Original Article

Outcomes of patients admitted to the intensive care unit with community-acquired pneumonia in a tertiary care center in Riyadh, Saudi Arabia

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Abstract:

BACKGROUND: Community-acquired pneumonia (CAP) is a leading cause of intensive care unit (ICU) morbidity and mortality. Despite extensive international epidemiological and clinical studies to improve those patients' outcomes, local statistics in Saudi Arabia are limited. The objective of this study is to describe the clinical characteristics and outcomes of patients admitted to the ICU with the diagnosis of CAP reflecting the experience of a tertiary center over an 18-year period.

METHODS: A retrospective cohort study included all consecutive adult ICU patients diagnosed with CAP between 1999 and 2017. Baseline demographics, patients' risk factors, and initial admission laboratory investigations were compared between survivors and nonsurvivors. A multivariate regression model was used to predict mortality.

RESULTS: During the study period, there were 3438 patients admitted to the ICU with CAP (median age 67 [Quartile 1, 3 (Q1, Q3) 51, 76] years) and 54.4% were males, of whom 1007 (29.2%) died. The survivors compared with nonsurvivors were younger (65 vs. 70 years), less likely to have chronic liver disease (2.4% vs. 10.5%), chronic renal failure (8.1% vs. 14.4%), and be immunocompromised (10.2% vs. 18.2%), and less frequently required mechanical ventilation or vasopressors (46.2% vs. 80.5% and 29.6% vs. 55.9%, respectively). Acute Physiology and Chronic Health Evaluation (APACHE) II score was significantly higher among nonsurvivors (median score 26 vs. 20) with a longer duration of mechanical ventilation and ICU stay. Using a multivariate regression model, age, APACHE II score, bilirubin level, vasopressors, and mechanical ventilation were significantly associated with increased mortality, while diabetes was associated with lower mortality.

CONCLUSION: Around one-third of patients admitted to the ICU with CAP died. Mortality was significantly associated with age, APACHE II score, vasopressor use, and mechanical ventilation. A comprehensive national registry is needed to enhance epidemiological data and to guide initiatives for improving CAP patients' outcomes.

Keywords:

Community-acquired pneumonia, critical care, hospital mortality, retrospective

Community-acquired pneumonia (CAP) is a leading cause of hospitalization, mortality, and health-care expenditure.[1] There are 102,000 annual deaths in the US due to CAP, with mortality rates at 1, 6, and 12 months of 13%, 23%, and 30%, respectively.[2] In Europe, CAP is responsible for at least 23,000 deaths annually.[3]

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Similarly, in Saudi Arabia, a point prevalence analysis of hospitalized CAP patients revealed a prevalence of 13.4%, with the highest being among older adults over 50 years.[4] These rates are widely variable depending on the healthcare setting in which it is managed and the severity of illness.[5-7]

Over the past 15 years, the need for CAP management in the intensive care unit (ICU) is steadily rising concomitantly with the increase in severe CAP.[8] CAP-associated complications, such as severe respiratory failure, sepsis, or septic shock, frequently lead to high medical care hospitalization.[9] Patient characteristics (age and gender) and comorbidities (immunological state, microbiological infections, and lack of response to therapy) usually impact the disease severity and subsequent morbidity and mortality.[10] International data report that the main factors influencing poor outcomes in hospitalized patients with severe CAP are sepsis and cardiac-related events;[11] however, statistics from Saudi Arabia are limited. The objective of this study is to describe the clinical characteristics and outcomes of patients admitted to the ICU with the diagnosis of CAP reflecting the experience of a tertiary center over an 18-year period.

Methods

Study setting and design

This was a retrospective cohort study of adult patients admitted to the medical-surgical ICU of King Abdulaziz Medical City, a tertiary care academic center in Riyadh, Saudi Arabia, between 1999 and 2017. The ICU has, over these years, grown from a 21 to an 80-bed unit with 24/7 in-house coverage by board-certified intensivists admitting around 900-3000 patients per year. The study was approved by the institutional review board of the Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia (RC20/634/R), and because of the study's retrospective nature, consent was waived.

