

**ORIGINAL ARTICLE****To assess the acute exacerbations of chronic obstructive pulmonary disease (COPD) patients**<sup>1</sup>Braj Kishore Singh, <sup>2</sup>Santosh Kumar<sup>1</sup>Assistant Professor, Dept of Medicine, Major SD Singh Medical College and Hospital, Farrukhabad, U.P., India;<sup>2</sup>Assistant Professor, Dept of Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India**ABSTRACT:**

**Aim:** The purpose of this study is to assess the acute symptoms of chronic obstructive pulmonary disease (COPD). **Methods:** This research included all participants who had been hospitalised for COPD exacerbations. In this research, we classified COPD exacerbations as patients hospitalised with a main diagnosis of COPD or those admitted with a primary diagnosis of pneumonia and a secondary diagnosis of COPD. In-hospital mortality and one-year mortality following discharge were the outcomes of interest. Demographics, comorbid conditions, concomitant drugs, and COPD treatments are all discussed. COPD-related drugs, including as short- and long-acting b2 agonists, anticholinergics, inhaled corticosteroids, and theophyllines, were assessed in the six months before the first hospitalisation. **Results:** The average age of the overall population at the time of cohort entrance was 75.5 years, with 67.5 percent of them being male. The majority of the patients had comorbidities, with a Charlson comorbidity index score of 3.8. Hypertension (56.25 percent), coronary artery disease (32.5 percent), and stroke were the most often seen comorbidities (32.5 percent). Approximately three-fourths of the patients were put on #2 COPD drugs, and 80 percent of patients had #2 emergency visits for COPD. The average hospital stay was 13.5±15 days. 12.5 percent of patients were admitted to the ICU, with a 9-day average stay. Mechanical breathing was necessary in 7.5 percent of patients, with a median duration of 8 days. Non-invasive ventilation was used in 2.5 percent of the patients. During the index hospitalisation, 9 patients (11.25 percent) died. Nonsurvivors were older than survivors and had a higher Charlson comorbidity index score. **Conclusion:** In conclusion, even if it is the first-ever exacerbation necessitating hospitalisation, it predicts a bad long-term result in COPD patients.

**Keywords:** COPD, Exacerbation**Corresponding author:** Santosh Kumar, Assistant Professor, Dept of Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India**This article may be cited as:** Singh BK, Kumar S. To assess the acute exacerbations of chronic obstructive pulmonary disease (COPD) patients. J Adv Med Dent Scie Res 2017;5(12):154-159.**INTRODUCTION**

Chronic obstructive pulmonary disease (COPD) is a long-term condition with significant social, health-care, and economic consequences. After neoplastic illness, ischemic heart disease, and cerebrovascular disorders, it is the fourth leading cause of mortality. <sup>1</sup> However, only COPD mortality has climbed in recent years, and it is anticipated to become the third greatest cause of death in the world by 2020. <sup>2</sup> The prevalence of COPD illness was predicted to be over 251 million cases in 2016 and 3.17 million fatalities in 2015 worldwide, with a rate of roughly 5% deaths each year. <sup>3</sup> The incidence rates were greater in males than in women above the age of 60. <sup>4,5</sup> As of 2016, COPD was India's second leading cause of mortality. In several population-based studies conducted throughout India, the frequency varied between 2 and 22 percent among males and 1.2 to 19 percent among women. <sup>6</sup> Cigarette smoking is the most frequent cause of COPD, accounting for around 85 to 90 percent of cases. Exposure to ambient smoking, passive smoke, occupational exposure, and genetic susceptibility are some of the other causes of COPD. <sup>7</sup> Shortness of breath, cough (with or without expectoration), fever, chest tightness, and hemoptysis are all frequent symptoms of COPD. <sup>8</sup> The primary

aims of COPD therapy are to give clinical relief and lower the risk of recurrent exacerbations, to slow disease progression, and to reduce death. <sup>2</sup> The basic aims of pharmacotherapy are to minimise the intensity of symptoms, enhance general health, and reduce the frequency, complications, and severity of exacerbations. <sup>9</sup>

