RESEARCH ARTICLE

Predictors of mortality in patients with respiratory infection admitted to ICU in a tertiary care centre

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Mohan CK, Mahandra M. Predictors of mortality in patients with respiratory infection admitted to ICU in a tertiary care centre. J Pulmon 2019;3(1):4-7.

INTRODUCTION: Respiratory infections account for significant mortality and morbidity throughout the world. In spite of advances in the development of newer antibiotics, respiratory infections continue to be an important cause for mortality. It is important to study the predictors of mortality in patients with respiratory infection in Indian patients as there is scarce data

METHODS: A prospective observational study was done in a tertiary care center from August 2017 to February 2018. Patients admitted to ICU with acute respiratory infection were included in the study. Data on demographic variables such as age, gender, diagnosis, and reason for ICU admission were recorded. We also noted the presence of co-morbidities. Modified CPI score was calculated on day 1 and day 2. Cox regression univariate and multivariate analysis along with Kaplan Meier analysis was done for assessing factors associated with mortality.

RESULTS: 303 patients satisfied the inclusion criteria and were included in the study. The mean age of the cohort was 56.05 ± 16.37 years and 62% were men. The most common diagnosis was Pneumonia (66%) followed by COPD (43.5%). Mean duration of hospital stay was 7.29 ± 3.76 days. The mortality rate was 17.8%. On multivariate Cox regression analysis CPI score >4 on day 1, CPI score >6 on day 2, number of antibiotics >2 were independently associated with increased hazard for mortality.

CONCLUSION: We found on multinominal Cox regression analysis, modified CPI score >4 on day 1, CPI score >6 on day 2, Usage of >2 antibiotics were independently associated with increased hazard for mortality in patients admitted to ICU with a respiratory infection.

Key Words: *Respiratory infection; mortality; Pneumonia*

INTRODUCTION

Respiratory infections account for significant mortality and morbidity throughout the world. In spite of advances in the development of newer antibiotics, respiratory infections continue to be an important cause for mortality. Acute respiratory infections are responsible for 4.25 million deaths worldwide each year and are the 3rd largest cause of death after cardiac disease and stroke in developed countries and in middle and low-income countries acute respiratory infections top the list (1). Low immunization, poor nutrition, overcrowding, HIV infection accounts for a high burden of acute respiratory infections (2).

Various risk factors like advanced age, presence of comorbid illness, higher APACHE II score, high CURB65 score, extensive pulmonary involvement, septic shock, renal failure, tachypnea, elevated blood urea nitrogen, hypotension, requirement of mechanical ventilation, decreased level of consciousness, underlying chronic lung disease, prior episode of large volume aspiration have been studied which are responsible for increased mortality in patients with acute respiratory infections (3-7). It is important to study the predictors of mortality in patients with respiratory infection in Indian patients as there is scarce data.

METHODOLOGY

We conducted a prospective observational study in a tertiary care center from August 2017 to February 2018. All patients admitted to ICU with acute respiratory infection were included in the study after obtaining informed consent. Data on demographic variables such as in-patient registration number, age, gender, diagnosis, and reason for ICU admission were recorded. We also noted the presence of comorbidities like Obesity, COPD, cirrhosis of the liver, Asthma, Chronic kidney disease, diabetes, heart failure, hypertension. A detailed history of previous ICU admissions and treatment details were collected. Patients with respiratory distress requiring NIV or invasive mechanical ventilation, receiving inotropes were admitted to ICU. Exclusion criteria were patients less than 18 years, who had HIV, patients died within 48 hours of admission were excluded from the study. Clinical Pulmonary Infection Score (CPIS score) was obtained on day 1 and day 2 of admission which included data on tracheal secretions (rare, abundant, abundant and purulent), chest X-ray infiltrates (None, diffuse, localized), temperature (≥ 36.5 and ≤ 38.4, ≥ 38.5 and ≤ 38.9, ≥ 39 and ≤ 36), Leukocyte count/mm^3 (≥ 4000 and ≤ 11000, ≤ 4000 and ≥ 11000, ≤ 4000 and ≥ 11000 with band forms ≥ 500). The severity of each parameter was given scoring 0, 1, 2 with increasing order of severity. The total score was calculated adding up each parameter and final CPIS score was calculated.

