Incidence, risk factors and outcomes of Acute Kidney Injury in Chronic Obstructive Pulmonary Disease patients with Acute exacerbation.

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ABSTRACT

Background: There is little data on the incidence, risk factors and outcomes of the AKI among COPD patients who are admitted to critical care units with exacerbation of symptoms. This observational study was conducted to evaluate the incidence and outcome of AKI with AECOPD.

Method: We performed an observational study of patients who were admitted in the intensive care unit from August 2021 to February 2023 for acute exacerbation of COPD.

Results: During the study period, a total of 108 patients were admitted to the ICU with acute respiratory failure attributed to COPD exacerbation. AKI occurred in 49 patients (45.4%). Independent risk factors for AKI in patients with AECOPD were advanced age, coronary artery disease, anemia, acute respiratory failure, and mechanical ventilation. Patients with AKI had worse prognostic implications and were more likely to require mechanical ventilation (42.8% vs 22.03%, P<0.05), had a longer ICU stay (6 ±1.3 days vs 5.41±1.1 days, P<0.05) and longer hospitalization (7.65±1.42 days vs 6.9±1.2 days, P<0.05); and higher in-hospital mortality (28.5 % vs 11.8 %, P<0.05) than those without AKI. Compared to patients without AKI who had in-hospital mortality rate of 11.8%, those with stage 2, or 3 AKI had rates of 41.6% and 85.7% respectively, that is 2.1-fold and 6.0-fold increased risk of in-hospital death, respectively.

Conclusion: Incidence of AKI is relatively high in patient with AECOPD requiring intensive care. Patient with AKI had poor outcomes compared to non-AKI patient with AECOPD. AKI can be a prognostic factor for determining patient survival.

Keywords: acute kidney injury; acute exacerbation of chronic obstructive pulmonary disease; incidence; risk factor.

INTRODUCTION

COPD is one of the leading causes of morbidity and mortality in Nepal with a prevalence of 12% in adults.[1] The global prevalence of COPD among people aged 30–79 years is 10·3%.[2] Exacerbation of COPD has a profound effect on patients, resulting in overall poor health and high mortality.[3,4] One of the severe complications of Acute Exacerbation of COPD(AECOPD) is Acute Kidney Injury (AKI) and it is reported that AKI is an independent risk factor for in-hospital mortality in patients with AECOPD.[5]

Previous study conducted by Barakat et al has shown that the incidence of AKI in patients with COPD was 128/100,000 person-years, and the prevalence of concomitant AKI at exacerbation was 9%. In addition, the mortality rate in AECOPD patients with AKI was 52/1000 person-years.[6]

However, the incidence, risk factors, and prognostic implications of AKI in the patients admitted in intensive care unit with AECOPD remain unknown. In this observational study, we determined the incidence of AKI in patients with AECOPD, evaluated the requirement for mechanical ventilation, length of mechanical ventilation and Intensive Care Unit (ICU) stay, duration of hospital stay and in hospital mortality in the AECOPD patient with AKI. We hypothesized that AKI leads to adverse outcomes and increase in-hospital mortality.

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METHODS

This study was conducted in tertiary hospital from August 2021 to February 2023. Study participants were enrolled to the study after obtaining informed written consent from the patient and accompanying family members The diagnostic criteria for AECOPD was based on Global Initiative for Chronic Obstructive Lung Disease 2023 Report : (i) history of COPD (forced expiratory volume in one second [FEV1]/forced vital capacity [FVC] <0.70 in the clinically stable state) and (ii) an acute worsening of respiratory symptoms such as dyspnea, cough, or purulent sputum, warranting hospital admission.[7] The inclusion criterion was patients with exacerbation of COPD requiring ICU hospitalization. The exclusion criteria were: patients without full medical records, patients with urinary tract infection, patients with a history of chronic kidney disease (CKD) stage 5, and patients undergoing dialysis prior to hospital admission.(Figure 1)