**METHODS AND MATERIALS**

The Department of Medicine conducted this prospective research with the agreement of the protocol review committee and the institutional ethics committee. This research included all participants who had been hospitalised for COPD exacerbations. In this research, we classified COPD exacerbations as patients hospitalised with a main diagnosis of COPD or those admitted with a primary diagnosis of pneumonia and a secondary diagnosis of COPD. <sup>10-13</sup> We added the pneumonia codes since it is sometimes difficult to determine whether or not COPD exacerbations are accompanied by pneumonia, and the coexistence of COPD exacerbations and pneumonia is prevalent. <sup>14</sup> In addition, the study group had to have at least two outpatient COPD visits and be prescribed at least two COPD-related drugs within a year. The index hospitalisation was defined

as the first admission for COPD exacerbations during the research period.

In-hospital mortality and one-year mortality following discharge were the outcomes of interest. Demographics, comorbid conditions, concomitant drugs, and COPD treatments are all discussed. COPD-related drugs, including as short- and long-acting b<sub>2</sub> agonists, anticholinergics, inhaled corticosteroids, and theophyllines, were assessed in the six months before the first hospitalisation. If comorbidities were present prior to the initial hospitalisation, they were indicated in the Table 1. The Charlson comorbidity index was computed in the manner previously reported.<sup>15</sup> We also gathered data on the index hospitalisation, such as length of stay, frequency and length of intensive care unit (ICU) admission, acute cardiovascular events, use of non-invasive ventilatory assistance, use of mechanical ventilation, and ventilator days. Acute myocardial infarction, unstable angina, acute heart failure, transient ischemic attack, and ischemic stroke were among the cardiovascular events of interest.

## RESULTS

This research involved 80 participants. Table 1 summarises the patients' baseline characteristics. The average age of the overall population at the time of cohort entrance was 75.5 years, with 67.5 percent of them being male. The majority of the patients had comorbidities, with a Charlson comorbidity index score of 3.8. Hypertension (56.25 percent), coronary artery disease (32.5 percent), and stroke were the

most often seen comorbidities (32.5 percent). Approximately three-fourths of the patients were put on #2 COPD drugs, and 80 percent of patients had #2 emergency visits for COPD. The average hospital stay was 13.5±15 days (Table 3). 12.5 percent of patients were admitted to the ICU, with a 9-day average stay. Mechanical breathing was necessary in 7.5 percent of patients, with a median duration of 8 days. Non-invasive ventilation was used in 2.5 percent of the patients.

## OUTCOME

During the index hospitalisation, 9 patients (11.25 percent) died. Nonsurvivors were older than survivors and had a higher Charlson comorbidity index score. Comorbidities such as heart failure, cancer, and stroke were more likely in nonsurvivors; nevertheless, hyperlipidemia was more common in survivors. In individuals who survived the initial hospitalisation, angiotensin II receptor blockers, b blockers, and statins were more typically administered. Nonsurvivors, as predicted, had a lengthier hospital stay and were more likely to need ICU admission and ventilatory assistance (Table 3). Furthermore, nonsurvivors had greater cardiovascular events throughout their hospital stay. According to multivariate logistic regression analysis, increasing age and Charlson comorbidity index score independently predicted in-hospital death (Table 4). Furthermore, using angiotensin II receptor blockers or b blockers was linked to decreased in-hospital mortality.

**Table 1: Baseline characteristics of the patients with COPD**

Gender	Number	%
Male	54	67.5
Female	26	32.5
Age in years		
Below 30	6	7.5
30-50	11	13.75
50-70	34	42.5
Above 70	29	36.25
Co morbidities		
Coronary artery disease	26	32.5
Hypertension	45	56.25
Liver cirrhosis	29	36.25
Heart failure	22	27.5

**Table 2: COPD medications**

COPD medications	Total	Survivor	Non survivor	P value
Anticholinergic	22	20	2	0.55
ICS	12	13	1	0.77
Theophylline	53	50	3	0.26
SABA	38	35	5	0.36
LABA	10	8	2	0.87