Study population

The data were extracted from a database consisting of all the patients admitted to the ICU, in which a full-time data collector prospectively collected data. This study's target population was all ICU adult patients (age ≥ 14 years) diagnosed with CAP. CAP was defined clinically by the presence of symptoms and signs of lower respiratory tract infection, e.g., (fever, cough, dyspnea, and sputum production) with chest infiltrates on X-ray. For patients admitted more than once to the ICU within the same hospitalization, the initial admission was only considered in the analysis. We included the patient's demographics (age and sex) and medical history of chronic medical conditions as defined by the Acute Physiology and Chronic Health Evaluation (APACHE) II system, including chronic cardiac, respiratory, liver, and renal diseases, and immunosuppression. We also documented the presence of diabetes. Furthermore, we included the following variables in the first 24 h of ICU admission: Glasgow Coma Scale (GCS), APACHE II score, ratio of partial pressure of oxygen in arterial blood to fractional inspired oxygen (PaO_2/FiO_2 ratio), need for mechanical ventilation, and vasopressor therapy. The following first 24-h laboratory findings: creatinine, serum bilirubin, international normalized ratio (INR), and lactic acid were also documented.

Statistical plan and analysis

Patients were grouped into hospital survivors and nonsurvivors. Continuous variables were presented as medians and quartiles 1 and 3 (Q1 and Q3) and compared using *t*-test. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test. Multivariate logistic regression was used to identify factors associated with hospital mortality and the results were reported as odds ratios and 95% confidence intervals (CI). We used Statistical Analysis System, (version 9.0; SAS Institute, CARY, NC, USA) to analyze the data, and a $P < 0.05$ was considered statistically significant.

Results

During the study period, there were 3,438 patients admitted to the ICU with CAP. The median age was 67 (Q1, Q3: 51, 76) years, and 54.4% were males. Concomitant chronic medical conditions were prevalent: 29.4% for chronic lung disease, 27.1% for chronic cardiac disease, 12.8% for immunosuppression, 10.0% for chronic renal disease, and 4.8% for chronic liver disease. Around half of the patients (46.9%) were diabetic. One-third of patients (37.4%) needed vasopressors, and (56.3%) required mechanical ventilation, with a median APACHE II score of 22 [Table 1].

Around one-third (29.2%) of the CAP patients died. Compared to survivors, nonsurvivors were older, with a higher APACHE II score (26 vs. 20), and had more frequent chronic liver disease (10.5% vs. 2.4%) and chronic renal disease (14.4% vs. 8.1%). They had a lower GCS (median 11 vs. 15) and PaO2/Fio2 ratio (153 vs. 185). They were more likely to require mechanical ventilation (80.7% vs. 46.2%) and tracheostomy (13.3% vs. 6.6%) and had a longer duration of mechanical ventilation (6 days vs. 0 days). They more frequently required vasopressors (55.9% vs. 29.6%). Nonsurvivors, compared to survivors, also had more elevated bilirubin, creatinine, lactic acid, and INR. Furthermore, their length of stay in the ICU was longer (7.8 days vs. 3.4 days), although the in-hospital stay was not different (22 days vs. 19 days) [Tables 1 and 2].

Table 1: Comparison of baseline characteristics of patients admitted to the intensive care unit with community-acquired pneumonia based on survival status

