

Associated factors for admission among acute exacerbation of chronic obstructive pulmonary disease patients presenting at the emergency department of a tertiary care center in Eastern Nepal: a cross-sectional study

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ABSTRACT

Introduction: The burden of COPD continues to increase over the years. COPD exacerbations require frequent hospitalizations and accelerate the decline of lung function. Hence, it is significant to understand the factors that can predict hospitalization due to acute exacerbation of COPD.

Method: A cross sectional study was conducted for a period of one year in total of 99 cases with an aim to identify factors associated with hospitalization due to acute exacerbation of COPD in patients visiting emergency department of BPKIHS, eastern Nepal. We obtained data of sociodemographic, clinical, and biochemical parameters. We analyzed their association with hospital admission with a multivariate analysis using a logistic regression model.

Result: Among 99 cases 50 were admitted and 49 were discharged. In multivariate analysis, the significant factors predictive of hospital admission in COPD exacerbations were domiciliary oxygen (OR 0.162, 95% CI 0.977-1.138), SpO₂ with O₂ (OR 0.864, 95% CI 0.146-0.864), neutrophil count (OR 1.274, 95% CI 1.045-1.554), lymphocyte count (OR 1.297, 95% CI 1.027-1.639) and serum urea level (OR 1.045, 95% CI 1.003-1.089).

Conclusion: In patients presenting to the emergency department with acute exacerbation of COPD, if the value of any one of the predicting factors (domiciliary oxygen, SpO₂ with O₂, neutrophil count, lymphocyte count and serum urea level) deteriorates by one unit, then there is 1.420 times increase in hospital admission.

Keywords: acute exacerbations, COPD, emergency department, hospital admissions, risk factors

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is now one of the top three causes of death worldwide.¹ Globally, the COPD burden is projected to increase in the coming decades because of continued exposure to COPD risk factors and aging of the population.² Some subnational studies conducted in Nepal have reported the prevalence of COPD is ranging from 23% to 43%.³ From 1990 to 2016, COPD continued to remain one of the major public health problems in Nepal. If the current situation prevails, it is expected that the burden of COPD will continue to increase over the years.⁴

COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.⁵ Spirometry is required to make the diagnosis in this clinical context; the presence of a post bronchodilator FEV1/FVC < 0.7 confirms the presence of persistent airflow limitation and thus of COPD.⁶ Although COPD is defined on the basis of airflow limitation, in practice the decision to seek medical help is usually determined by the impact of symptoms on a patient's functional status.⁵ A person may seek medical attention either because of chronic respiratory symptoms or because of an acute, transient episode of exacerbated respiratory symptoms.⁵ The course of COPD shows periods of abrupt worsening of the symptoms, known as exacerbations, which may have multiple etiologies.

Exacerbations of COPD are important events in the management of COPD because they negatively impact health status, rates of hospitalization and readmission, and disease progression.⁷

Economic analyses have shown that >70% of COPD related health care expenditures are due to emergency department visits.⁶ The best predictor of having frequent exacerbations (defined as two or more exacerbations per year) is a history of earlier events.⁸ COPD exacerbations represent the large majority of COPD treatment costs. Hospitalizations due to exacerbations of COPD account for major economic costs in addition to causing disease progression.⁹

COPD exacerbations impair the quality of life (QOL), require frequent hospitalizations, and also accelerate the decline of lung function.¹⁰ Due to its importance, there is special interest in understanding the factors associated with the development of COPD exacerbations and the

factors that can predict hospitalization. The study aims to identify factors associated with hospitalization due to acute exacerbation of COPD in patients of BP Koirala Institute of Health Sciences (BPKIHS), eastern Nepal. The identification of these factors would help us to recognize high-risk patients in whom medical intervention should be more intensive to avoid hospitalizations for such patients, with an improvement in health parameters and the consequent reduction in costs that hospitalization entails.

METHOD

Our study was conducted in the Emergency Department (ED) of BPKIHS, from 2nd June 2020 for one year. Patients presenting with COPD exacerbations at the ED were taken as participants. Exacerbations were described as episodic acute worsening of respiratory symptoms, including increased dyspnea, cough, wheezing, and/or change in the amount and character of sputum in previously diagnosed cases of COPD.⁶ The diagnosis of COPD was established based on valid medical documents confirmed either by spirometry reports or in absence of spirometry reports by documents showing physician-diagnosed cases taking prescribed medications for COPD.

Patients with lung cancer, active pulmonary tuberculosis, interstitial lung disease and mental incapacity to answer questionnaires were excluded from the study.