Sputum collection was obtained within 24 h of admission to ICU in a sterile wide mouthed container. Adequacy of the sample was if the quantity was 15 ml and was mucopurulent on visual examination.

In patients who needed immediate mechanical ventilation, tracheal aspirate was collected within 24 hours and sent for analysis. Bronchoalveolar lavage was done in selected patients. The Institutional Ethics Committee approved the study. Informed consent from the patient/patient's legally authorized representative was taken prior to inclusion in the study. We defined sepsis as life-threatening organ dysfunction with an increase of two points or more in sequential organ function assessment score (8).

Statistical analysis

Descriptive data are presented as frequencies (percentages) for discrete variables and as means (SDs) for continuous variables. Inferential statistics like the chi-square test was used. Cox regression univariate and multivariate analysis along with Kaplan Meier analysis was done for assessing factors associated with mortality. All statistical tests were 2-tailed, and factors were considered statistically significant at $p<0.05$. IBM SPSS version 22 and CDC Epi Info version 7 was used for analysis.

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Received: May 02, 2019, Accepted: May 11, 2019, Published: May 16, 2019

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RESULTS

We screened 330 patients admitted to RICU and 27 patients were excluded from the study (Figure 1), Three hundred and three patients satisfied inclusion criteria and were included in the study. The mean age of the cohort was 56.05 ± 16.37 years and 62% were men. The most common diagnosis was Pneumonia (66%) followed by COPD (43.5%), Empyema (12.5%), Bronchiectasis (4.6%), Interstitial Lung Disease (4.29%) and Tuberculosis (2.6%). Diabetes was the most common comorbidity (33%) followed by hypertension 28.38%, Cardiac failure 5.2%, Asthma 3.9%.

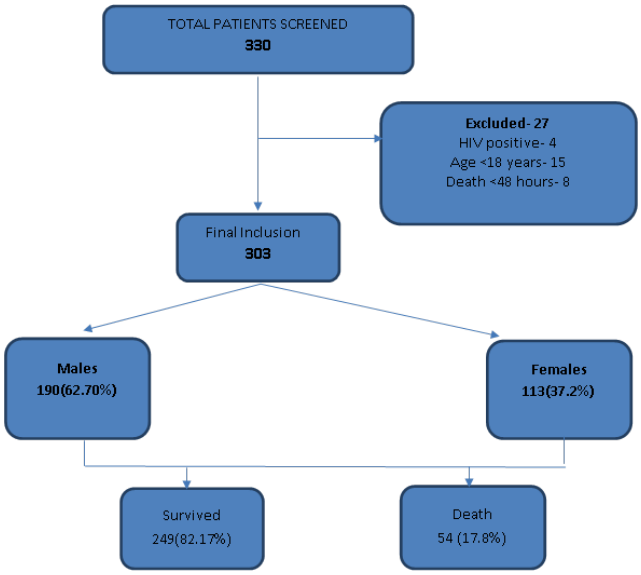

Figure 1) *Flowchart of inclusion and exclusion criteria of the cohort*

In our study, 103 patients were managed only on NIV and 200 patients needed mechanical ventilation. Twenty percent of patients developed Ventilator-associated pneumonia (VAP). In 46.2% (140/303) of patients, causative Organisms were isolated. *Acinetobacter baumanii* was the most common organism isolated. Mean duration of hospital stay was 7.29 ± 3.76 days. Mean duration of ICU stay was 5.2 ± 2.3 days. The mortality rate was 17.8%. ARDS was the most common cause of death.

Comparison of survivors and non-survivors

On univariate Cox regression analysis, we found Diabetes mellitus, COPD, modified CPI score on day 1 and day 2, >2 antibiotic usages, Ventilator-associated pneumonia were statistically significant risk factors for mortality (Table 1). On multivariate Cox regression analysis CPI score >4 on day 1, CPI score >6 on day 2, number of antibiotics >2 were independently associated with increased hazard for mortality (Table 2) Kaplan Meier analysis of Modified CPI score >4 on day1 (Figure 2) and modified CPI score >6 on day 2 confirms significant association with mortality (Figure 3).

DISCUSSION

Respiratory infections incur significant mortality, morbidity and increased healthcare burden throughout the world. In developing countries like India, affordability to access critical care becomes an important factor due to financial constraints (9). Mortality in critically ill patients with respiratory infection remains high despite advances in ventilation strategies and newer antimicrobial chemotherapy (10). Identification of poor prognostic factors in patients admitted to ICU enables critical care physician to take timely appropriate action and manage those cases better. We found in our study on multivariate Cox regression analysis CPI score >4 on day 1, CPI score >6 on day 2, Usage of >2 antibiotics were independently associated with increased hazard for mortality.