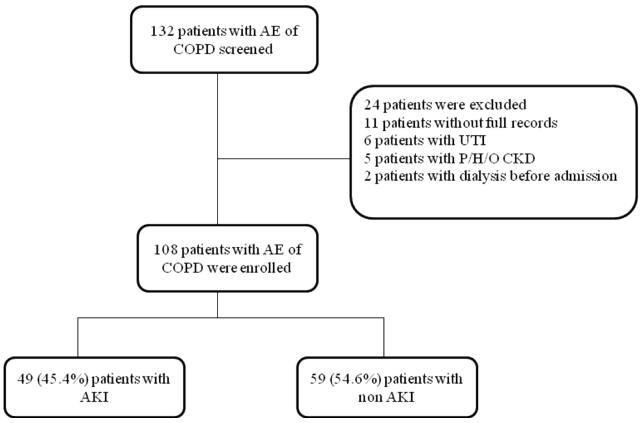

Figure 1 Flowchart of patient selection.

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; AKI, acute kidney injury, UTI, urinary tract disease, CKD, Chronic kidney disease

According to the 2012 Kidney Disease Improving Global Outcomes (KDIGO) criteria, AKI was defined as per the change in SCr level, which defined AKI as an increase in SCr by ≥0.3 mg/dl within 48 hours or increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days. We staged AKI using the difference between baseline and peak serum creatinine levels according to the KIDGO criteria.[8] Cor pulmonale can be defined as pulmonary arterial hypertension resulting from diseases affecting the structure and/or function of the lungs. Pulmonary hypertension results in right ventricular enlargement and may lead with time to right heart failure.[7]

All the required demographics and in hospital information were recorded in the Performa. Data were entered in Microsoft excel and statistically analyzed by using statistical package for the social sciences (SPSS) software version 20.0 (SPSS Ltd, Chicago, IL, USA). Categorical data were presented as percentage and frequency while continuous data were presented as mean and standard deviation. Chi Square test and Independent T test were used for statistical analysis. A two sided P value <0.05 was considered statistically significant.

RESULTS

Out of 132 patients admitted in ICU with AECOPD, 24 (18%) were excluded. 108 patients of AECOPD were enrolled in the final analysis with the mean age of 69.0 ± 5.5 years among which most of the study population consisted of males (63.9%). AKI was observed in 49 patients (45.4%), including 27.8 % stage 1 AKI, 11.1 % stage 2 AKI, and 6.5 % stage 3 AKI.

The demographic data, comorbidities and complications of the study sample are shown in Table 1. Compared with non-AKI group, there was no significant difference in gender for AKI group with male: female ratio of 2:1, but patients with AKI was of an advanced age (74 years vs 66 years; P < 0.05). Patients with AKI were more commonly complicated with acute respiratory failure (ARF) (51 % vs 32.2%; P < 0.05). Hypercapnic encephalopathy was present in 8.2% in patient with AKI compared to 3.4% in non-AKI. Patients with AKI had higher incidence of Coronary Artery Disease (36.7% vs 18.6%) and Anemia (55.1% vs 30.5%) compared with patient with non-AKI. While comparison of the other incidence of comorbidities in patients with AKI and non-AKI, there was no clinical significant difference however patients with AKI had a higher proportion of Cor pulmonale (51.0 % vs 32.2 %; P = 0.048), renal replacement therapy (4.1% vs 0%, P= 0.117), atrial fibrillation (22.4 % vs 10.2 %; P = 0.081), hypertension (67.3 %vs 50.8%; P = 0.083), diabetes mellitus (24.5% vs 16.9%; P = 0.33), CLD (4.1% vs 3.4%; P = 0.85), cerebrovascular disease (16.3% vs 11.9%; P = 0.504), and cancer (4.1% vs 1.7%; P = 0.452).