Taking reference from the study done by Garcia-Sanz MT et al., among the factors associated with admission in acute exacerbation of COPD, one of the major associated factor was found to be neutrophilia.¹¹ A sample size of 99 was calculated using the following formula $N = 2p' * (1-p') * (z\sim/2 + zb)^2 / d^2$

Where, $p' = p1 + p2 / 2$

P1 = neutrophil count in non-admitted cases in the study¹¹

P2 = neutrophil count in admitted cases in the study¹¹

$z\sim/2$ = value at 95% CI

zb = value at 80% power

d^2 = level of precision

A cross-sectional study was done to determine if the prevailing factors at a certain point in time might correlate with admission. All the required information was recorded in a structured Pro

forma. Study variables included sociodemographic parameters, clinical parameters and biochemical parameters. Those parameters were then classified into nominal and numerical variables for statistical analysis.

All statistical analysis was performed using a statistical software package (SPSS for Windows, version 25). Frequency, percentage, mean \pm SD, median and inter-quartile range were calculated for baseline variables. Nominal variables were compared using Pearson's chi-square test and Fischer's exact test. Numerical variables were differentiated as parametric and non-parametric. Parametric variables were compared with the outcome using the independent t-test while non-parametric variables were compared using Man-Whitney U test. Binary logistic regression was carried out to determine the factors predicting admission in patients with acute exacerbation of COPD visiting ED of BPKIHS. In bivariate analysis, those variables significant at < 0.200 were included for regression analysis, and some variables were found to be confounders (cough, short acting bronchodilator agonists [SABA], cooking medium and edema) for the analysis.

After controlling all the confounders, multivariate binary logistic regression analysis was performed. Factors predicting hospital admission were concluded using multivariate analysis. A regression equation was made for significant factors for hospital admission.

RESULT

During the study period of one year, among a total of 99 patients, 50 (50.5%) were admitted and 49 (49.5%) were discharged. A comparison of categorical variables between the admitted and non-admitted cases are shown in Table 1.

Among categorical variables between admitted and non-admitted patients the significant parameters were found to be mean age, cough, other symptoms (symptoms indirectly related to the respiratory system i.e., altered sensorium and bilateral limb swelling), use of short acting bronchodilator agonists (SABA), use of domiciliary oxygen, vaccination status (against either one or both of Influenza and Pneumococcal vaccine), previous hospital admissions, previous ED visits, cooking medium and edema.

Mean age in years in admitted group was slightly higher than in non-admitted group. The most common presenting complain was dyspnea followed by cough as seen in 97 and 64 patients,

respectively. Majority of patients with cough did not require hospitalization. Among 41 patients presenting with other symptoms more than half were admitted.

As shown in figure no. 1, the most common drug used by patients presenting with acute exacerbations of COPD was inhaled SABA followed by inhaled corticosteroids (ICS) and inhaled long-acting beta agonists (LABA). A significant relationship existed between patients taking SABA and hospitalization. Interestingly, all the patients prescribed with antibiotics were admitted. This may be due to an overlap between antibiotic prescription and concurrent chest infection.

Only 27 (27.3%) patients were under domiciliary oxygen. Among them 19 (19.2%) were hospitalized indicating that patients under domiciliary oxygen may have had a severe form of exacerbation than patients not under domiciliary oxygen, therefore, required hospitalization.

A total of eight patients gave a history of vaccination against either pneumococcal or influenza vaccine. Admission rate was found to be less in patients who were vaccinated.

Nineteen patients had a history of previous hospitalization for COPD exacerbations within the past one year. Among them 15(15.2%) patients needed admission. Whereas, among 13(13.1%) patients, who had a history of at least one visit to the emergency department within the past three months, only one got admitted. An assumption can be made that people who had recently visited the ED were more likely to be under medication for acute exacerbations of COPD which might have resulted in decreased rate of hospitalization.

The admission rate was found to be more in patients not using biomass for cooking currently. This improbable finding could be explained by the possibility that those patients must have been exposed to biomass fuel in the past.

Our study showed that on general examination, the most common finding was edema. 23 out of 28 patients presenting with edema required admission. We can presume that patients presenting to the ED with acute exacerbations along with edema could have also developed cor pulmonale that resulted in the need of hospitalization.

Likewise, the significant parameters between admitted and non-admitted patients among

numerical variables were found to be mean respiratory rate, partial pressure of arterial oxygen (PaO₂), serum lactate level, neutrophil count, monocyte count, serum urea and serum sodium as shown in Table 2.