TABLE 1 Univariate Cox regression analysis of factors associated with mortality in patients admitted to ICU with a respiratory infection

Variables	Total (303)	Survivors (249)	Non-survivors (54)	P value
Age in years, mean (SD)	56.05 (16.37)	56.41 (16.4)	54.37 (16.17)	0.848
Gender, male n (%)	190 (62.7)	156 (62.7)	34 (63)	0.54
Comorbidities, n (%)	204 (67.3)	167 (67.1)	37 (68.5)	0.87
Diabetes, n (%)	100 (33)	75 (30.1)	25 (46.3)	0.026
Cardiac failure, n (%)	16 (5.3)	13 (5.2)	3 (5.6)	0.921
Hypertension, n (%)	86 (28.4)	72 (28.9)	14 (25.9)	0.741
COPD, n (%)	116 (38.3)	102 (41)	14 (25.9)	0.04
Previous antibiotics usage, n (%)	110 (36.3)	91 (36.5)	19 (35.2)	0.877
Number of antibiotics used, n, mean (SD)	2.27 (0.95)	2.10 (0.9)	3.04 (0.77)	0.0001
Modified CPI score (Day 1), mean (SD)	3.91 (1.44)	3.61(1.2)	5.33 (1.25)	0.0001
Modified CPI score (Day 2), mean (SD)	4.33 (1.57)	3.93 (1.3)	6.19 (1.16)	0.0001
VAP, n (%)	53 (17.5)	29 (11.6)	24 (44.4)	0.0001
Length of ICU stay, n (%)	6.29 (3.86)	6.16 (3.8)	6.85 (4.08)	0.124

TABLE 2 Multinominal cox regression analysis of factors associated with mortality in patients admitted to a ICU with a respiratory infection

Variables	Hazard ratio (95%CI)	p-value	Multinomial Hazard ratio (95%CI)	p value
Age >60 years	0.94 (0.54-1.65)	0.848	1.14 (0.57-2.25)	0.705
Modified CPI score >4 (on day 1)*	4.17 (2.15-8.07)	0.0001	2.45 (1.22-4.90)	0.011
Modified CPI score >6 (on day 2)	6.49 (3.51-11.97)	0.0001	4.11 (2.09-8.08)	0.0001
Diabetes Mellitus	1.10 (0.63-1.90)	0.73	0.90 (0.51-1.58)	0.786
COPD**	0.74 (0.40-1.37)	0.352	1.05 (0.52-2.16)	0.882
Number of antibiotics, >2	1.81 (1.35-2.44)	0.0001	2.04 (1.01-4.10)	0.045
Ventilator Associated Pneumonia	1.45 (0.81-2.58)	0.202	0.83 (0.46-1.48)	0.552

*Clinical Pulmonary Infection score; **Chronic Obstructive Pulmonary Disease

Various critical illness scoring systems such as APACHE II score, SOFA score, SAPS 2 score are well validated for predicting mortality in critically ill patients (11-13). Drawbacks of these scoring systems are that they are cumbersome and need multiple parameters including arterial blood gas analysis. So we used the Modified Clinical Pulmonary Infection Scoring System (CPIS) for prognosticating pulmonary illness. CPIS was initially developed to assist the physician to diagnose VAP clinically which involves 6 parameters which include arterial blood gas. Due to complexities involved in the calculation of CPIS which needs invasive technique like arterial blood gas analysis, a modified CPIS was created mainly to assess the severity of the disease at admission and subsequent day. CPI score involves 4 parameters namely tracheal secretions, chest X-ray, temperature and leukocyte counts as these are easily available during admission. We found CPI score >4 on day 1 and >6 on day 2 were independent predictors of mortality.

