

RABMS Journal of Research in Applied and Basic Medical Sciences



Impact of Comorbidities on the Management Outcome of Acute Exacerbation of COPD

Ronak Jain¹, Pratik Akhani², Deepak Nagar³, Ramesh Agrawal^{*4}

Abstract

Background & Aims: Chronic obstructive pulmonary disease (COPD) is an important cause of mortality and morbidity globally. COPD, if associated with multiple comorbidities, has a greater impact on treatment outcome and hospital stay, hence effective control of COPD is crucial for enhancing quality of life. Our study assesses the effect of comorbidities on management outcomes in acute exacerbations of COPD patients.

Materials & Methods: An analytical cross-sectional study was planned on 630 patients. Patients with acute exacerbations of COPD who were admitted to pulmonary ward and ICU were enrolled in the study. Data analysis was done using MS Excel and SPSS version 21.0. Unpaired students't-test was used and p < 0.05 was taken to be statistically significant.

Results: 61.9% of patients had at least one associated comorbidity e.g. CAD (37.2%), hypertension (28.2%), diabetes mellitus (24.3%), and CVD (10.3%). We found that acute exacerbation of COPD patients with comorbidities had prolonged hospital stay, greater ICU admissions, and need for invasive ventilation as compared to those without comorbidities. Presence of comorbidities with COPD was significantly associated with duration of hospital stay.

Conclusion: Comorbidities associated with acute exacerbations of COPD increase the hospital stay, need for ICU admission and more invasive ventilation, and reduce the impact of treatments.

Keywords: Comorbidity, Chronic Obstructive Pulmonary Disease, Diabetes Mellitus, Hypertension

Received 21 May 2021; accepted for publication 18 September 2021

Introduction

Chronic obstructive pulmonary disease (COPD) is still an emerging threat to global health and a challenging public health problem leading to morbidity and mortality globally (1). COPD frequently coexists with other co-morbid conditions that may cause potentially serious health consequences such as a decrease in pulmonary function and diminished survival rate, e.g. cardiovascular diseases (hypertension, atherosclerotic coronary artery disease, congestive heart

¹ Department of TB & Chest, Government Medical College, Ratlam, Madhya Pradesh, India.

² Department of Physiology, Nandkumar Singh Chouhan Government Medical College, Khandwa-450001, Madhya Pradesh, India.

³ Department of TB & Chest, Government Medical College, Ratlam, Madhya Pradesh, India.

⁴ Department of Microbiology, Nandkumar Singh Chouhan Government Medical College, Khandwa-450001, Madhya Pradesh, India

^{*}Corresponding authors: Ramesh Agrawal, Address: Department of Microbiology, Nandkumar Singh Chouhan Government Medical College, Khandwa-450001, Madhya Pradesh, India, Email: drrameshagrawal22@gmail.com, Tel: (+91) 7568775748

failure, pulmonary hypertension, peripheral vascular disease and stroke), musculoskeletal disorders (skeletal muscle dysfunction, loss of muscle mass, osteoporosis, osteopenia & osteoarthritis), psychological disturbances (depression, anxiety), diabetes and lung cancer; and among them, ischemic heart disease (IHD) is a major cause of mortality and morbidity in the COPD population as a whole (2). COPD enhances the risk of developing hypertension and diabetes mellitus. On the other hand, major risk factors of IHD including hypertension, diabetes mellitus, hyperlipidemia and obesity, which are known as metabolic syndrome, have a higher prevalence in COPD patients (3).

Comorbidities in COPD can occur at any stage of the disease (4). There is evidence that comorbidities coexisting with the COPD are associated with increased risk for exacerbations, prolonged hospitalizations, reduced health status, and increased mortality (5). Conditions frequently linked with COPD are increased age, smoking, systemic inflammatory changes, and airflow restriction (6). Comorbidities among COPD patients enhance overall cost burden and also increase health care resources utilization. Patients with multiple comorbidities may also show decreased effectiveness to treatment (7). Coexisting asthma also significantly increases the frequency of severe exacerbations in COPD patients (8).

Proper management of multimorbidity in patients with COPD involves early detection and treatment of comorbidities. Therefore, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend that the presence of comorbidities should be separately evaluated while assessing COPD patients (9). Management of COPD patients with comorbidities is often very complex and unclear because of lack of a standardized protocol for their determination and difficulties in differentiating comorbidities from severe COPD

Hence, this study was planned to assess the effect of comorbidities on management outcomes in acute

exacerbations of COPD patients.

Materials and Methods

Ethical approval: The study received ethical approval from the Ethics & Research Committee of Shri Aurobindo Medical College and Post Graduate Institute, Indore, Madhya Pradesh, India.