In multivariate analysis, the significant factors predictive of hospital admission in COPD exacerbations were domiciliary oxygen (OR 0.162,

95% CI 0.977-1.138), SpO₂ with O₂ (OR 0.864, 95% CI 0.146-0.864), neutrophil count (OR 1.274, 95% CI 1.045-1.554), lymphocyte count (OR 1.297, 95% CI 1.027-1.639) and serum urea level (OR 1.045, 95% CI 1.003-1.089). If the value of these predicting factors deteriorates by one unit, then there is 1.420 times increase in admission as depicted in Table 3.

Table 1. Comparison of categorical variables among admitted and non – admitted cases^a

Characteristics	Categories	Admission status		p-value
		No	Yes	
Female		32 (54.2)	27 (45.8)	0.252
Male		17 (42.5)	23 (57.5)	
Mean age in years ± SD		72.10 ± 9.12	75.72 ± 8.63	0.045
Findings on history taking :				
Shortness of breath	Absent	0 (0.0)	2(100.0)	0.495
	Present	49 (50.5)	48(49.5)	
Cough	Absent	12 (34.3)	23(65.7)	0.025
	Present	37 (57.8)	27(42.2)	
Expectoration	Absent	28 (44.4)	35 (55.6)	0.184
	Present	21 (58.3)	15 (41.7)	
Hemoptysis	Absent	49 (50.5)	48 (49.5)	0.495
	Present	0 (0.0)	2(100%)	
Wheezing	Absent	46 (49.5)	47 (50.5)	1.000
	Present	3 (50.0)	3 (50.0)	
Chest pain	Absent	39 (48.1)	42 (51.9)	0.570
	Present	10 (55.6)	8 (44.4)	
Fever	Absent	39 (47.0)	44 (53.0)	0.256
	Present	10 (62.5)	6 (37.5)	
Anorexia	Absent	45 (49.5)	46 (50.5)	1.000
	Present	4 (50.0)	4 (50.0)	
Other symptoms	Absent	34 (58.6)	24 (41.4)	0.031
	Present	15 (36.6)	26 (63.4)	
Domiciliary oxygen	Yes	8 (29.6)	19 (70.4)	0.015
	No	41 (56.9)	31 (43.1)	
Vaccination	Yes	7 (87.5)	1 (12.5)	0.031
	No	42 (46.2)	49 (53.8)	
Previous hospital admission	Yes	4 (21.1)	15 (78.9)	0.006
	No	45 (56.3)	35 (43.8)	
Previous ED visits	Yes	12 (92.3)	1(7.7)	0.001
	No	37 (43.0)	49 (57.0)	
Smoking history	Yes	40 (47.1)	45 (52.9)	0.232
	No	9 (64.3)	5 (35.7)	
Cooking medium	Biomass fuel	35 (66.0)	18 (34.0)	<0.001
	LPG	14 (30.4)	32 (69.6)	
Findings on clinical examination :				
Altered sensorium	Absent	47 (48.5)	50 (51.5)	0.242
	Present	2 (100.0)	0 (0.0)	
Pallor	Absent	44 (50.0)	44 (50.0)	0.776
	Present	5 (45.5)	6 (54.5)	
Dehydration	Absent	46 (48.9)	48 (51.1)	0.678
	Present	3 (60.0)	2 (40.0)	
Oedema	Absent	44 (62.0)	27 (38.0)	<0.001
	Present	5 (17.9)	23(82.1)	

^acomparison done using Pearson's chi-square test and Fischer's exact test. **Bold** represents statistically significance (p-value < 0.05). SD: standard deviation, ED: emergency department, LPG: Liquid Petroleum Gas