Table 1 Demographics of Patients with or Without AKI

Variables	AKI (n= 49)	Non AKI (n=59)	P - value
Age(years)	74.1±4.0	66.3±3.8	<0.05
Male (%)	46.3	53.6	0.78
Female (%)	43.5	56.4	0.78
Complications, n (%)			
Acute Respiratory Failure	25(51)	19(32.2)	<0.05
Hypercapneic Encephalopathy	4(8.2)	2(3.4)	0.28

Comorbidities, n (%)			
Hypertension	33(67.3)	30(50.8)	0.08
Diabetes Mellitus	12(24.5)	10(16.9)	0.33
Atrial Fibrillation	11(22.4)	6(10.2)	0.08
Anemia	27(55.1)	18(30.5)	<0.05
Cor pulmonale	26(53.1)	22(37.3)	0.10
Pulmonary artery HTN	3(6.1)	2(3.4)	0.50
Coronary Artery Disease	18(36.7)	11(18.6)	<0.05
Chronic Liver Disease	2(4.1)	2(3.4)	0.85
Cerebrovascular Disease	8(16.3)	7(11.9)	0.50
Cancer	2(4.1)	1(1.7)	0.45

In-hospital outcomes for patients with or without AKI are shown in Figure 2and Table 2.

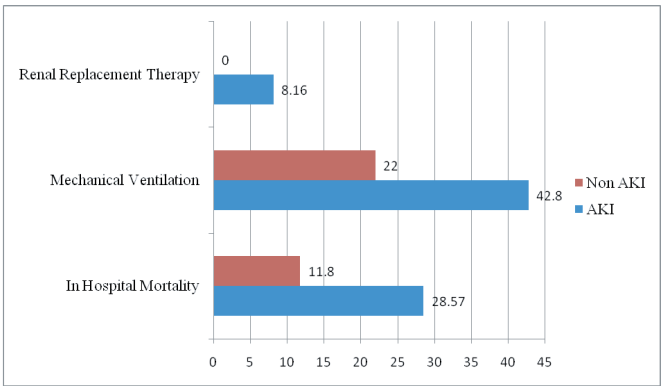

Figure 2: In hospital outcome inpatient with or without AKI.

Table 2: Duration of treatment of patient with or without AKI

Variables	AKI	Non AKI	P-value
Duration of mechanical Ventilation (Days)	5.52±0.98	5.23±0.59	0.34
Duration of ICU stays (Days)	6.0±1.29	5.4±1.13	<0.05
Duration of Hospitalization (Days)	7.65±1.42	6.92±1.20	<0.05

Patients with AKI were more likely to require mechanical ventilation (42.8% vs 22.03%; P < 0.05) compared with the non- AKI group. However, there was no significant difference in duration of mechanical ventilation between AKI (5.52±0.98 days) and non-AKI groups (5.23±0.59 days; P = 0.34).

Out of 49 patients who had AKI, 4 patients required renal replacement therapy (RRT), which accounted for 8.1% of all patients with AKI. Moreover, the in-hospital mortality of this group was 100%.

Patients with AKI had a longer duration of hospitalization (7.65±1.422 days) compared with the non-AKI group (6.92±1.20; P < 0.05).

During the hospitalization, the overall in-hospital mortality was 19.4% (21/108). In-hospital mortality was 28.5% in the patient with AKI was (28.5% vs 11.8%, P< 0.05) compared with non-AKI patients. In particular, 85.7 % (6/7) of the patient with AKI stage 3 died during hospitalization while only 11.8% (7/59) of the patient with non-AKI died during hospitalization.(Figure 3)

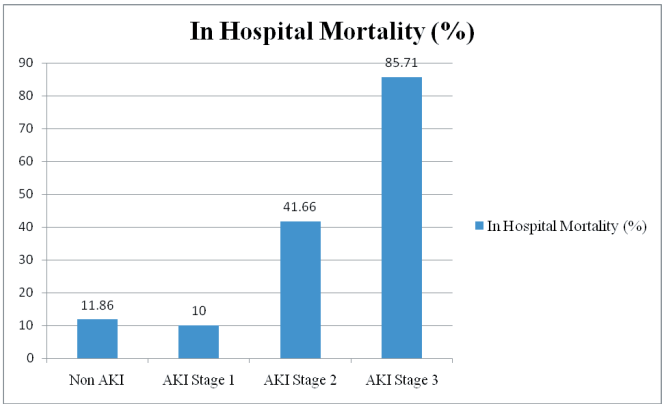

Figure 3: Shows the in-hospital mortality according to AKI stages.

