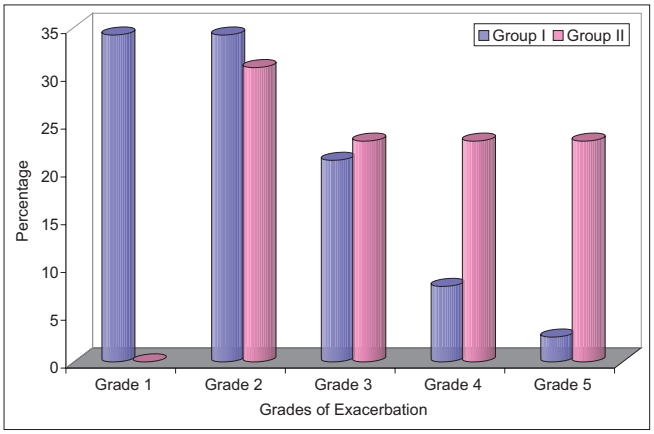

Chart 1: Distribution of cases in two groups according to severity of exacerbations
Group I = Only COPD, Group II = Overlap

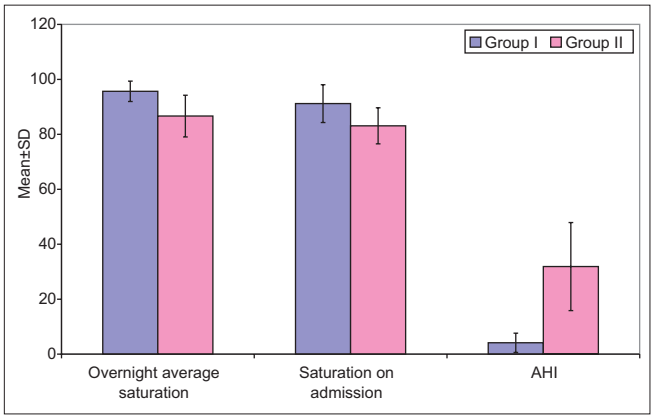

Chart 2: Comparison of cases in two groups according to oxygen saturation findings
Group I = Only COPD, Group II = Overlap

The comparison of patients in two groups according to the blood sugar and lipid parameters has been shown in Table 2 and Chart 4. As compared to only COPD, the mean fasting blood sugar, serum cholesterol and low density lipoprotein (LDL) levels were significantly high in overlap ($P < 0.001$). Serum very low-density lipoprotein (VLDL) level was also higher in overlap as compared to only COPD but the difference was not significant statistically ($P > 0.05$). Four out of thirty-eight patients (10.5%) in only COPD and 13/13 patients (100%) in overlap were detected to have hypertension. The association was statistically significant ($P < 0.001$) i.e. $\chi^2 = 34.895$ (df = 1). Overall the metabolic syndrome was observed in only two out of thirty-six (5.3%) patients in only COPD and 6/13 (46.2%) patients in overlap. The difference between the two group was $\chi^2 = 12.246$ (df = 1) i.e. statistically significant ($P < 0.001$). Multiple regression analysis to show that obesity, OSAS or combined effect of both was responsible for the presence of metabolic syndrome could not be done due to a small number of patients with overlap syndrome and obesity.

Table 3: Agewise distribution of cases in two groups

Age group (years)	Total	Only COPD (*n*=38)		Overlap (*n*=13)	
		No.	%	No.	%
<50	9	9	23.7	0	0.0
51-60	19	9	23.7	10	76.9
61-70	18	15	39.5	3	23.1
>70	5	5	13.2	0	0.0
Mean age±SD (range)	58.98±7.42	59.18±8.56		58.38±2.90	
(Median) in years	(40-71) (60)	(40-71) (61)		(52-63) (58)	

χ^2=12.897 (df=3), *P*=0.005. SD: Standard deviation, COPD: Chronic obstructive pulmonary disease

Table 4: Distribution of cases in two groups according to GOLD COPD stage

COPD stage	Total	Only COPD (*n*=38)		Overlap (*n*=13)	
		No.	%	No.	%
I	3	3	7.9	0	0.0
II	6	5	13.2	1	7.7
III	23	15	39.5	8	61.5
IV	19	15	39.5	4	30.8

