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Clinico-epidemiological Profile of Pneumonia in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a common cause of morbidity and mortality in the adult population, with a high burden in Nepal. Pneumonia is a common cause of COPD exacerbations. The study aimed to determine the clinico-epidemiologic characteristics of pneumonia in COPD patients.

Methods: This hospital-based, cross-sectional study was conducted at Birat Medical College Teaching Hospital, using a structured proforma that recorded patient sociodemography, clinical history, examination, and laboratory data. The pneumonia severity was documented using the Pneumonia Severity Index (PSI) score and CURB-65 score.

Results: Out of a total of 152 COPD patients with pneumonia, there were 84 (55.26%) patients with atypical pneumonia and 68 (44.74%) with typical pneumonia, 107(70.39%) had a smoking history, dyspnea was present in 75 (58.59%) atypical pneumonia patients and 53 (41.41%) typical pneumonia patients. Respiratory failure was present in 130 (85.53%), and 30 (19.74%) patients had altered sensorium. Patients admitted to ICU were 106 (69.74%), with 57 (53.77%) classed PSI IV and 31 (29.25%) as PSI Class V. CURB-65 score of ≥3 had sensitivity of 23.9%, specificity of 94.4%, positive predictive value of 97% and a negative predictive value of 14.3% in predicting need for ICU admission.

Conclusions: COPD patients with pneumonia commonly present with atypical pneumonia, have chronic co-morbidities, and have high PSI classification on admission. The PSI is preferred over CURB-65 score in predicting ICU admission.

Keywords: *Pneumonia; Pulmonary Disease, Chronic Obstructive; Respiratory Insufficiency.*

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INTRODUCTION

Chronic Obstructive Pulmonary Disease is a major contributor to morbidity and mortality in general population. WHO estimates more than 6% death annually is attributed to chronic obstructive pulmonary disease (COPD).[1] In Nepal, the prevalence of COPD is 22.7%.[2] The highest national age-standardized death and disability-adjusted life years (DALY) rate of COPD in 2019 was observed in Nepal (3,318).[3]

Pneumonia is a common cause of out-patient visits and hospital admissions in patients with COPD, and is a common infection implicated in COPD exacerbations.[4] Age more than 65 years and presence of co-morbidities are risk factors for pneumonia. Presence of COPD may impact the natural history of pneumonia. Management of COPD involves use of inhaled and systemic corticosteroids, which may contribute to the pathogenesis of pneumonia.[5-9]

The clinicoepidemiologic characteristics of pneumonia in COPD patients in Nepal is unknown. COPD has not been shown as a risk factor for mortality in pneumonia patients.[10] Hence, this study aimed to determine the clinicoepidemiological characteristics of pneumonia in patients with COPD.

METHODS

The study was hospital-based, cross-sectional and analytical, conducted from November 1, 2022 to April 31, 2023, in the Department of Internal Medicine, Birat Medical College Teaching Hospital, Biratnagar, Nepal. COPD patients admitted in the Department of Internal Medicine with diagnosis of pneumonia, and giving informed written consent were included in the study.

As the prevalence of pneumonia in COPD patients is underreported, the sample size was estimated at 138 COPD patients, and, keeping margin of error at 7%, with prevalence of COPD in adult population in Nepal at 22.7%, and considering 10% as non-respondents, a sample size of 152 was calculated.

Typical pneumonia refers to an acute illness acquired outside the hospital or healthcare facility, comprising of fever, new-onset cough with or without expectoration, breathlessness, or pleuritic chest pain, with presence of infiltrates in chest x-ray.[11] Atypical Pneumonia refers to an acute illness caused by atypical organisms, that are not detectable in gram stain and are not cultured by standard techniques, with symptom complex of cough, fever, malaise, alteration in sensorium or gastrointestinal symptoms such as diarrhea, with chest x-ray findings other than typical pneumonic consolidations, such as absent or minimal imaging findings on initial chest x-ray, or an unusual distribution of the pulmonary opacities in a patient presenting with respiratory and systemic symptoms.[12]

Chronic Obstructive Pulmonary Disease (COPD) is defined as presence of chronic cough, dyspnea, wheezing or chest heaviness in subjects more than 40 years, with spirometry findings of post bronchodilator FEV1/FVC ratio <70% or below the lower 95% limit of normal (LLN) value, or known clinical diagnosis of chronic obstructive pulmonary disease.

Bronchial Asthma is defined as presence of cough, dyspnea, wheezing and/or chest tightness, with spirometry findings suggestive of post bronchodilator (400 micrograms of salbutamol inhalation) reversibility of 12% or more in FEV1, or known clinical diagnosis of Bronchial Asthma.