Variable	All (*n*=3438)	Survivor (*n*=2424)	Nonsurvivor (*n*=1007)	*P*
Demographics				
Age (years), median (Q1–Q3)	67 (51–76)	65 (47–75)	70 (58–78)	<0.001
Sex (male), *n* (%)	1870 (54.4)	1282 (52.9)	586 (58.2)	
Chronic diseases, *n* (%)				
Chronic liver disease	163 (4.8)	58 (2.4)	105 (10.5)	<0.001
Chronic lung disease	1009 (29.4)	774 (32.0)	232 (23.1)	<0.001
Chronic renal disease	343 (10.0)	195 (8.1)	145 (14.4)	<0.001
Immunocompromised state	440 (12.8)	247 (10.2)	193 (18.2)	<0.001
Chronic cardiac disease	930 (27.1)	640 (26.5)	287 (28.6)	0.200
Diabetes	1611 (46.9)	1129 (46.6)	477 (47.4)	0.670
MV, *n* (%)	1936 (56.3)	1119 (46.2)	813 (80.7)	<0.001
Vasopressors, *n* (%)	1287 (37.4)	718 (29.6)	563 (55.9)	<0.001
APACHE II, median (Q1-Q3)	22 (17–28)	20 (15–25)	26 (21–32)	<0.001
Laboratory findings in the first 24 h, median (Q1–Q3)				
Bilirubin (mmol/L)*	13 (8–24)	11 (7–19)	18 (10–40)	<0.001
Creatinine (μmol/L)*	103 (63–200)	90 (60–172)	139 (77–246)	<0.001
Lactic acid (mg/dL)*	1.7 (1.1–2.9)	1.6 (1.1–2.5)	2.2 (1.4–4.4)	<0.001
INR*	1.2 (1.1–1.5)	1.1 (1.0–1.4)	1.4 (1.1–1.9)	<0.001
PaO_2/Fio_2 ratio*	174 (115–258)	185 (124–268)	153 (96–225)	<0.001
GCS, median (Q1–Q3)*	14 (10–15)	15 (11–15)	11 (7–15)	<0.001

*Data on these variables is available for the following number of patients-Bilirubin=2445, creatinine=3181, Lactic acid=2716, INR=3109, PaO_2/FiO_2 ratio=3217, GCS=3293. Categorical data are presented as frequencies and percentages. Continues data are presented as median and quartiles 1 and 3 (Q1–Q3). APACHE=Acute Physiology and Chronic Health Evaluation, PaO_2/FiO_2 ratio=The ratio of arterial oxygen partial pressure to fractional inspired oxygen, GCS=Glasgow Coma Scale, INR=International normalized ratio, MV=Mechanical ventilation

Table 2: Outcomes of patients admitted to the intensive care unit with community-acquired pneumonia on survival status

Variable	Median (Q1–Q3)			*P*
	All (*n*=3438)	Survivors (*n*=2424)	Nonsurvivors (*n*=1007)	
ICU LOS	4.2 (1.3–11.0)	3.4 (1.0–8.7)	7.8 (2.5–16.7)	<0.001
Hospital LOS	3 (2–43)	19 (11–41)	22 (9–46)	0.750
MV duration	2 (0–8)	0 (0–4)	6 (1–16)	<0.001
Tracheostomy, *n* (%)	294 (8.5)	159 (6.6)	134 (13.3)	<0.001

Categorical data are presented as frequencies and percentages. Continues data are presented as median and interquartile 1 and 3 (Q1–Q3). ICU=Intensive care unit, LOS=Length of stay, MV=Mechanical ventilation

On multivariate logistic regression, increasing age, APACHE II score, and bilirubin were found to be associated with increased hospital mortality (age: odds ratio [OR] 1.02, 95% CI: 1.01,1.02; APACHE score: OR 1.07, 95% CI: 1.05,1.08, and bilirubin: OR: 1.01, 95% CI: 1.01,1.01 for each unit increase, respectively). In addition, mechanical ventilation, as well as vasopressor use, was also associated with increased hospital mortality (mechanical ventilation: OR 3.49, 95%CI: 2.87, 4.24; vasopressor use: OR: 1.45, 95%CI: 1.22, 1.73, respectively). However, diabetes was associated with decreased mortality by 25% [OR: 0.75, 95%CI: 0.63, 0.89, Table 3].

Discussion

We report the clinical characteristics and outcomes of patients admitted to the ICU with the diagnosis of CAP, reflecting the experience of a tertiary center over an 18-year period. Our findings showed that less than a third of CAP patients who needed ICU management died. Mortality was associated with age, APACHE II score, bilirubin, mechanical ventilation, and vasopressor therapy.