COPD: Chronic obstructive pulmonary disease

Table 5: Distribution of cases in two groups according to BMI and waist circumference

BMI category (BMI in kg/m^2)	Total	Only COPD (*n*=38)		Overlap (*n*=13)	
		No.	%	No.	%
Underweight (<18.5)	22	21	55.3	1	7.7
Normal weight (18.5-24.9)	13	12	31.6	1	7.7
Overweight (25.0-29.9)	0	0	0	0	0
Obese (>30)	16	5	13.2	11	84.6
Mean BMI±SD		20.70±8.03		31.82±5.80*	
Mean waist circumference±SD		58.21±20.07		96.62±17.61*	

χ^2=23.015 (df=2), *P*<0.001, **P*<0.001 (*t*-test). BMI: Body mass index, SD: Standard deviation

DISCUSSION

McNicholas *et al.*[15] has recently stated that sleep disorder in COPD is a forgotten dimension. Indeed, there are very few studies available on overlap syndrome. None of the available studies have been focused on the influence of overlap syndrome on the severity of AECOPD. There are four significant findings of our cross-sectional prospective study on patients admitted with AECOPD. 1) The severity of exacerbation of COPD is significantly worse in patients with overlap compared to those without overlap. 2) The prevalence of OSAS in our study on AECOPD is higher than that seen in other studies performed on stable COPD patients. 3) Patients in overlap syndrome admitted with AECOPD are significantly more obese and the majority have stage 3 and 4 COPD. 4) Those with AECOPD and overlap syndrome have significantly higher likelihood of metabolic syndrome compared to those without overlap syndrome.

The significant finding for which the study was performed and on which no cross-sectional study has been done earlier suggests that the patients with AECOPD are at a significantly higher risk of severe exacerbation leading to

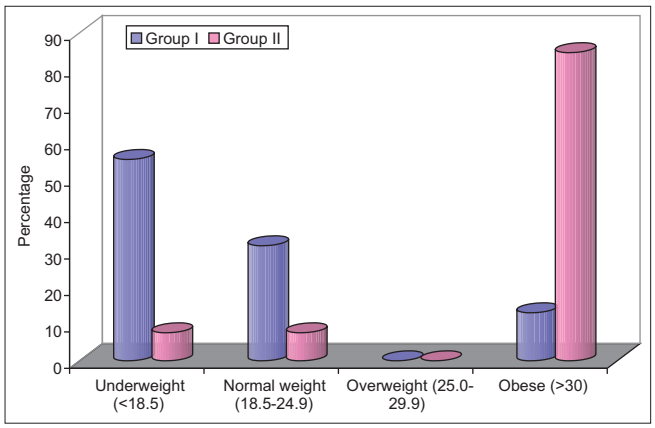

Chart 3: BMI Category in both the groups
Group I = Only COPD, Group II = Overlap

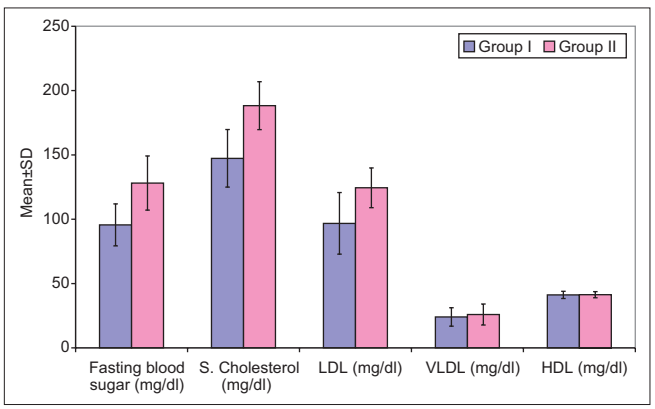

Chart 4: Distribution of cases in two groups according to blood sugar and lipid parameters
Group I = Only COPD, Group II = Overlap