Study Design & study population: We performed an analytical cross-sectional study. 630 patients who were admitted with acute exacerbation of COPD in Shri Aurobindo Medical College and Post Graduate Institute, Indore from June 2016 to June 2017 participated in the study. Diagnosis and severity of COPD were confirmed by the most recent digital spirometry testing. Demographic and other detailed information on comorbid conditions were obtained and diagnosed by appropriate standard tests.

Inclusion criteria: IPD patients of acute exacerbation of COPD, who were above 40 years of age were included in the study.

Exclusion criteria: Patients with severe chest trauma/facial abnormalities, post-operative respiratory failure, respiratory failure due to acute respiratory distress syndrome (ARDS), respiratory failure secondary to infection, brainstem lesions and left ventricular failure (cardiogenic pulmonary edema), sleep apnea and upper airway obstruction were excluded from the study.

Statistical Methods: The data were analyzed using Microsoft Excel 2016 and SPSS® (Statistical Package for Social Sciences) version 21. Mean and standard deviation were calculated for the continuous variables, whereas proportion for the nominal variables. Unpaired students't-test was used to compare means between two groups. p < 0.05 was considered to be statistically significant.

Results

Table 1 shows age-wise distribution of patients. Majority (n=290, 46.03 %) of the patients were in the 61-70 years of age group.

Table 1: Age-Wise Distribution of Patients

Age (Years)	Frequency (n)	Percentage (%)
41-60	150	23.81
61-70	290	46.03
71-80	120	19.04
>80	70	11.12
Total	630	100

Out of total 630 patients with COPD with acute exacerbation, 390 (61.9%) had at least one associated comorbidity (Figure 1). Most of the patients (n =41) required 2 days of ICU admission (Figure 2).

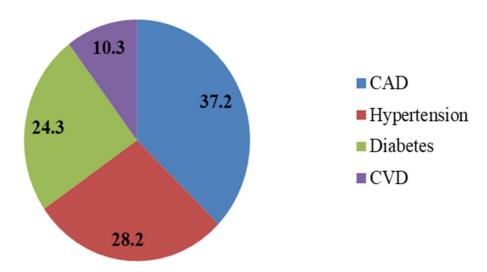


Fig 1: Comorbidities (%) associated with COPD (n=390)

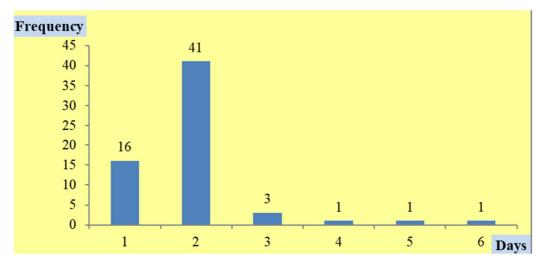


Fig 2: 2-Duration of ICU stay in acute exacerbation of COPD patients

We found that comorbidities associated with acute exacerbation of COPD significantly increase the hospital stay of the patients and reduce the impact of treatment. (Tables 2-5).

Table 2: Effect of CAD on hospital stay in acute exacerbation of COPD

Mode of treatment	With CAD (145)	Without CAD (240)	p-value
ST [days]	3.6 ± 0.54 (86)	$3.35 \pm 0.78 (148)$	0.0092*
ST+NIV [days]	5 ± 3.082 (52)	3.90 ± 0.80 (87)	0.0019*
ST+NIV+IV [days]	$8 \pm 4 \ (07)$	$6.66 \pm 3.05 (5)$	0.5447

^{*}p < 0.05 statistically significant; unpaired students' t test.

ST = Standard Therapy, NIV = Non-invasive Ventilation, IV = Invasive Ventilation

Table 3: Effect of Hypertension on hospital stay in acute exacerbation of COPD

Mode of treatment	Hypertension (110)	Without Hypertension (240)	p-value
ST [days]	3.5 ± 0.51 (66)	3.35 ± 0.78 (148)	0.1539
ST+NIV [days]	4.83 ± 2.16 (38)	3.90 ± 0.80 (87)	0.0006*
ST+NIV+IV [days]	$8 \pm 4 (6)$	$6.66 \pm 3.05 (5)$	0.5549

^{*}p < 0.05 statistically significant; unpaired students' t test.

ST = Standard Therapy, NIV = Non-invasive Ventilation, IV = Invasive Ventilation

Table 4: Effect of Diabetes Mellitus on hospital stay in acute exacerbation of COPD

Mode of treatment	Diabetes (95)	Without Diabetes (240)	p-value
ST [days]	4.31 ± 0.72 (58)	3.35 ± 0.78 (148)	< 0.0001*
ST+NIV [days]	4.60 ± 0.61 (30)	3.90 ± 0.80 (87)	< 0.0001*
ST+NIV+IV [days]	$7.3 \pm 2.63 (7)$	$6.66 \pm 3.05 (5)$	0.7050

^{*}p < 0.05 statistically significant; unpaired students' t test.