To the extent of our knowledge, this is the largest study in Saudi Arabia of severe CAP.[12-14] Globally, the in-hospital mortality rate in severe CAP requiring ICU management remains high despite this continuous medical improvement.[15] In West China Hospital, Dong Huang and his group reported that CAP-associated mortality reached 40% for data collected between 2011 and 2018.[16] Another single-center Spanish study included 3719 severe CAP patients, confirming this high (38%) in-hospital mortality.[17]

Age is inversely related to individual immunity defense, leading to morbidity and mortality. A 1-year

Table 3: Multivariate regression to define the association with survival among patients admitted to the intensive care unit with community-acquired pneumonia

Variables	OR	95% CI	*P*
Age (for every year increase)	1.02	1.01–1.02	<0.001
APACHE II (for every unit increase)	1.07	1.05–1.08	<0.001
Bilirubin (for every unit increase)	1.01	1.01–1.01	<0.001
MV	3.49	2.87–4.24	<0.001
Vasopressors	1.45	1.22–1.73	<0.001
Diabetes	0.75	0.63–0.89	0.001

APACHE=Acute Physiology and Chronic Health Evaluation, OR=Odds ratio, CI=Confidence interval, MV=Mechanical ventilation

increase over 65 has a higher likelihood of severe CAP and ICU hospitalization. We reported a significant 5-year difference between survivors and nonsurvivors, confirming previous literature results.[18,19] Although the prevalence of CAP notably rises five times with age, chronological age fails to predict a poorer outcome for elderly patients hospitalized with CAP according to few studies;[20] however, our findings showed that with each year increase, CAP-related mortality risk increased by 2%.

Chronic pulmonary disease is a CAP risk factor that increases CAP incidence by two to four times.[21,22] Kaplan *et al*. compared 158,960 CAP patients and 794,333 hospitalized controls matched for age, sex, and race hospitalized for reasons other than CAP.[19] The incidence of chronic pulmonary disease was significantly higher in CAP patients than in controls ($P < 0.001$), with more frequent hospital mortality. Similarly, in our study, chronic pulmonary disease was present in one-third of CAP patients and significantly associated with mortality. Furthermore, most patients with severe CAP face respiratory failure and require mechanical ventilator support and endotracheal intubation. That is consistent with other studies where mortality was higher in mechanically ventilated patients.[23] Mechanical ventilation was also significantly associated with mortality (OR: 3.49 [95% CI: 2.87–4.24]; $P < 0.0001$).

The PaO_2/FiO_2 measures the extent of lung injury and may be associated with mortality. Our study population had a median PaO_2/FiO_2 ratio that was significantly higher in the survivors, which was 185 compared to 153. Likewise, 144 adult mechanically ventilated patients for respiratory failure caused by CAP were found to have significantly higher mean PaO_2/FiO_2 ratio for survivors (166 vs. 101).[24]

Not surprisingly, survivors had a lower APACHE II with a median of 20 versus 26, and every unit of measurement increase in APACHE II score was significantly associated with increased mortality (OR: 1.07 [95% CI: 1.05–1.08]; $P < 0.0001$).

Diabetes, the most common chronic disease observed locally, was unexpectedly significantly associated with lower mortality (OR.75 [95% CI: 0.63–0.89]). This paradoxical association has been reported frequently in the literature.[25,26] This lack of association has been described before and referred to as the diabetes paradox, which may also be related to the obesity paradox.[25,26]

Strengths of our study include the large sample size and prospective data collection. Limitations include being a single-center study and the lack of microbiological data.

Conclusion

CAP was a common cause of ICU admission. Around one-third of patients admitted to the ICU with CAP died. Mortality was significantly associated with age, APACHE II score, bilirubin, and mechanical ventilation. A comprehensive national registry is needed to enhance epidemiological data and improve CAP patients' outcomes.

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Conflicts of interest
There are no conflicts of interest.

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