respiratory failure. The majority of only COPD cases had mild to moderate exacerbations i.e. normal blood gas level on admission whereas majority of cases in overlap group had severe, very severe or life-threatening exacerbations i.e., either type 1 or type 2 respiratory failure. Also, with increasing severity of exacerbation, the mean AHI increased. Statistically, the difference between the two groups was significant ($P = 0.021$). Our study is the first study to show that the patients with overlap syndrome presenting with AECOPD are significantly more vulnerable to respiratory failure during exacerbation. The only other study to have evaluated exacerbation with respect to overlap syndrome was a study by Marin *et al.*[16] It was a large longitudinal study with more than 200 patients in three arms consisting of only COPD, overlap treated with continuous positive airway pressure (CPAP) and overlap not treated with CPAP. The study showed that overlap syndrome not treated with CPAP have a higher mortality i.e. death from any cause ranging from cardiovascular, cancer to pulmonary compared to only COPD. It was also shown that the overlap syndrome patients who were not treated with CPAP are likely to suffer COPD exacerbation requiring hospitalization compared to only COPD. The severity of exacerbation in patients with only COPD, however, was not compared to overlap syndrome not treated with CPAP.

The second finding is that out of 51 patients enrolled in the study, 13 have coexisting OSAS. Thus, the prevalence of overlap syndrome in patients admitted with AECOPD is 25.5%. Studies on prevalence of overlap syndrome show that the prevalence of OSAS is not greater in stable COPD patients compared with the non-COPD population.[15] Sleep Heart Health Study with 5,954 participants showed the prevalence of OSAS among the stable COPD subjects was 14.0% and those without COPD was 18.6%.[1] Thus, our prevalence of 25.5% is higher than that found in stable COPD patients. Though there is a plenty of data on the prevalence of overlap syndrome in stable COPD patients,[1,2] there is a paucity of data on the prevalence of overlap syndrome in patients admitted with AECOPD. One such study available in the literature shows a very high prevalence (51.4%) of overlap syndrome in patients hospitalized with AECOPD.[17] In this study a limited polysomnography (type 3 study) was performed in only 35 out of 101 patients admitted with AECOPD. We had performed type 1 sleep study i.e., full polysomnography in all 51 patients admitted with AECOPD. Thus the results cannot be compared. Nevertheless, the prevalence in this only available study is also very high. Hence, more studies are required to establish this finding of 'high' prevalence of OSAS in patients admitted with AECOPD. Also, it can be deducted that the examination focused on the search for OSAS in patients hospitalized for COPD exacerbation is likely to increase the probability of OSAS detection.[17]

Another significant finding of our study is that both mean BMI and waist circumference in those with overlap syndrome compared to only COPD is significantly high. Many authors have studied the prevalence of obesity in COPD patients. The overall prevalence of obesity in population is reported to be 18%, with the highest prevalence in GOLD stages 1 and 2 (16-24%) and the lowest in GOLD stage 4 (6%).[18,19] The prevalence of obesity in our patients with overlap syndrome is 84% and the majority of patients these patients had COPD GOLD stages 3 and 4. It is a very unusual have obese patients with stage 3 and 4 COPD. It has been shown that mortality reduces with higher BMI also known as "reverse epidemiology of obesity" or the "obesity paradox."[20-23] However, this 'better mortality' has not been studied with respect to the presence or absence of overlap syndrome. We hypothesize that the apparent contradiction of reduced mortality in obese patients may possibly not be true for a subgroup of patients with overlap of COPD and OSAS and it needs to be studied in detail.

The fourth significant finding of our study is that the patients with overlap have significantly higher incidence of metabolic syndrome compared to those with only COPD. Many authors have evaluated obesity and its impact on lung function, exercise capacity and prognosis in COPD patients.[20-25] Many others have evaluated metabolic syndrome in patients of COPD and shown that metabolic syndrome is more prevalent in overweight or obese COPD patients than in BMI-matched healthy subjects.[26-29] A few others have evaluated OSAS with COPD without comparing metabolic syndrome.[30,31] But none have evaluated metabolic syndrome, obesity, OSAS and COPD all together. As compared to those with only COPD mean fasting blood sugar, serum cholesterol and LDL levels are significantly higher in patients of overlap syndrome. Four out of thirty-eight (10.5%) patients in only COPD and 13/13 (100%) patients in overlap are detected to have hypertension. Overall metabolic syndrome is observed in significantly higher number of patients with overlap syndrome compared to only COPD patients. The important risk factors, which have been shown to cause metabolic syndrome in COPD are smoking, genetics, obesity, physical inactivity, and airflow limitation.[24] However, none of the studies have shown that OSAS in these patients can also be the cause of metabolic syndrome especially with the growing evidence suggesting that OSAS, beyond their epidemiologic relationship, may be causally related to metabolic syndrome. Our study shows that the presence of OSAS in patients of COPD can also be a risk factor for metabolic syndrome, though it could not be proven beyond doubt, as regression analysis could not be done. It has been stated that patients with overlap syndrome may have more chances of cardiovascular consequences because of greater hypoxia predisposing to atherosclerosis more than COPD and OSA alone, though it has not been proven.[30,32,33] We can add that a greater prevalence of metabolic syndrome due to overlap syndrome in COPD patients might further increase the likelihood of atherosclerosis.