**Table 3: Outcome**

	Total	outcome		P value
		Survivor	Nonsurvivor	
	80	71	9	
Mechanical ventilation	6	4	2	0.001
Duration of Mechanical ventilation (days)	14	6	8	0.55
Non-invasive ventilation	2	1	1	0.001
Cardiovascular events	3	2	1	0.01
Length of hospital stay(days)	13.5± 15	12.5± 12	31.5± 44	0.001
ICU admission	10	8	2	0.001
Length of ICU stay(days)	9± 8	8± 7	12 ± 11	0.005

**Table 4: Logistic regression analysis**

Parameter	Odds ratio	95% CI	P value
Age, per year	1.16	1.13–1.16	0.001
CCI, per point	1.19	1.11–1.25	0.01
Heart failure	1.45	0.84–1.82	0.12
Hyperlipidemia	0.93	0.62–1.40	0.44
Malignancy	1.48	0.99–2.29	0.17
Stroke	1.28	0.95–1.76	0.43
Use of ARB	0.72	0.48–0.88	0.05
Use of b blocker	0.74	0.51–0.85	0.03
Use of statin	0.51	0.24–1.24	0.09

## DISCUSSION

Several studies have shown a significant death risk after hospitalisation for acute COPD exacerbations. Although COPD exacerbations have been extensively researched, the exacerbation under investigation is seldom the first in the patient's disease cycle. A recent research on first-time COPD hospitalizations revealed the likelihood of later severe exacerbations and long-term death in these individuals.<sup>16</sup> Our research also sheds light on the short- and long-term mortality risk factors for a first-time hospitalisation for COPD exacerbations, as well as important events such as in-hospital death and the requirement for ICU care and ventilatory support during the initial hospital stay. The patient ages in both groups were comparable, as were the one-year death rates. Furthermore, both studies showed that greater age and comorbidity scores were significant predictors of death. As a result of their collaboration, the two studies produced a more complete picture of a first-ever severe exacerbation for clinicians caring for COPD patients.

Our findings demonstrate the significant incidence of comorbidities in patients hospitalised for COPD exacerbations, as well as their significance in terms of in-hospital and one-year prognosis in this cohort. Comorbidity severity, as defined by the Charlson comorbidity index, is a well-established predictor of death in stable COPD patients.<sup>17,18</sup> However, the data for hospitalised COPD exacerbations is less consistent. Several studies found no independent relationship between comorbidity load and in-hospital<sup>19</sup> or longer-term mortality<sup>20,21</sup>, despite the fact that several comorbidity indices have been demonstrated to be independently predictive of in-

hospital death<sup>22-24</sup> and post-discharge mortality.<sup>25</sup>

Differences in research design, source population, and comorbidity grading technique might explain the disparities. In actuality, the GOLD has placed increasing focus over the last decade on the diagnosis and treatment of concomitant diseases in COPD because to their potential influence on patient prognosis. Our data support the notion that an individual patient's health state has a major impact on mortality risk in COPD patients. Because of overlapping risk factors or a direct link, COPD is often related with cardiovascular disorders such as coronary artery disease, heart failure, hypertension, and stroke.<sup>26</sup>

Angiotensin II receptor blockers, b blockers, and statins are popular therapeutic medication classes used in the care of cardiovascular patients, and several studies have shown that they have a protective impact on cardiovascular outcomes.<sup>27-29</sup> These drugs were also related with better outcomes in individuals with severe COPD exacerbations, according to our findings. Statins, as a family of lipid-lowering medicines, have an additional immunomodulatory impact that may reduce neutrophil infiltration, cytokine generation, and matrix remodelling in COPD;<sup>30</sup> hence, statin usage seems physiologically plausible to be related with a reduced risk of COPD exacerbations and death.<sup>31</sup> Despite the findings of a recent large-scale randomised controlled trial<sup>33</sup>, it is still recommended that COPD patients with other reasons get a statin. The use of b blockers has long been regarded a contraindication for COPD patients;<sup>33</sup> however, recent studies have argued that starting or continuing b blocker medication in COPD patients with or