ST = Standard Therapy, NIV = Non-invasive Ventilation, IV = Invasive Ventilation

Table 5: Effect of CVD on hospital stay in acute exacerbation of COPD

Mode of treatment	With CVD (40)	Without CVD (240)	p-value
ST [days]	4.5 ± 0.70 (24)	3.35 ± 0.78 (148)	< 0.0001*
ST+NIV [days]	$5 \pm 1.5 (11)$	3.90 ± 0.80 (87)	0.0002*
ST+NIV+IV [days]	7.80 ± 2.10 (5)	$6.66 \pm 3.05 (5)$	0.5107

p < 0.05 statistically significant; unpaired students' t test.

ST = Standard Therapy, NIV = Non-invasive Ventilation, IV = Invasive Ventilation

Discussion

The present study showed that acute exacerbation of COPD patients with comorbidities had prolonged hospital stay and greater risk of ICU admission as compared to patients without comorbidities. This may occur due to a more complicated course requiring a longer hospital stay and increasing the risk of ICU

admission and death. Acute exacerbations of COPD with comorbidities patients require invasive ventilation therapy as compared to those without comorbidities. Presence of comorbidities in COPD was significantly associated with the length and cost of hospitalization, which was similar to other studies like Volpe G et al (10). Among the overall COPD patients, 61.9% had at

least one chronic comorbidity associated with COPD. Systemic hypertension, diabetes, and heart diseases (coronary heart disease) were the most frequently reported comorbidities which were in concordance with other studies like E Crisafulli et al (11). The prevalence of coronary artery disease reported was 37.2% in patients with COPD which was similar to Hillas et al (12). but lower compared to Schwab et al (13) (47.8%).

In our study, patients with COPD reported hypertension in 28.2% of cases which was in concordance with Van Manen et al (14). But, some previous studies like Fumagalli et al (52%), Mapel et al (45%), Frei et al (42%), Koskela et al (41%) reported a much higher prevalence of hypertension in patients with CPOD.

The prevalence of diabetes associated with COPD was 24.3% which was congruent with the findings of Koskela et al (18). and Cazzola et al (19). and incongruent with the findings of other previous studies like Sidney et al., van Manen et al., Lopez Varela et al., Fumagalli et al., and Mapel et al. that reported lower diabetes prevalence of 2%, 5%, 8% and 11% and 12%, respectively. Present study reported cerebrovascular disease in 10.3% of cases which was similar to the findings of Van Manen et al. Many studies such as Mapel et al. Koskela et al. Lopez Varela et al. Anecchino et al, and Miyazaki et al. reported a much higher prevalence of cerebrovascular disease (68%, 65%, 41%, 32%, and 27%, respectively).

An exacerbation episode of COPD increases the risk of future exacerbations and can lead to a vicious cycle of patient deterioration. Therefore, understanding the predictors of increased exacerbation risk and prevention of COPD exacerbations should be the key focus of COPD clinical research. Comorbidities associated with acute exacerbations of COPD prolong the hospital stay of the patients and reduce the impact of treatments which affect the quality of life. Comorbidities may also lower the quality of COPD-related care, which can be a potential area for further research. Our findings could also provide insight into future quality improvement strategies in patients with COPD.

Conclusion

Comorbidities associated with acute exacerbations of COPD increase the hospital stay, need for ICU admission and more invasive ventilation, and reduce the impact of treatment. Therefore, greater attention needs to be paid to the assessment and management of comorbidities in COPD.

Acknowledgements

Authors acknowledge the guidance, support, and motivation provided by Dr. Satish Motiwale, Professor and Head of the Department of Tuberculosis and Respiratory Diseases, SAMC & PGI, Indore.

Conflict of Interest

Authors have no conflicts of interest to declare.

References

- Lamprecht B, Soriano JB, Studnicka M, Kaiser B, Vanfleteren LE, Gnatiuc L, et al. Determinants of underdiagnosis of COPD in national and international surveys. Chest 2015;148 (4):971–85.
- Patel AR, Hurst JR. Extrapulmonary comorbidities in chronic obstructive pulmonary disease: state of the art. Expert Rev Respir Med 2011;5(5): 647-62.
- Smith MC, Wrobel JP. Epidemiology and clinical impact of major comorbidities in patients with COPD. Int J Chron Obstruct Pulmon Dis 2014; 9: 871-88.
- Agusti A, Calverley PM, Celli B, Coxson HO, Edwards LD, Lomas DA, et al. Characterisation of COPD heterogeneity in the ECLIPSE cohort. Respir Res 2010; 11: 122.
- Cavaillès A, Brinchault-Rabin G, Dixmier A, Goupil F, Gut-Gobert C, Marchand-Adam S, et al. Comorbidities of COPD. Eur Respir Rev 2013;22(130):454-75. Epping-Jordan JE, Galea G, Tukuitonga C, Beaglehole R. Preventing chronic diseases: taking stepwise action. Lancet 2005; 366: 1667-71.
- Simon-Tuval T, Scharf SM, Maimon N, Bernhard-Scharf BJ, Reuveni H, Tarasiuk A. Determinants of elevated healthcare utilization in patients with COPD. Respir Res 2011;12:7.