There are a few drawbacks of our study. Firstly, there were only 51 patients in the study. A larger study could

have established our findings more firmly and enabled us to do regression analysis for metabolic syndrome in COPD and overlap syndrome. Thus, a similar study with a large number of patients needs to be performed. Secondly, the design of the study is such that the number of exacerbation in terms of the past history and the follow up is not available. Also, the outcome of exacerbation in terms mortality is not evaluated, as only those patients who survived could be further analyzed for presence of OSAS and COPD were included. More information of exacerbation would have further improved our knowledge on long-term outcome of AECOPD with OSAS.

Nevertheless, it is important for the clinician to know and explain to the patient that the treatment of OSAS in COPD is very essential to prevent a life-threatening exacerbation. If they are explained about treatment on experiencing such life-threatening condition, the probability of compliance towards treatment is likely to increase. Also, the patients admitted with AECOPD should be evaluated for OSAS to improve the probability of OSAS detection. Future studies should evaluate the association between COPD and obesity with respect to OSAS and metabolic syndrome, as the mortality may be high in 'obese COPD' patients with OSAS.

REFERENCES

1. Sanders MH, Newman AB, Haggerty CL, Redline S, Lebowitz M, Samet J, O'Connor GT, *et al*. Sleep Heart Health Study. Sleep and sleep-disordered breathing in adult with predominantly mild obstructive airway disease. Am J Respir Crit Care Med 2003;167:7-14.
2. Lee R, McNicholas WT. Obstructive sleep apnea in chronic obstructive pulmonary disease patients. Curr Opin Pulm Med 2011;17:79-83.
3. Zamarrón C, García Paz V, Morete E, del Campo Matías F. Association of chronic obstructive pulmonary disease and obstructive sleep apnea consequences. Int J Chron Obstruct Pulmon Dis 2008;3:671-82.
4. Minai OA, Ricaurte B, Kaw R, Hammel J, Mansour M, McCarthy K, *et al*. Frequency and impact of pulmonary hypertension in patients with obstructive sleep apnea syndrome. Am J Cardiol 2009;104:1300-6.
5. Hawryłkiewicz I, Sliwiński P, Górecka D, Pływaczewski R, Zieliński J. Pulmonary haemodynamics in patients with OSAS or an overlap syndrome. Monaldi Arch Chest Dis 2004;61:148-52.
6. Dwarakanath A, Elliott MW. Noninvasive ventilation in the management of acute hypercapnic respiratory failure. Breathe 2013;9:339-48.
7. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al*. ATS/ERS Task Force: Standardisation of spirometry. Eur Respir J 2005;26:319-38.
8. Global strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease, Revised 2011. Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2011_Feb21.pdf. [Last accessed on 2014 Dec 23].
9. Burge S, Wedzicha JA. COPD exacerbations: Definitions and classifications. Eur Respir J 2003;21(suppl 41):46-53s.
10. Epstein L, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, *et al*. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009;5:263-76.
11. Global Database on Body Mass Index. Word Heath Organization. Available from: http://apps.who.int/bmi/index.jsp. [Last accessed on 2014 Dec 23].
12. Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication No. 02-5215. Available from: http://www.nhlbi.nih.gov/files/docs/resources/heart/atp3full.pdf.
13. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2011;34(Suppl 1):S62-9.
14. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, *et al*. Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: Blood pressure measurement in humans: A statement for professionals from the subcommittee of professional and public education of the American Heart Association Council on high blood pressure research. Hypertension 2005;45:142-61.