The mMRC (modified Medical Research Council) scale is a tool to measure patient's

disability due to breathlessness on daily activities using a self-rated scale of 0 to 4. Scale 0 refers to no breathlessness except on strenuous exercise; scale 1 refers to presence of breathlessness when hurrying on the level or walking up a slight hill; scale 2 refers to presence of breathlessness causes the patient to walk slower than people of same age on the level, or if the patient has to stop to catch breath when walking at their own pace on the level; scale 3 refers to the state when patient stops for breath after walking approximately 100 meters or after few minutes on the level; and scale 4 refers to the state when patient is too breathless to leave the house, or breathless when dressing or undressing.[13]

The pneumonia severity index (PSI) is a prediction tool for prognosis of pneumonia. It utilizes 3 demographic characteristics (age, gender, nursing home residence), 5 coexisting illnesses (active neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, renal disease), 5 physical examination findings (acutely altered mental state, respiratory rate >30 cycles/minute, systolic blood pressure <90mmHg, temperature <35 or ≥40◦C, pulse ≥125 beats/minute), (6 laboratory measurements (blood urea nitrogen, glucose, hematocrit, and sodium levels; partial pressure of arterial oxygen; and arterial pH), and 1 radiographic finding (pleural effusion). The score is classed as I-II when score ≤70; class III when score 71 – 90; class IV when score 91 – 130, and class V when score >130.[14]

CURB-65 score is a tool to assess severity of pneumonia, comprising of confusion, urea >7mmol/L, respiratory rate ≥30 cycles/minute, systolic blood pressure <90mmHg or diastolic blood pressure <60mmHg, and age ≥65 years, stratifying pneumonia patients according to increasing risk of mortality as score 0, 0.7%; score 1, 3.2%; score 2, 3%; score 3, 17%; score 4, 41.5% and score 5, 57%.[15]

A current smoker is a patient who has been smoking more than 10 cigarettes per day for at least 10 years prior to enrollment in study. A reformed smoker is a patient who has smoked at least 100 cigarettes in a lifetime and has quit smoking for at least 1 year prior to enrollment.

A structured proforma was used to record patient information, sociodemographic data, clinical history and physical examination, chest x-ray, CT chest and laboratory data such as complete blood count, blood sugar, renal function test, ESR, CRP titer. The severity of pneumonia was documented using Pneumonia Severity Index (PSI) scoring system, and CURB-65 score.

Data were entered in Microsoft Excel 2007 and statistically analyzed by SPPS software version 25. Descriptive statistical data were presented as mean, standard deviation and percentages, and presented in tabular format.

RESULTS

There were 152 COPD patients admitted for pneumonia, 81 (53.29%) were female, 71 (46.71%) male. The mean age was 71.68 years (±10.13). There were 50 (32.9%) current smokers and 57 (37.5%) reformed smokers, with mean pack years of 16.05 (±10.67) and mean smoking index 291.56 (±187.83). There were 45 (29.61%) non-smokers and 29 (19.1%) alcohol consumers.

There were 84 (55.26%) with atypical pneumonia and 68 (44.74%) patients with typical pneumonia. Table 1 depicts the symptom complex of pneumonia in COPD patients.

There were 30 (19.74%) patients with altered sensorium; 12 (7.89%) had lethargy, 6 (50%) each in typical and atypical pneumonia; stupor in 6 (60%) with atypical and 4 (40%) with typical pneumonia; obtundation in 6 (100%) and coma in 2 (100%) patients with atypical pneumonia. Hyponatremia was present in 58 (38.16%) patients, of which 45 (77.57%) were cases of atypical pneumonia. The mean BMI

was 23.47 kg/m2 (±5.19) and mean SpO2 was 84.8% (±7).

The sputum culture showed growth in 41 patients, namely *Acinetobacter baumanii* in 10 patients (6.58%), *Klebsiella pneumoniae* in 7 (4.6%), *Streptococcus pneumoniae* in 13 (8.55%), *Staphylococcus aureus* in 3 (1.97%), *Pseudomonas aeruginosa* in 2 (1.32%), *Escherichia coli* in 2 (1.32%) and yeast in 4 (2.63%).

Of the 64 (42.1%) patients with complications, 31 (48.44%) had sepsis, 11 (35.48%) septic shock and 22 (34.38%) acute kidney injury. In atypical pneumonia patients 35 (54.69%) had complications, of which 15 (48.39%) had sepsis, 6 (54.54%) septic shock and 14 (63.63%) acute kidney injury. In typical pneumonia patients, 29 (45.31%) had complications, of which, 16 (51.61%) had sepsis, 5 (45.45%) septic shock and 8 (36.36%) acute kidney injury.

