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Predictors of mortality in severe community acquired pneumonia in an intensive care unit of Sri Lanka

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Abstract

Background: Severe community-acquired pneumonia (SCAP) carries high mortality. This study describes the predictors of mortality in SCAP.

Method: A prospective cross-sectional study was conducted in the Medical Intensive Care Unit (MICU) of National Hospital of Sri Lanka (NHSL) recruiting patients with SCAP admitted from July to December 2023. Disease outcome, complications and organ support received were documented.

Results: Among 56 participants, 36 (64.3%) were males and 33 (58.9%) were ≥50 years of age. Septic shock requiring vasopressors was seen in 36 (69.6%), acute kidney injury (AKI) in 24 (42.9%) and 40 (71.4%) required mechanical ventilation (MV). There were 20 (35.7%) deaths.

A higher number of non-survivors had respiratory failure (100% vs 55.6%, p<0.0001), PaO_2/FiO_2 ratio<250 (100% vs 77.8%, p=0.02) and required MV (100% vs 55.6%, p<0.0001) compared to survivors. Length of MV was higher in non-survivors than survivors (8 vs 2.5 days p<0.001).

History of chronic renal failure (OR 6.214, 95% CI 1.84 - 20.99, p=0.003), presence of AKI (OR 9.0, 95% CI 2.54 - 31.80, p=0.001) and need for renal replacement therapy (OR 13.44, 95% CI 3.07 - 58.71, p=0.001) were associated with mortality. Patients who had septic shock and required vasopressors (OR 15.2, 95% CI 1.833 - 126.07, p=0.01) had a higher risk of death. In a multivariable logistic regression model, AKI independently predicted mortality (adjusted OR 5.3, 95% CI 1.26 - 28.28, p<0.02).

Conclusion: Presence of respiratory failure, AKI and septic shock predicts mortality in patients with SCAP.

Key words: severe pneumonia, community acquired pneumonia, mortality, intensive care unit, predictors

Introduction

Community-acquired pneumonia (CAP) is a pervasive and serious health concern, frequently ranking among the leading causes of morbidity and mortality throughout the world.[1] It significantly affects vulnerable groups, such as the elderly, those with chronic illnesses, and compromised immune systems.[2] CAP is an acute infection of the lung tissue that occurs in individuals who have not been recently hospitalized or regularly exposed to healthcare facilities, setting it apart from healthcare-associated or hospital-acquired pneumonia. Despite progress in medical care, CAP continues to place a considerable burden on health-care systems due to its broad spectrum of clinical manifestations, which can vary from mild, self-limiting illness to severe, life-threatening conditions that necessitate hospitalization and intensive care treatment.

The management of CAP is further complicated by the wide range of pathogens responsible for the infection, the increasing prevalence of antibiotic resistance, and the differences in patient responses

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to treatment. The diversity in CAP cases, influenced by differences in pathogen virulence, host immune response, and preexisting health conditions, makes it difficult to predict outcomes accurately and tailor treatment strategies effectively. This has resulted in a heightened emphasis on understanding the clinical, microbiological, and demographic factors that impact the severity and prognosis of CAP.

In this context, severe community-acquired pneumonia (SCAP) constitutes a crucial subset of CAP cases, associated with elevated mortality rates and increased utilization of healthcare resources.[3] SCAP often demands intensive treatment and poses notable challenges in terms of timely diagnosis, effective antimicrobial therapy, and supportive care. Identifying the predictors of severity in SCAP, such as age, underlying health conditions, microbial etiology, and complications such as sepsis or acute respiratory distress syndrome (ARDS), is vital for enhancing patient outcomes and guiding clinical decision-making. There are limited data regarding predictors of mortality in SCAP in Sri Lanka. The unique healthcare challenges in Sri Lanka, including variable access to advanced medical care, different patient demographics, and pathogen profiles, necessitate region-specific studies. Furthermore, while SCAP is a globally recognized concern, factors influencing mortality and treatment outcomes may differ significantly based on local healthcare infrastructure, patient characteristics, and microbial patterns. Thus, this study was conducted to provide localized data that can help guide ICU management strategies for SCAP in Sri Lanka, potentially improving patient outcomes.

This study explores the complex interplay of factors that influence the severity and outcomes of SCAP. By conducting a prospective cross-sectional study in the Medical Intensive Care Unit (MICU) of the National Hospital of Sri Lanka, we identified the clinical characteristics, microbial patterns, treatment methods, and outcomes of patients with SCAP. In addition, determinants of mortality in this high-risk patient group were identified to provide practical guidance for clinicians to enhance management strategies.