DISCUSSION

In this study, more than two-third of in-patients with AECOPD admitted in ICU had an AKI and patients with AKI had worse prognostic implications than patients without AKI. Patients with AECOPD with AKI were of more advanced age and it was also independently associated with an increased risk of requiring mechanical ventilation, a longer duration of ICU stay and hospitalization and increased in-hospital mortality

We found that the incidence of AKI was 45.4% in inpatients with AECOPD. In previous studies conducted by Wan X et al, Barakat et al and Fabbian et al, incidence rates for AKI in a stable COPD and AECOPD ranged from 1.9% to 21% which was much less than our study.[9,6,5] The higher incidence in our study could be because we only included the AECOPD patient requiring ICU admission compared to Wan X et al, Barakat et al and Fabbian et al, who enrolled stable COPD patient admitted in general ward.[9,6,5] Furthermore, in the studies by Fabbian et al and Barakat et al, AKI was diagnosed by the International Classification of Diseases.[6,5] However, the performance of International Classification of Diseases in identifying AKI reported that the sensitivity was only 17%, and specificity was >98%, which might underestimate the incidence ofAKI.[10] Macedo E et al, in his study showed that the

critically ill patients admitted in ICU had higher incidence of AKI 28% to 60% based upon the criteria for diagnosing AKI and Luo X et al, also showed the incidence of AKI of 51% in critically ill patients using KDIGO as a diagnostic criteria of AKI which was similar to our study.[11,12]

Our study showed that the risk factors for AKI are advanced age, coronary artery disease, anemia, acute respiratory failure and mechanical ventilation which was similar to the studies by Barakat et al which reported that advanced age, hypertension, angina, heart failure, and CKD were independently associated with AKI in patients with AECOPD.[6] Similar to our study Wan X et al, found that the independent risk factors for AKI in patients with AECOPD were advanced age, coronary artery disease, anemia, cancer, chronic kidney disease, hypercapnic encephalopathy, acute respiratory failure, and mechanical ventilation. [9]

Mechanical ventilation is an important step for treatment of patients for AECOPD.[14] On the other hand, it is also independent risk factor for AKI. Reduction in renal blood flow (RBF) due to hypoxemia or hypercapnia, decreased preload and increased right ventricular afterload, and ultimately decreased cardiac output causes an inflammatory reaction in the lung and inflammatory mediators released into the systemic circulation by the effect of mechanical ventilation were the main mechanisms for explaining AKI caused by mechanical ventilation.[14, 15]

Finding from our study show that patient with AECOPD with AKI had increased risk of requiring mechanical ventilation, a longer length of ICU stay, a longer length of hospitalization, and higher in-hospital mortality. Individually, patient with advanced age and AKI with Stage 2 and stage 3 requiring RRT were independent risk factor for in-hospital death. Our study findings were comparable to the study conducted by Wan X et al, who concluded that AKI is common in patients with AECOPD requiring hospitalization with increased risk of mechanical ventilation (38.7% vs 19.1%, P<0.001), a longer ICU stay (9 days vs 8 days, P=0.033) and longer hospitalization (13 days vs 10 days, P<0.001); and higher in-hospital mortality (18.0% vs 2.7%, P<0.001) than those without AKI. Alaithan et al ,evaluated 119 patients with COPD who were admitted to ICU and found that AKI was identified as an independent risk factor associated with in-hospital mortality.[15]Advanced age and ARF are two common risk factors for in-hospital death in patients with AECOPD.[16]

LIMITATIONS

This is a single center based study with moderate sample size and involvement of multiple center with more patients would have improved the statistical power of the study. Also data such as body mass index, COPD severity stage, and smoking were not available, which may be associated with AKI. We did not assess urine output in determining the presence of AKI. Although AKI is partly defined by urine volume, most AKI staging studies have used only SCr levels, and not urine output. [8,17]

CONCLUSIONS

Patients with AECOPD are at an increased risk of developing AKI. AKI can further worsen the prognosis and outcome of COPD patients leading to ICU stay and hospitalization with higher mortality rates.