without an exacerbation is safe and even beneficial.<sup>34</sup> Aside from cardiovascular protection, b blockers may possibly benefit COPD patients by counteracting sympathetic tone or alleviating ischemia load.<sup>35</sup> Furthermore, as with asthma, persistent dosage of b blockers in COPD patients may give bronchoprotective benefits such as decreased inflammation, mucosal metaplasia, and production of different spasmogenic proteins via activation of b2 adrenoceptors.<sup>36</sup> The renin-angiotensin system may be involved in the aetiology of COPD via its role in the control of pro-inflammatory mediators in the lung. Angiotensin II, in particular, promotes the release of interleukin-6, tumour necrosis factor- $\alpha$ , and monocyte chemoattractant protein-1, as well as having an immunomodulatory influence on T cell responses that mediate lung damage in COPD.<sup>37,37</sup> Angiotensin II receptor blockers were shown to decrease the cytokine response of type I alveolar cells to lung damage in a recent research.<sup>38,39</sup> Our results and clinical observations confirm angiotensin II receptor blockers' therapeutic effect in COPD patients.<sup>31,40</sup> Taken together, the beneficial benefits of these medicines on COPD outcomes need special consideration. On the one hand, they highlight the significance of comorbidity control in COPD care. These drugs, on the other hand, may have direct lung protective characteristics and affect the prognosis of COPD patients.

In accordance with previous research<sup>41,42</sup>, the current study found that patients with a longer hospital stay and ICU admission had a poorer in-hospital outcome during a COPD exacerbation hospitalisation. We further show that the two factors were independent predictors of death one year after discharge. Longer hospital stays and ICU admission both indicate the severity of acute diseases, which has a detrimental influence on in-hospital prognosis and, to a lesser extent, post-discharge result.<sup>43</sup> Thus, the outcomes of this research suggest that starting post-discharge case management in patients receiving ICU treatment or a lengthy hospital stay during a COPD exacerbation may be beneficial and significant in the goal of improving long-term prognosis.

We discovered that mortality for COPD exacerbations was 11.25 percent in the first year following hospital release, which is comparable to another study's findings.<sup>16</sup> Our one-year death rate, however, did not seem to be lower than that of comparable studies that included patients with past severe COPD exacerbations.<sup>25</sup> Indeed, our research cohort was older, which is an independent predictor of post-discharge mortality<sup>43</sup>, when compared to previous study participants, but our findings highlight the importance of a hospitalised COPD exacerbation, even if it is the first of its kind. In summary, past studies<sup>44</sup>, as well as ours, indicate that hospitalizations for a COPD exacerbation identify a COPD subgroup with a bad prognosis. Based on the findings of this research, it is advised that more

comprehensive planning and follow-up for these high-risk patients may be necessary, especially if they were older, comorbid, or released after a COPD hospitalisation including a protracted hospital stay or ICU care.

## CONCLUSION

In conclusion, even if it is the first-ever exacerbation necessitating hospitalisation, it predicts a bad long-term result in COPD patients. Comorbidities have an important influence in determining mortality risks and should be thoroughly examined and controlled.