Methodology

This was a single-center, prospective cross-sectional study conducted in the Medical Intensive Care Unit (MICU) at the National Hospital of Sri Lanka (NHSL) from July to September 2023. The study enrolled 56 participants above 18 years who were admitted to MICU, NHSL with SCAP. Diagnosis of CAP was made in the presence of signs and symptoms related to lower respiratory tract infection (temperature >38°C, cough, sputum production, dyspnea, tachypnea, pleuritic pain), signs of invasion of alveolar space AND new or changed lung infiltrate on chest imaging.

Study participants were recruited following informed written consent. Consent was obtained directly from patients who were conscious and capable of rational decision-making at the time of admission to the MICU. For patients who were unconscious or intubated and therefore unable to provide direct consent, proxy consent was obtained from the bystander or next of kin. To ensure that the vulnerable population, such as unconscious or critically ill patients, was protected ethically, proxy consent was obtained from their closest relatives or bystander.

Clinical information including demographics, comorbidities, lifestyle factors, and microbiological data were obtained from the records and participants were followed up to identify complications and the outcome. SCAP was defined based on Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) criteria.[4] Ethical approval was obtained from the Ethics Review Committee of the NHSL.

The data collected was analyzed using IBM SPSS Statistics for Windows, Version 25.0. Variables were described using frequencies and appropriate 'Z' test, chi-square test and multi-variable logistic regression was used to identify associations of mortality.

Results

There were 56 participants recruited to the study, with a male predominance (n=36, 64.3%). Majority were less than 50 years of age (n=23, 41.07%), while 22 participants (39.29%) belonged to the age group of 50-65 years, with the remainder being more than 65 years (n=11, 19.64%) and comorbidities were seen in 45 participants (80.4%). Diabetes mellitus (n=25, 44.6%), chronic kidney disease (n=19,33.9%), COPD (n=12, 21.4%), cardiovascular disease (n=18, 32.1%), stroke (n=2,3.6%) and neoplastic disease (n=2,3.6%) were seen among the study group. There were 15 (26.8%) smokers and 7 (12.5%) alcohol consumers.

Characteristics of SCAP in the study population

All study participants (n=56) had SCAP according to IDSA/ATS criteria. Factors determining severity (Table 1) revealed that a significant proportion required vasopressors to maintain their blood pressure (n=39, 69,6%) and required mechanical ventilation for respiratory failure (n=40, 71.4%).

Table 1. Presence of variables of disease severity in the study population

IDSA/ATS criteria	*Frequency (%) N=56*
Major criteria	
Septic shock with the need of vasopressors	39 (69.6)
Respiratory failure requiring mechanical ventilation	40 (71.4)
Minor criteria	
Respiratory rate ≥30/min	53 (94.6)
PaO_2/FiO_2 ≤250	48 (85.7)
Multi-lobar infiltrates	42 (75)
Confusion/disorientation	13 (23.2)
Uraemia (BUN ≥20 mg/dl)	19 (33.9)
Leukopenia (WBC <4000/µl)	12 (21.4)
Thrombocytopenia (Platelet <100,000/µl)	6 (10.7)
Hypothermia	0 (0)
Hypotension requiring aggressive fluid resuscitation	11 (19.6)

Causative organism was identified only in 36 (64.2%) of the study participants, with a bacterial organism isolated in 28 (50%), viral in 1 (1.8%) and polymicrobial organisms in 7 (12.5%) participants. Majority (75%) of chest x-ray findings showed multilobar involvement.

There were 20 (35.7%) deaths among the SCAP patients admitted to the MICU. Age, gender and most comorbidities were not associated with mortality (Table 2). Presence of chronic renal failure was the only comorbidity associated with a higher risk of death in SCAP (p=0.002). Chest X-ray findings and the causative organism were also not associated with the outcome of SCAP.

Majority of patients who died in the ICU had either septic shock or respiratory failure. The presence of AKI, need for hemodialysis, mechanical ventilation and vasopressor support increased the risk of death among the participants. Also, AKI was identified to be an independent risk factor for mortality in a multivariable logistic regression model (adjusted OR 5.3, 95% CI 1.26-28.28, p<0.02). In contrast, High-Flow Nasal Oxygen (HFNO) (P=0.094) and Non-Invasive Ventilation (NIV) (P=0.140) did not show significant associations with ICU mortality, suggesting these supports are not strongly linked to patient outcomes in the ICU.