Respiratory failure developed in 130 (85.53%) patients; 92 (60.53%) had Type 1 respiratory failure, of which 46 (67.65%) occurred in typical, and another 46 (54.76%) in atypical pneumonia; 38 (25%) had Type 2 respiratory failure, of which 28 (33.33%) occurred in atypical, and 10 (14.71%) in typical pneumonia. Mechanical ventilator support was required in 12 (7.89%) patients, 8 (9.52%) of which had atypical, and 4 (5.88%) had typical pneumonia.

Of 31 diabetes mellitus patients, 22 (70.97%) had typical pneumonia; of 66 hypertension patients, 36 (54.54%) had atypical pneumonia; of 15 ischemic heart disease patients, 10 (66.67%) had atypical pneumonia; of 11 stroke patients, 8 (72.72%) had atypical pneumonia; of 9 asthma patients, 7 (77.78%) had atypical; of 7 bronchiectasis patients, 6 (85.71%) had atypical pneumonia. There were 106 patients admitted to ICU and 46 to ward, with a pattern of admission based on the pneumonia severity index depicted in Table 2, and Table 3 depicts the pattern of admission based on CURB-65.

Table 1. Clinical symptoms in COPD patients with pneumonia (n = 152)

Symptoms	**N (%)**	**Pneumonia (N, %)**	
		Typical	**Atypical**
Cough	126 (82.9)		
Productive cough	84 (66.67)	52 (61.9)	32 (38.09)
Non-productive cough	42 (33.33)	13 (30.95)	29 (69.05)
Median duration (IQR))	6 (6)		
Fever	61 (40.13)	32 (52.46)	29 (47.54)
Median duration (IQR)	4 (3)		
Dyspnea	128 (84.21)	53 (41.41)	75 (58.59)
mMRC Grade 0	2 (1.56)	0	2 (100)
mMRC Grade 1	15 (11.72)	6 (40)	9 (60)
mMRC Grade 2	50 (39.06)	17 (34)	33 (66)
mMRC Grade 3	51 (39.84)	26 (50.1)	25 (49.02)
mMRC Grade 4	10 (7.81)	4 (40)	6 (60)
Median duration (IQR)	4 (2)		
Chest Pain	33 (21.71)	22 (66.67)	11 (33.33)
Median duration (IQR)	3 (5.5)		
Hemoptysis	6 (3.95)	4 (66.67)	2 (33.33)
Loose Bowel Motion	20 (13.16)	2 (10)	18 (90)

mMRC: modified Medical Research Council

Table 2. The pattern of admission based on the Pneumonia Severity Index (PSI) in COPD patients with pneumonia

PSI	ICU	Ward
Class I-II	1	17
Class III	17	24
Class IV	57	5
Class V	31	0

PSI: Pneumonia Severity Index
ICU: Intensive Care Unit

Table 3. Pattern of admission based on CURB-65 Score in COPD patients with pneumonia

CURB-65	ICU	Ward
0	1	12
1	31	28
2	41	6
3	26	0
4	7	0
5	0	0

CURB-65: confusion, uremia, respiratory rate, BP, age ≥ 65 years

In using CURB-65 score as predictive tool to decide on admission to ICU, the study observed that a score of ≥3 had sensitivity of 23.9%, specificity of 94.4%, positive predictive value of 97% and a negative predictive value of 14.3%.

DISCUSSION

In the study of 152 COPD patients with pneumonia, the mean age was 71.68 years (±10.13). In a study by Janson et al, COPD patients with pneumonia had mean age 65.9 years (±10.1).[16] In the same study, pneumonia was common in males, irrespective of the severity of COPD. The present study observed pneumonia predominantly in females, 81 (53.29%) as compared to males, 71 (46.71%). There were 68 (44.74%) patients with typical pneumonia and 84 (55.26%) patients with atypical pneumonia. In a study of 4121 pneumonia patients, 983 (23.9%) pneumonia were occurred in patients with COPD. Many were active and reformed smokers, 80.6%, as compared to pneumonia patients without COPD, 50.5%, frequent alcohol consumers, and had co-morbid conditions such as chronic cardiovascular diseases.[17] These patients presented with typical pneumonia features such as productive cough, dyspnea, and respiratory failure, and less frequently with atypical pneumonia. In the present study, 70.39% had a smoking history, and dyspnea was present in 75 (58.59%) atypical pneumonia patients and 53 (41.41%) typical pneumonia patients. Loose bowel motion was present in 18 (90%) atypical pneumonia patients, while only 2 patients (10%) with typical pneumonia had loose bowel motion. In a study by Gomez-Junyet et al., 78% pneumonia patients with COPD had dyspnea as compared to non-COPD pneumonia (57.4%), and productive cough was observed in 74.8% of pneumonia patients with COPD as compared to 58% in non-COPD pneumonia; loose bowel motion was observed in 8.7% pneumonia patients with COPD as compared to 16.6% in non-COPD pneumonia; more pneumonia patients with COPD developed respiratory failure (76.2%) as compared to non-COPD pneumonia (66.1%).[17] In the present study, a total of 130 (85.53%) pneumonia patients with COPD developed respiratory failure.