## REFERENCE

1. World Health Organization(2000). World Health Report. Geneva: World Health Organization.
2. Murray CJL, Lopez AD(1997). Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet*;349:1269–76.
3. Raheison C, Girodet P-O et al (2009) *Eur Respir J* 18:213–221
4. Doucet M, Rochette L, Hamel D (2016) Incidence, prevalence and mortality trends in chronic obstructive pulmonary disease over 2001 to 2011: a public health point of view of the burden. *Can Respir*:01–10
5. Sogaard M, Madsen M, Lokke A, Hilberg O, Sorensen HT, Thomsen RW (2016) Incidence and outcomes of patients hospitalized with COPD exacerbation with and without pneumonia. *Int J Chron Obst Pulmon Dis* 11:455–465
6. Joseph T. DiPiro, Robert L. Talbert, Gary C. Yee, Gary R. Matzke, Barbara G. Wells, L. Michael Posey, *Pharmacotherapy a pathophysiologic approach*, 10th edition, Mc Graw Hill Education, 543-554.
7. A Bourdin, P R. Burgel, P. Chanez, G. Garcia, T. Perez, N. Roche. Recent advances in COPD: pathophysiology, respiratory physiology and clinical aspects, including comorbidities. *Eur. Respir. J.* 2009. 18 114 196-212.
8. Donnell DEO, Parker CM (2006) COPD exacerbations – pathophysiology. *Thorax.* 61:4,354–4,361
9. A Bourdin, P R. Burgel, P. Chanez, G. Garcia, T. Perez, N. Roche. Recent advances in COPD: pathophysiology, respiratory physiology and clinical aspects, including comorbidities. *Eur. Respir. J.* 2009. 18 114 196-212.
10. Lieberman D, Gelfer Y, Varshavsky R, Dvoskin B, Leinonen M, et al. (2002) Pneumonic vs nonpneumonic acute exacerbations of COPD. *Chest* 122: 1264–1270.
11. Gil A, Gil R, Oyaguez I, Carrasco P, Gonz Lez A (2006) Hospitalization by pneumonia and influenza in the 50–64 year old population in Spain (1999–2002). *Hum Vaccin* 2: 181–184.
12. Soyseth V, Brekke PH, Smith P, Omland T (2007) Statin use is associated with reduced mortality in COPD. *Eur Respir J* 29: 279–283.
13. Vaz Fragoso CA, Concato J, McAvay G, Van Ness PH, Gill TM (2012) Respiratory impairment and COPD hospitalisation in older persons: a competing risk analysis. *Eur Respir J* 40: 37–44.
14. Wang MT, Lo YW, Tsai CL, Chang LC, Malone DC, et al. (2013) Statin use and risk of COPD exacerbation