Table 2. Factors associated with mortality in SCAP

Factors	*Outcome*		*P Value*
	Death (N=20)	*Survived (N=36)*	
Age			
<50 years	8 (40.0)	15 (41.7)	0.069
50-65 years	11 (55.0)	11 (30.6)	
>65 years	1 (5%)	10 (27.8%)	
Gender			
Male	16 (80.0)	20 (55.6)	0.086
Lifestyle factors			
Smoking	6 (30.0)	9 (25.0)	0.686
Alcohol	1 (5.0)	6 (16.7)	0.402
Comorbidities			
Chronic respiratory disease/COPD	3 (15.0)	9 (25.0)	0.506
Congestive heart failure/cardiovascular disease	5 (25.0)	13 (36.1)	0.394
Neoplastic disease	0 (0.0)	2 (5.6)	0.532
Stroke/Neurological illness	2 (10.0)	0 (0.0)	0.123
Chronic renal disease	12 (60.0)	7 (19.4)	0.002
Diabetes mellitus	11 (55.0)	14 (38.9)	0.245
Clinical features and laboratory findings			
Respiratory rate ≥ 30/min	20 (100.0)	33 (91.7)	0.545
$PaO_2/FiO_2 \leq 250$	20 (100.0)	28 (77.8)	0.041
Confusion/disorientation	4 (20.0)	9 (25.0)	0.752
Uraemia (BUN ≤ 20 mg/dl)	9 (45.0)	10 (27.8)	0.192
Leukopenia (WBC <4000/µl)	6 (30.0)	6 (16.7)	0.313
Thrombocytopenia (Platelet <100,000/µl)	1 (5.0)	5 (13.9)	0.405
Chest x-ray findings			
Single lobar consolidation	5 (25.0)	5 (13.9)	0.375
Multilobar infiltrates	15 (75.0)	27 (75.0)	
Interstitial infiltrates	0 (0.00)	2 (5.6)	
None	0 (0.00)	2 (5.6)	

(Continued)

Factors	*Outcome*		*P Value*
	Death (N=20)	*Survived (N=36)*	
Causative Organism			
Bacterial	8 (40.0)	20 (55.6)	0.281
Viral	1 (5.0)	0 (0.00)	
Poly-microbial	4 (20.0)	3 (8.3)	
Unidentified	7 (35.0)	13 (36.1)	
Complications			
Septic shock	19 (95.0)	20 (55.6)	0.002
Respiratory failure	20 (100.0)	20 (55.6)	<0.0001
Acute kidney injury	15 (75.0)	9 (25.0)	0.001
Parapneumonic effusion	0 (0.00)	4 (11.1)	0.285
Lung cavitation and abscess	3 (15.0)	2 (5.6)	0.336
Other	1 (5.0)	9 (25.0)	0.078
Organ support received			
HFNO	7 (35.0)	21 (58.3)	0.094
NIV	7 (35.0)	20 (55.6)	0.140
MV	20 (100.0)	20 (55.6)	<0.0001
Vasopressor support	18 (90.0)	20 (55.6)	0.008
HD/SLED/CRRT	11 (55.0)	3 (8.3)	

COPD; chronic obstructive pulmonary disease, BUN; blood urea nitrogen, WBC; white blood cells, HFNO; high flow nasal oxygen, NIV; non-invasive ventilation, MV; mechanical ventilation, HD; heamodialysis, SLED; sustained low-efficiency dialysis, CRRT; continuous renal replacement therapy.

Table 3. Logistic regression analysis of factors associated with mortality

Parameter	*OR (univariate analysis)*	*95% CI*	*P value*	*Adjusted OR (multivariate analysis)*	*95% CI*	*P value*
History of chronic renal failure	6.214	1.84-20.99	0.003	2.7	0.45-16.6	NS
Presence of AKI	9.0	2.54-31.80	0.001	5.3	1.26-28.28	<0.02
Need for renal replacement therapy	13.44	3.07-58.71	0.001	4.3	0.638-29.35	NS
Septic shock required vasopressors	15.2	1.833-126.07	0.01	6.8	0.69-67.28	NS

*NS – Not significant (p≥0.05)

Discussion

SCAP is a progressive disease evolving from a local to a systemic infection with the spectrum of sepsis-related complications requiring ICU admission.[5] Various tools are available to define SCAP, of which the 2007 IDSA/ATS was adopted in our study. CURB-65 score evaluates confusion, urea levels, respiratory rate, blood pressure, and age. It has shown high predictive accuracy for in-hospital mortality. Higher CURB-65 scores correlate with increased mortality rates.[6]

Pneumonia Severity Index (PSI) stratifies patients based on clinical and demographic factors. It is widely used but may be less effective in specific populations, such as kidney transplant recipients.[7]

The Quick Sequential Organ Failure Assessment (qSOFA) score is useful for identifying patients at risk of severe pneumonia. A modified version incorporating procalcitonin has been shown to enhance predictive accuracy.[8]

The requirement for mechanical ventilation or vasopressor support because of septic shock were universally accepted as indications for ICU admission and are the major criteria recommended by the IDSA/ATS along with nine minor criteria with a recommendation that patients with three or more criteria be considered for ICU admission[4]. As there is limited data regarding SCAP in relation to the outcome and factors affecting the outcome, our study focused on assessing them.