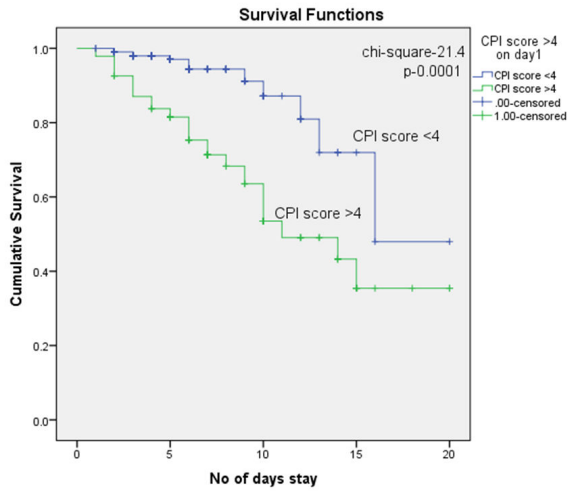

Figure 2) Kaplan Meier survival analysis of patients with respiratory infection with modified CPI score on day 1

Poly antimicrobial therapy (>2 antibiotics) was found to be a predictor of mortality may be because patients who received >2 antibiotics were more critically ill requiring a broader spectrum of antibiotics and hence higher mortality compared to rest (14).

Mortality in our study was 17.8% which was lower compared to studies done in Riyadh (24.4% and 25.9%) (15,16), Turkey (31%) (17), Egypt (49%) (18), Australia (32) (19) but was higher compared to studies done in Pakistan (11%), Canada (8.1%) (20), Sweden (4%) (21). A meta-analysis showed an average mortality of 36.5% for Community acquired pneumonia patients admitted in the ICU, with a range of 21.7% to 57.3% (22).

Numerous studies have been all over the globe for identifying predictors of mortality in ICU patients with a respiratory infection like Pneumonia, ARDS. A meta-analysis consisting of 122 studies dealing with the prognostic factors in patients with community-acquired pneumonia and found 10 independent predictors of death, including male sex, diabetes mellitus, malignancy, neurologic disease, tachypnoea, hypotension, hypothermia, leucopenia, bacteremia, and multilobar infiltrates (22). A Swedish study done showed that low serum albumin and the occurrence of secondary infection, but also the absence of chills and airway colonization, were correlated to higher mortality (21). A Spanish study found age, CURB score 3-4, septic shock, ARDS, and acute renal failure during the first 24 h of ICU admission were found to be independent predictors of mortality in SCAP patients (23).

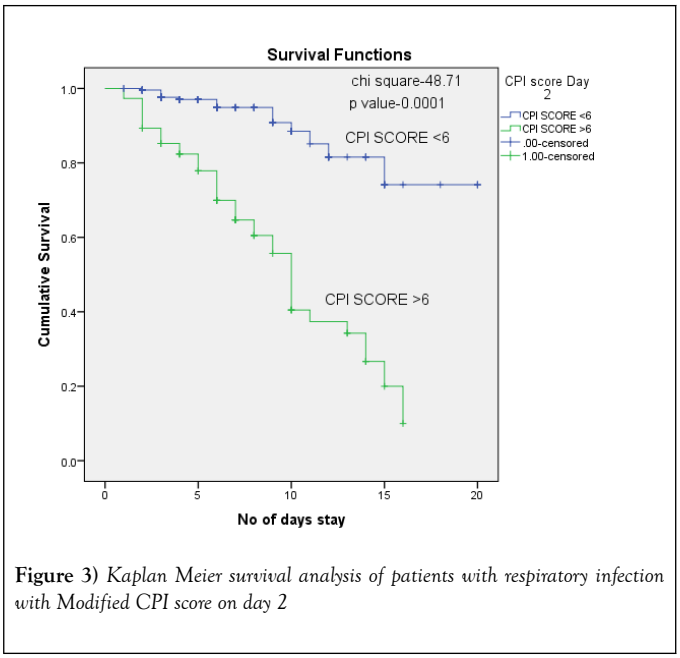

Figure 3) *Kaplan Meier survival analysis of patients with respiratory infection with Modified CPI score on day 2*

There are several limitations in our study, firstly this study needs to be repeated in ICUs in multicenter for generalization of our results. Secondly, we did not use severity of illness scores like APACHE2 and SOFA score. Thirdly modified CPIS score system which we have used needs further validation in larger studies.

CONCLUSION

We found on multinominal Cox regression analysis, modified CPI score >4 on day 1, CPI score >6 on day 2, Usage of >2 antibiotics were independently associated with increased hazard for mortality in patients admitted to ICU with a respiratory infection. Modified CPI score could be a simple tool for prognosticating patients in ICU with a respiratory infection.

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