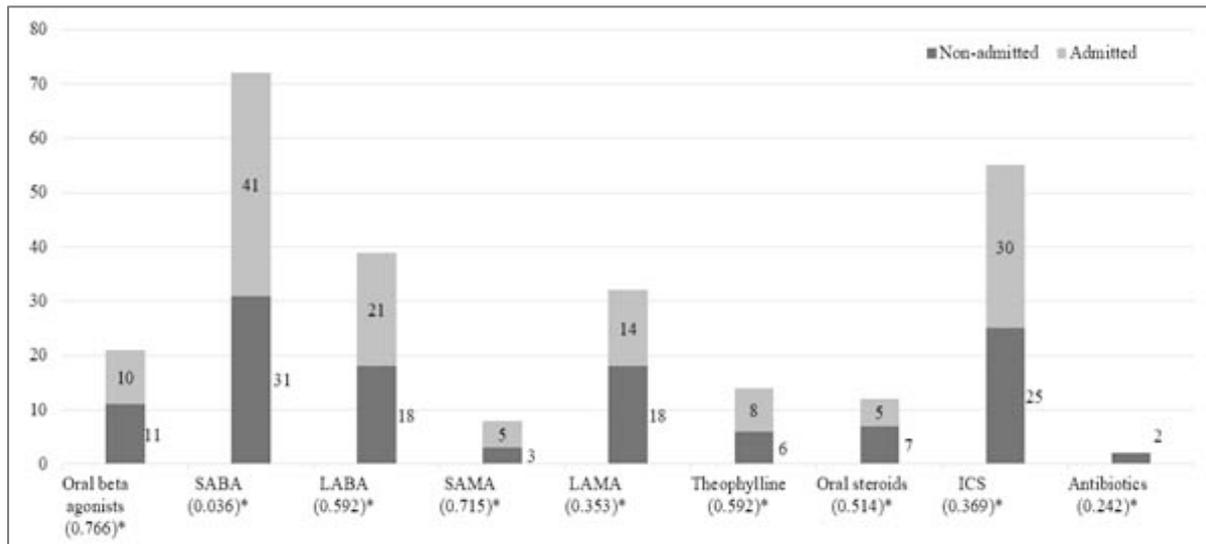


Figure 1. Comparison of drug history in admitted and non-admitted cases. *p: value; SABA: Short acting beta agonists; LABA: Long-acting bronchodilator agonists; SAMA: Short acting muscarinic agonists; LAMA: Long acting muscarinic agonists; ICS: Inhaled corticosteroids

Table 2. Comparison of numerical variables among admitted and non-admitted cases.^a

Variables	Admitted	Non-admitted	p-
Vitals [Mean value(±SD)]			
Pulse in beats per min	97.52 (14.27)	102.45 (18.71)	0.143
SBP in mm Hg	118.00 (20.21)	121.84 (23.07)	0.381
DBP in mm Hg	73.20 (15.31)	75.92 (13.37)	0.350
RR in breaths per min	28.00 (5.40)	24.73 (4.74)	0.002
Temperature in deg. Fah.	98.08 (0.63)	97.98 (0.32)	0.305
SaPO ₂ (at room air) mm Hg	75.44 (15.89)	78.96 (15.51)	0.267
SaPO ₂ (with oxygen) mm Hg	90.60 (6.44)	92.80 (5.77)	0.077
ABG parameters [Mean value(±SD)]			
pH	7.34 (0.14)	7.36 (0.096)	0.307
PaO ₂	63.43 (21.67)	75.56 (20.04)	0.005
PaCO ₂	56.81 (17.43)	53.71 (18.99)	0.400
HCO ₃	25.81 (7.22)	26.71 (8.82)	0.585
Lactate	2.05 (1.28)	1.34 (0.63)	0.001
Lab parameters [Mean value(±SD)]/[Median value(IQR)]			
Hemoglobin in gm/dl	12.27 (3.18)	13.097 (2.71)	0.167
TLC in cells/mm	9466.00(4939.62)	9442.86(3559.26)	0.979
Neutrophils in %	80.16 (10.26)	74.10 (11.05)	0.006
Lymphocytes in %	14 (7.5 - 20) ^b	15 (10 - 21) ^b	0.160
Monocytes in %	4 (2 - 8) ^b	8 (5 - 9) ^b	<0.001
Eosinophils in %	0 (0 - 2) ^b	0 (0 - 2) ^b	0.364
Platelets in cells/mm	131000 (99,550.25 - 2,14,000) ^c	160000 (101000 - 256000) ^c	0.445
Blood glucose in gm/dl	130.24 (48.45)	120.69 (46.42)	0.319
Urea in mg/dl	47 (25 - 69) ^c	32 (23 - 49) ^c	0.021
Creatinine in mg/dl	1.09 (0.57)	0.93 (0.38)	0.113
Serum Na ⁺ in mmol/L	136.34 (6.65)	138.57 (4.66)	0.057
Serum K ⁺ in mmol/L	4.31 (0.96)	4.12 (0.74)	0.261
Serum albumin in gm/dl	3.61 (0.45)	3.67 (0.696)	0.591

^a comparison done using Independent t-test and Man-Whitney U test; ^bexpressed in median value (IQR) **Bold** represents statistical significance (p-value < 0.05); SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RR: Respiratory rate; SaPO₂: Saturation of peripheral oxygen; ABG: Arterial blood gases; pH: Potential of hydrogen; PaO₂: Partial pressure of oxygen; PaCO₂: Partial pressure of carbon dioxide; IQR: Inter quartile range; TLC: Total leukocyte count