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REFERENCES

1. Bista B, Dhimal M, Bhattarai S, Neupane T, Xu YY, Pandey AR, et al. Prevalence of non-communicable diseases risk factors and their determinants: Results from STEPS survey 2019, Nepal.2021;16:1–20.[Internet] [Pubmed]
2. Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. Lancet Respir Med. 2022;10(5):447–58. [Pubmed]
3. Celli BR, Barnes PJ. Exacerbations of chronic obstructive pulmonary disease. Eur Respir J. 2007;29(6):1224–38. [Pubmed]
4. Seemungal TAR, Hurst JR, Wedzicha JA. Exacerbation rate, health status and mortality in COPD--a review of potential interventions. Int J Chron Obstruct Pulmon Dis. 2009;4:203–23. [Pubmed]
5. Fabbian F, De Giorgi A, Manfredini F, Lamberti N, Forcellini S, Storari A, et al. Impact of renal dysfunction on in-hospital mortality of patients with severe chronic obstructive pulmonary disease: a single-center Italian study. Int Urol Nephrol. 2016;48(7):1121–7. [Pubmed]
6. Barakat MF, McDonald HI, Collier TJ, Smeeth L, Nitsch D, Quint JK. Acute kidney injury in stable COPD and at exacerbation. Int J COPD. 2015;10(1):2067–77. [Pubmed]
7. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. Eur Respir J. 2023;2300239. [Internet] [Pubmed]
8. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, et al. Diagnosis, evaluation, and management of acute kidney injury: A KDIGO summary (Part 1). Crit Care. 2013;17(1):1–15. [Pubmed]
9. Wan X, Chen D, Tan Y, Ma M, Zhang F, Liu Z, et al. Incidence, risk factors, and prognostic implications of acute kidney injury in patients with acute exacerbation of copd. Int J COPD. 2020;15:1085–92. [Pubmed]

10. Grams ME, Waikar SS, MacMahon B, Whelton S, Ballew SH, Coresh J. Performance and limitations of administrative data in the identification of AKI. Clin J Am Soc Nephrol. 2014;9(4):682–9. [Pubmed]
11. MacEdo E, Malhotra R, Claure-Del Granado R, Fedullo P, Mehta RL. Defining urine output criterion for acute kidney injury in critically ill patients. Nephrol Dial Transplant. 2011;26(2):509–15. [Pubmed]
12. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. Crit Care. 2014;18(4):1–8. [Pubmed]
13. Kuiper JW, Groeneveld ABJ, Slutsky AS, Plötz FB. Mechanical ventilation and acute renal failure. Crit Care Med. 2005;33(6):1408–15. [Pubmed]
14. Alaithan AM, Memon JI, Rehmani RS, Qureshi AA, Salam A. Chronic obstructive pulmonary disease: Hospital and intensive care unit outcomes in the Kingdom of Saudi Arabia. Int J COPD. 2012;7:819–23. [Pubmed]
15. Hu GP, Zhou YM, Wu ZL, Li YQ, Liang WQ, Wei LP, et al. Red blood cell distribution width is an independent predictor of mortality for an acute exacerbation of COPD. Int J Tuberc Lung Dis. 2019;23(7):817–23. [Pubmed]
16. Thomas ME, Blaine C, Dawnay A, Devonald MAJ, Ftouh S, Laing C, et al. The definition of acute kidney injury and its use in practice. Kidney Int. 2015;87(1):62–73.[Internet] [Pubmed]