When considering the outcomes of SCAP, our study revealed that 20 (35.7%) patients died in ICU and 36 (64.3%) patients survived to be discharged to the ward. Mortality is 24% in a study done in Cairo, which studied 54 patients[9]. Mortality rates in studies including fewer than 90 patients ranged between 21% and 54%.[10] These results show comparable mortality rates to our study.

Our study revealed a significant association between the outcome and respiratory failure requiring mechanical ventilation (p value<0.001) and septic shock requiring vasopressors (p value 0.002), as well as $PaO_2/FiO_2 \leq 250$. Walden et al., found that the isolation of *Staphylococcus aureus* in blood, presence of septic shock, need for mechanical ventilation and renal replacement therapy all showed a strong association with outcome in patients with pneumonia.[11] Shock was identified to increase the risk of death by four fold in a Chinese study.[12] Septic shock and requirement of mechanical ventilation were strongly associated with mortality of patients with pneumonia in many other studies.[13-15] Septic shock is characterized by a cytokine storm with elevated serum inflammatory markers and interleukins. This excessive systemic inflammatory response leads to host tissue damage and multi-organ failure contributing to the mortality. In addition, during sepsis, neutrophils have many abnormalities including impaired migration, bacterial clearance, cytokine secretion and there is increased release of immature neutrophils, which are all associated with increased mortality risk in sepsis. The anti-inflammatory response during septic shock causes leukocyte reprogramming and changes to the immune status. Lymphocyte depletion and dysfunction in septic shock result in immunosuppression, thus affecting the patient outcome.[16-19] The increased mortality associated in septic shock could be explained by the above processes.

Jingjing Pan et al., reported that a lower the PaO_2/FiO_2 ratio was associated with a higher risk of death in pneumonia.[12] A study done in Italy, found that impaired PaO_2/FiO_2 had a three-fold risk of mortality in patients with COVID-19 pneumonia.[20] These findings were consistent with our study. PaO_2/FiO_2 ratio reflects the respiratory status of the patient and low values indicate the presence of acute respiratory distress syndrome, thus a measure of mortality.[12] Patients who had SCAP requiring MV due to severe respiratory failure indicating a more severe lung involvement had higher mortality.

Our study revealed that the need for renal support (HD, SLED, CRRT) [p value <0.001) was also significantly associated with a poor outcome from SCAP. Similarly in a retrospective record review of patients with SCAP, conducted in South Africa found that, need for mechanical ventilation, inotropes and dialysis were independent predictors of mortality.[21] The presence of AKI was identified to have a higher mortality risk in patients with pneumonia as supported by many previous studies, especially in those with pre-existing chronic kidney disease.[22-25] Respiratory failure following pneumonia could affect gas exchange and activation of renin-angiotensin-aldosterone system resulting in fluid retention, yet renal hypoxia and vasoconstriction contributing to AKI. Use of MV may contribute to release of systemic inflammatory mediators causing renal injury.[26] Septic shock per say can affect renal perfusion due to dysregulated immune responses resulting in AKI.[27] AKI can lead to systemic fluid

overload, retention of uremic toxins and metabolic acidosis, resulting in a higher mortality rate.[28] Hence, it highlights the need to monitor renal functions in patients with pneumonia and consider early ICU admission with aggressive treatment in those with deteriorating renal functions.

Our study identified chronic kidney disease to increase mortality. Similarly, previous studies showed that the infection-related mortality rates were higher in individuals with lower baseline eGFR levels. Lower eGFR levels were associated with higher hazard ratios for infection-related death after adjustment for age, race/ethnicity, sex and other confounders.[29,30] A systematic review reported a positive association of underlying chronic kidney disease with mortality.[31] The pooled adjusted risk for all-cause mortality in patients with respiratory tract infections almost doubled in patients with kidney disease.[31] Increased susceptibility to bacterial infections is due to immune dysfunction, with defective phagocytosis, impaired monocyte function and T lymphocyte immaturity seen in those on chronic dialysis. Thus, sepsis associated mortality risk is high in pre-existing renal disease.[32]

This study was carried out at a single center with a limited number of patients as the enrolled participants, which may reduce the generalizability of the findings. Although our study sample was small, we were able to give important inferences. The causative organisms were not specifically identified which could be considered as a limitation.

Conclusion

In conclusion, in patients with SCAP, the presence of respiratory failure requiring mechanical ventilation, previous history of chronic kidney disease, presence of AKI, need for renal replacement therapy and septic shock requiring inotrope support, predicts the mortality consistent with other studies. Identifying such complications early would necessitate escalation to intensive care, more stringent monitoring and treatment.

Author declaration

Competing interests

Authors do not have any conflicts of interest.

Criteria for authorship

WP, TN: conceptualization, methodology, data acquisition and analysis. LD, HG, PR, NP, WP: data analysis and drafting the manuscript. All authors were involved in writing and revising the manuscript.

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