15. McNicholas WT, Verbraecken J, Marin JM. Sleep disorders in COPD: The forgotten dimension. Eur Respir Rev 2013;22:365-75.
16. Marin JM, Soriano JB, Carrizo SJ, Boldova A, Celli BR. Outcomes in patients with chronic obstructive pulmonary disease and obstructive sleep apnea: The overlap syndrome. Am J Respir Crit Care Med 2010;182:325-31.
17. Turcani P, Skrickova J, Pavlik T, Janousova E, Orban M. The prevalence of obstructive sleep apnea in patients hospitalized for COPD exacerbation. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2014. [Epub ahead of print].
18. Franssen FM, O'Donnell DE, Goossens GH, Blaak EE, Schols AM. Obesity and the lung: 5. Obesity and COPD. Thorax2008;63:1110-7.
19. Steuten LM, Creutzberg EC, Vrijhoef HJ, Wouters EF. COPD as a multicomponent disease: Inventory of dyspnoea, underweight, obesity and fat free mass depletion in primary care. Prim Care Respir J 2006;15:84-91.
20. Cao C, Wang R, Wang J, Bunjhoo H, Xu Y, Xiong W. Body mass index and mortality in chronic obstructive pulmonary disease: A meta-analysis. PLoS One 2012;7:e43892.
21. Landbo C, Prescott E, Lange P, Vestbo J, Almdal TP. Prognostic value of nutritional status in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1999;160:1856-61.
22. Kalantar-Zadeh K, Horwich TB, Oreopoulos A, Kovesdy CP, Younessi H, Anker SD, *et al*. Risk factor paradox in wasting diseases. Curr Opin Clin Nutr Metab Care 2007;10:433-42.
23. Naik D, Joshi A, Paul TV, Thomas N. Chronic obstructive pulmonary disease and the metabolic syndrome: Consequences of a dual threat. Indian J Endocrinol Metab 2014;18:606-16.
24. O'Donnell DE, Hamilton AL, Webb KA. Sensory-mechanical relationships during high- intensity, constant-work-rate exercise in COPD. J Appl Physiol (1985) 2006;101:1025-35.
25. Schols AM, Broekhuizen R, Weling-Scheepers CA, Wouters EF. Body composition and mortality in chronic obstructive pulmonary disease. Am J Clin Nutr 2005;82:53-9.
26. Poulain M, Doucet M, Drapeau V, Fournier G, Tremblay A, Poirier P, *et al*. Metabolic and inflammatory profile in obese patients with chronic obstructive pulmonary disease. Chron Respir Dis 2008;5:35-41.
27. Akpınar EE, Akpınar S, Ertek S, Sayın E, Gülhan M. Systemic inflammation and metabolic syndrome in stable COPD patients. Tuberk Toraks 2012;60:230-7.
28. Breyer MK, Spruit MA, Hanson CK, Franssen FM, Vanfleteren LE, Groenen MT, *et al*. Prevalence of metabolic syndrome in COPD patients and its consequences. Plos One 2014;9:e98013.
29. Lazovic B, Stajic Z, Mazic S, Đelić M. Prevalence of metabolic syndrome in patients suffered from chronic obstructive pulmonary disease. Journal of Regional Section of Serbian Medical Association in Zajecar 2012;37:229-32.
30. McNicholas WT. Chronic obstructive pulmonary disease and obstructive sleep apnea: Overlaps in pathophysiology, systemic inflammation, and cardiovascular disease. Am J Respir Crit Care Med 2009;180:692-700.
31. Weitzenblum E, Chaouat AR, Kessler R, Canuet M. Overlap syndrome: Obstructive sleep apnea in patients with chronic obstructive pulmonary disease. Proc Am Thorac Soc 2008;5:237-41.
32. Lee R, McNicholas WT. Obstructive sleep apnea in chronic obstructive pulmonary disease patients. Curr Opin Pulm Med 2011;17:79-83.
33. Mieczkowski B, Ezzie ME. Update on obstructive sleep apnea and its relation to COPD. Int J Chron Obstruct Pulmon Dis 2014:9 349-62.

How to cite this article: Gothi D, Gupta SS, Kumar N, Sood K. Impact of overlap syndrome on severity of acute exacerbation of chronic obstructive pulmonary disease. Lung India 2015;32:578-83.

Source of Support: Nil, **Conflict of Interest:** None declared.