- Lee H, Rhee CK, Lee BJ, Choi DC, Kim JA, Kim SH, et al. Impacts of coexisting bronchial asthma on severe exacerbations in mild-to-moderate COPD: results from a national database. Int J Chron Obstruct Pulmon Dis 2016;11:775–83.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD). From the global strategy for the diagnosis, management and prevention of COPD. 2017. Available from: http://goldcopd.org. Accessed March 16, 2020.
- Terzano C, Colamesta V, Unim B, Romani S, Meneghini A, Volpe G, et al. Chronic obstructive pulmonary disease (COPD) exacerbation: impact of comorbidities on length and costs during hospitalization. Eur Rev Med Pharmacol Sci 2017;21:3680–9.
- Crisafulli E, Costi S, Luppi F, Cirelli G, Cilione C, Coletti O, et al. Role of comorbidities in a cohort of patients with COPD undergoing pulmonary rehabilitation. Thorax 2008;63:487–92.
- Hillas G, Perlikos F, Tsiligianni I, Tzanakis N. Managing comorbidities in COPD, Int J Chron Obstruct Pulmon Dis 2015;10: 95–109.
- Schwab P, Dhamane AD, Hopson SD, Moretz C, Annavarapu S, Burslem K, et al. Impact of comorbid conditions in COPD patients on health care resource utilization and costs in predominantly Medicare population. Int J Chron Obstruct Pulmon Dis 2017;12: 735–44.
- Van Manen JG, Bindels PJ, Lizermans CJ, van der Zee JS, Bottema BJ, Schadé E. Prevalence of comorbidity in patients with chronic airway obstruction and controls over the age of 40. J Clin Epidemiol 2001;54(3):287–93.
- 14. Fumagalli G, Fabiani F, Forte S, Napolitano M, Marinelli P, Palange P, et al. INDACO project: a pilot study on incidence of comorbidities in COPD patients referred to pneumology units. Multidiscip Respir Med 2013;8(1):28.
- 15. Mapel DW, Hurley JS, Frost FJ, Petersen HV, Picchi

- MA, Coultas DB. Health care utilization in chronic obstructive pulmonary disease. A case-control study in a health maintenance organization. Arch Intern Med 2000;160(17):2653–8.
- Frei A, Muggensturm P, Putcha N, Siebeling L, Zoller M, Boyd CM, et al. Five comorbidities reflected the health status in patients with chronic obstructive pulmonary disease: the newly developed COMCOLD index. J Clin Epidemiol 2014;67(8):904–11.
- Koskela J, Kilpeläinen M, Kupiainen H, Mazur W, Sintonen H, Boezen M, et al. Co-morbidities are the key nominators of the health related quality of life in mild and moderate COPD. BMC Pulm Med 2014;14(1):102.
- Cazzola M, Bettoncelli G, Sessa E, Cricelli C, Biscione G. Prevalence of comorbidities in patients with chronic obstructive pulmonary disease. Respiration 2010;80(2):112–9.
- Sidney S, Sorel M, Quesenberry CP Jr, DeLuise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease. Hospitalizations and mortality: Kaiser Permanente Medical Care Program. Chest 2005;128(4):2068–75.
- Lopez Varela MV, Montes de Oca M, Halbert RJ, Muiño A, Perez-Padilla R, Tálamo C, et al; PLATINO Team.
 Sex-related differences in COPD in five Latin American cities: the PLATINO study. Eur Respir J 2010;36(5):1034–41.
- 21. Anecchino C, Rossi E, Fanizza C, De Rosa M, Tognoni G, Romero M. Working Group ARNO Project. Prevalence of chronic obstructive pulmonary disease and pattern of comorbidities in a general population. Int J Chron Obstruct Pulmon Dis 2007;2(4):567–74.
- Miyazaki M, Nakamura H, Chubachi S, Sasaki M, Haraguchi M, Yoshida S, et al; Keio COPD Comorbidity Research (K-CCR) Group. Analysis of comorbid factors that increase the COPD assessment test scores. Respir Res 2014;15(1):13.