- requiring hospitalization. *Am J Med* 126: 598–606 e592.
15. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 40: 373–383.
  16. Ward A, Ishak K, Proskorovsky I, Caro J (2006) Compliance with refilling prescriptions for atypical antipsychotic agents and its association with the risks for hospitalization, suicide, and death in patients with schizophrenia in Quebec and Saskatchewan: a retrospective database study. *Clin Ther* 28: 1912–1921.
  17. Marti S, Munoz X, Rios J, Morell F, Ferrer J (2006) Body weight and comorbidity predict mortality in COPD patients treated with oxygen therapy. *Eur Respir J* 27: 689–696.
  18. Casanova C, Cote C, de Torres JP, Aguirre-Jaime A, Marin JM, et al. (2005) Inspiratory-to-total lung capacity ratio predicts mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 171: 591–597.
  19. Dransfield MT, Rowe SM, Johnson JE, Bailey WC, Gerald LB (2008) Use of beta blockers and the risk of death in hospitalised patients with acute exacerbations of COPD. *Thorax* 63: 301–305.
  20. Ranieri P, Bianchetti A, Margiotta A, Virgilio A, Clini EM, et al. (2008) Predictors of 6-month mortality in elderly patients with mild chronic obstructive pulmonary disease discharged from a medical ward after acute nonacidotic exacerbation. *J Am Geriatr Soc* 56: 909–913.
  21. Wildman MJ, Sanderson C, Groves J, Reeves BC, Ayres J, et al. (2009) Predicting mortality for patients with exacerbations of COPD and Asthma in the COPD and Asthma Outcome Study (CAOS). *QJM* 102: 389–399.
  22. Patil SP, Krishnan JA, Lechtzin N, Diette GB (2003) In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. *Arch Intern Med* 163: 1180–1186.
  23. Mohan A, Premanand R, Reddy LN, Rao MH, Sharma SK, et al. (2006) Clinical presentation and predictors of outcome in patients with severe acute exacerbation of chronic obstructive pulmonary disease requiring admission to intensive care unit. *BMC Pulm Med* 6: 27.
  24. Cheng Y, Borrego ME, Frost FJ, Petersen H, Raisch DW (2014) Predictors for mortality in hospitalized patients with chronic obstructive pulmonary disease. *Springerplus* 3: 359.
  25. Almagro P, Calbo E, Ochoa de Echaguen A, Barreiro B, Quintana S, et al. (2002) Mortality after hospitalization for COPD. *Chest* 121: 1441–1448.
  26. Fabbri LM, Luppi F, Beghe B, Rabe KF (2008) Complex chronic comorbidities of COPD. *Eur Respir J* 31: 204–212.
  27. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, et al. (1996) The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. *N Engl J Med* 335: 1001–1009.
  28. Hjalmarson A, Goldstein S, Fagerberg B, Wedel H, Waagstein F, et al. (2000) Effects of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure: the Metoprolol CR/XL Randomized Intervention Trial in congestive heart failure (MERIT-HF). MERIT-HF Study Group. *JAMA* 283: 1295–1302.
  29. Konstam MA, Neaton JD, Dickstein K, Drexler H, Komajda M, et al. (2009) Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial. *Lancet* 374: 1840–1848.
  30. Young RP, Hopkins R, Eaton TE (2009) Potential benefits of statins on morbidity and mortality in chronic obstructive pulmonary disease: a review of the evidence. *Postgrad Med J* 85: 414–421.
  31. Mancini GB, Etmann M, Zhang B, Levesque LE, FitzGerald JM, et al. (2006) Reduction of morbidity and mortality by statins, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers in patients with chronic obstructive pulmonary disease. *J Am Coll Cardiol* 47: 2554–2560.
  32. Criner GJ, Connett JE, Aaron SD, Albert RK, Bailey WC, et al. (2014) Simvastatin for the prevention of exacerbations in moderate-to-severe COPD. *N Engl J Med* 370: 2201–2210.
  33. Egred M, Shaw S, Mohammad B, Waitt P, Rodrigues E (2005) Under-use of beta-blockers in patients with ischaemic heart disease and concomitant chronic obstructive pulmonary disease. *QJM* 98: 493–497.
  34. Short PM, Lipworth SI, Elder DH, Schembri S, Lipworth BJ (2011) Effect of beta blockers in treatment of chronic obstructive pulmonary disease: a retrospective cohort study. *BMJ* 342: d2549.
  35. Andreas S, Anker SD, Scanlon PD, Somers VK (2005) Neurohumoral activation as a link to systemic manifestations of chronic lung disease. *Chest* 128: 3618–3624.
  36. Lipworth BJ, Williamson PA (2009) Beta blockers for asthma: a double-edged sword. *Lancet* 373: 104–105.
  37. Shrikrishna D, Astin R, Kemp PR, Hopkinson NS (2012) Renin-angiotensin system blockade: a novel therapeutic approach in chronic obstructive pulmonary disease. *Clin Sci (Lond)* 123: 487–498.
  38. Kaparianos A, Argyropoulou E (2011) Local renin-angiotensin II systems, angiotensin-converting enzyme and its homologue ACE2: their potential role in the pathogenesis of chronic obstructive pulmonary diseases, pulmonary hypertension and acute respiratory distress syndrome. *Curr Med Chem* 18: 3506–3515.
  39. Wong MH, Chapin OC, Johnson MD (2012) LPS-stimulated cytokine production in type I cells is modulated by the renin-angiotensin system. *Am J Respir Cell Mol Biol* 46: 641–650.
  40. Andreas S, Herrmann-Lingen C, Raupach T, Luthje L, Fabricius JA, et al. (2006) Angiotensin II blockers in obstructive pulmonary disease: a randomised controlled trial. *Eur Respir J* 27: 972–979.
  41. Rivera-Fernandez R, Navarrete-Navarro P, Fernandez-Mondejar E, Rodriguez-Elvira M, Guerrero-Lopez F, et al. (2006) Six-year mortality and quality of life in critically ill patients with chronic obstructive pulmonary disease. *Crit Care Med* 34: 2317–2324.
  42. Ai-Ping C, Lee KH, Lim TK (2005) In-hospital and 5-year mortality of patients treated in the ICU for acute exacerbation of COPD: a retrospective study. *Chest* 128: 518–524.
  43. Steer J, Gibson GJ, Bourke SC (2010) Predicting outcomes following hospitalization for acute exacerbations of COPD. *QJM* 103: 817–829.

44. Roche N, Zureik M, Soussan D, Neukirch F, Perrotin D (2008) Predictors of outcomes in COPD exacerbation cases presenting to the emergency department. *Eur Respir J* 32: 953–961.