COPD patients with pneumonia have more hospital admissions, higher duration of hospitalization, more severe form of pneumonia and poorer outcomes.[10] In present study, 106 (69.74%) were admitted to

ICU, 57 (53.77%) were classed PSI IV and 31 (29.25%) PSI Class V. In a study of pneumonia in COPD, 73.5% patients were classified as high-risk PSI (class IV and V) as compared to 54.1% pneumonia patients without COPD.[17]

Jansen et al., noted COPD patients with concurrent Asthma had higher risk of pneumonia as compared to those without asthma. In this study, of the 9 patients with asthma, 7 (77.78%) had atypical pneumonia and 2 (22.22%) typical pneumonia. The phenomena of increased risk of pneumonia in COPD and asthma patients are probably due to use of inhaled corticosteroids. In a Taiwan study of COPD with asthma cohort there was increased risk of pneumonia irrespective of use of inhaled corticosteroids.[18]

Lin et al., observed increased risk of pneumonia in patients with COPD and co-morbid cardiovascular disease.[19] Other co-morbid conditions in patients with COPD with increased risk of pneumonia were cerebrovascular accident, diabetes mellitus, smoking history and obesity.[20] In present study, pneumonia was present in 66 (43.42%) hypertension patients, 31 (20.4%) diabetes mellitus, 15 (9.87%) ischemic heart disease, 11 (7.24%) cerebrovascular accident, 9 (5.92%) asthma, 7 (4.61%) bronchiectasis, 4 each (2.63%) hypothyroidism and chronic kidney disease and 1 (0.66%) chronic liver disease patients. The mean BMI was 23.47 kg/m2 (±5.19), and 55 (36.18%) patients had BMI >25kg/m^2.

Typical organisms identified by culture were *Streptococcus pneumoniae* in 13 patients (8.55%) and *Staphylococcus aureus* in 3 patients (1.97%). Only 41 patients (26.97%) demonstrated growth. Various studies have observed that etiological organisms in pneumonia patients were not identified in 60% of cases.[21,22] *Pseudomonas aeruginosa* was isolated in sputum culture of 2 (1.32%) patients. In the study by Gomez-Junyet J et al., *Pseudomonas aeruginosa* was observed in 3.1% COPD patients with pneumonia, and in 0.6% in non-COPD cases.[17] This study observed less complications in COPD patients with pneumonia such as sepsis (9.1%) as compared to patients without COPD (13.3%). In the present study, sepsis was present in 31 patients (48.44%). While mechanical ventilator support in pneumonia patients with COPD was required in 4.5% in study by Gomez-Junyet et al., as compared to 5.9% non-COPD pneumonia patients, the present study observed need for mechanical ventilator in 12 (7.89%). [17]

As score point for presence of COPD in patient with pneumonia is not given in PSI, it may not accurately predict mortality or need for ICU care in such patients. In a study by Niederman MS, pneumonia patients with COPD had a higher mean PSI score (105 ± 32 vs 87 ± 34), and majority were admitted to the ICU (25% vs 18%) in comparison to those without COPD.[23] In present study, of the 106 COPD patients with pneumonia admitted to the ICU, 105 patients (99%) were classed as PSI III and above. In the present study, in predicting the need for intensive care unit admission, the CURB-65 score of COPD patients with pneumonia had sensitivity of 23.9%, specificity of 94.4%, positive predictive value of 97% and a negative predictive value of 14.3%. A study by Capelastegui et al., observed that the CURB-65 score was not able to predict need for ICU care, while other studies have observed that the CURB-65 was a better predictor for need for ICU admission as compared to PSI score.[24]

Limitations of the study were that pneumonia in patients without COPD was not evaluated, and as the study did not document outcomes of pneumonia, the interpretation of role of PSI and CURB-65 scores were limited.

CONCLUSION

COPD patients with pneumonia were mostly female and smokers, commonly presented with atypical pneumonia, which was predominantly in patients with chronic co-morbid conditions. Dyspnea, loose bowel motion, respiratory failure and altered sensorium were common clinical features of pneumonia patients with COPD. The PSI is preferred over CURB-65 score in deciding ICU admission.

CONFLICT OF INTEREST

None

SOURCES OF FUNDING

None

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