Table 3. Predictors of hospital admission according to multivariate analysis

Variables in the Equation	β coefficient	p values	Odd ratio	95% C.I. for OR	
				Lower	Upper
Age	0.053	0.175	1.054	0.977	1.138
Expectoration	-0.334	0.648	0.716	0.171	3.006
Domiciliary oxygen	-1.82	0.047	0.162	0.027	0.976
Previous hospital admission	0.424	0.68	1.528	0.203	11.5
PR	-0.049	0.075	0.952	0.902	1.005
RR	0.048	0.518	1.049	0.907	1.213
SaPO ₂ (with oxygen)	-0.146	0.046	0.864	0.749	0.997
PaO ₂	-0.024	0.179	0.976	0.942	1.011
Lactate	0.435	0.257	1.545	0.728	3.277
Hemoglobin	0.041	0.741	1.042	0.817	1.329
Neutrophils	0.242	0.017	1.274	1.045	1.554
Lymphocytes	0.26	0.029	1.297	1.027	1.639
Urea	0.044	0.036	1.045	1.003	1.089
Creatinine	-0.615	0.487	0.54	0.095	3.068
Sodium	-0.024	0.683	0.976	0.871	1.095
Constant	-5.203	0.683	0.005		

Bold represents statistical significance (p-value < 0.05); PR: Pulse rate; RR: Respiratory rate; SaPO₂: Saturation of peripheral oxygen; PaO₂: Partial pressure of oxygen

DISCUSSION

This study was carried out to determine the factors associated with hospital admission among adults who presented with AECOPD in the ED.

Neutrophil counts is an inflammatory marker which could also be used as a parameter to assess the severity of COPD exacerbations. A study showed that neutrophilic COPD cases had a fourfold increased risk of admission.¹² It reported significant relationship between neutrophilia (adjusted OR 3.8, 95% CI 1.8-8.0) in peripheral blood, exacerbation severity and hospital admission frequency in COPD exacerbations. Similar to our study which showed that neutrophilia (OR 1.274, 95% CI 1.045-1.554) was one of the predictive factors for hospitalization, a study done by Garcia – Sanz et al also found neutrophilia (OR 3.15, 95% CI 1.570-6.335) to be a significant predictor of hospital admission.¹¹

In this study we measured SpO₂ at room air and SpO₂ with oxygen aid. Results demonstrated that admitted patients had lower SpO₂ even with oxygen aid. Our study revealed lower SpO₂ with oxygen to be one of the significant predicting factors of hospitalization which is comparable to another study done by Alcazar B et. al which also showed that poorer SpO₂ were significantly associated with hospitalization.¹³

A raised serum urea considered an indirect marker of nonspecific systemic illness was seen as a significant predictor of admission in our study. Our finding is supported by a study which concludes

increased serum urea (>7.35mmol/l) as a risk factor for prediction of in patient mortality in admitted cases of AECOPD.¹⁴

In our study, though previous hospital admissions and PaO₂ showed statistical significance in admitted patients, it couldn't establish any significance as a predicting factor for admission in AECOPD. Contrarily, a study done by S. Vidal et. al shows PaO₂ (OR 2.7, 95% CI 2.12–3.44) and previous hospital admission due to COPD exacerbations (OR 2.03, 95% CI 1.32-3.11) as significant factors predictive of hospital admission.¹⁵

A study done in India also found previous hospital admission (OR 1.963, 95% CI 1.037-3.814) as a significant predictor of hospital admission along with increasing sputum purulence and existing comorbidities.⁹

We believe this is the first study from Nepal to gather information about predictors of hospitalization due to AECOPD.

However, our study has some limitations. Spirometry is required to confirm the diagnosis in COPD but we could not exclude patients without spirometry report due to unavailability of spirometry at ED. This study was conducted in a single center. It is a small observational cross sectional study which allows us to suggest associations but does not enable us to identify causal relationships. The sample size and duration of the study were relatively smaller. The possibility of observers' bias and the inaccuracy of the clinical history cannot be ruled out completely.

These outcomes, therefore, need to be confirmed by multicentric studies with a large sample size.

CONCLUSION

Out of 99 cases visiting the ED with AECOPD, 50 (50.5%) cases required admission. Need of domiciliary oxygen, lower SpO₂, presence of neutrophilia, lymphocytosis on differential count and higher serum urea levels were found to be associated with a greater likelihood of hospitalization among patients presenting with AECOPD at the emergency department. If the value of any one of the above mentioned predicting factors deteriorates by one unit, then there is 1.420 times increase in hospital admission.

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Consent

The study was approved by the IRC, BPKIHS and all the patients were enrolled in the study only after they signed the informed consent.

Conflict of Interest

None

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