

Patient characteristics and ICU mortality predictors in severe community acquired pneumonia

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Abstract

Background: Severe community-acquired pneumonia (CAP) is a potentially life-threatening infection worldwide and frequently requires ICU admission with relatively high mortality. **Objectives:** To describe patient's characteristics, mortality rate and etiological pathogens in patients with severe CAP who required ICU admission and to determine the predictors of mortality.

Methods: This prospective study included 95 consecutive patients admitted to the ICU with severe CAP. All patients were subjected to clinical examination, assessment by APACHE II and CURG-65 scoring as well as radiological, laboratory and microbiological examination. Different possible mortality risks were assessed for statistical analysis.

Results: The overall mortality was 44.2 %. The most frequently predicted high risk of mortality were requirement for MV , PaO₂/FiO₂ < 250, CURB-65 score ≥ 3 , multilobar infiltrate in chest x ray, age > 65 years, APACHE II score > 20 , serum urea > 30 mg/dL, serum creatinine >1.0 mg/dL, shock at admission, polymicrobial identification, current smoking, total leucocyte counts < 4 or > 11 x 10⁹/) and presence of \geq two comorbidities. CURB-65 score 2 and presence of no or only one comorbidity on admission showed more favorable outcome . Microbiological identifications were obtained in 58.9% and Streptococcus pneumonia and Staphylococcus aureus were the most common isolated pathogens.

Conclusion: ICU patients admitted with severe CAP are associated with high mortality. Early identifying mortality predictors is crucial for meticulous follow up and tailoring

more suitable therapeutic planning which may have the potential of improving the outcome of critically ill patients with severe CAP.

Keywords: Severe CAP, ICU, prognostic factors, microbial etiology, APACHE II score, CURB-65

Abbreviations: ICU (intensive care unit), APACHE (acute physiology and chronic health evaluation), CURB-65 (confusion, blood urea nitrogen, respiratory rate, blood pressure, age more than 65 years)

Introduction

Community-acquired pneumonia (CAP) is a serious and potentially life-threatening infection worldwide. Severe CAP is defined as pneumonia which requires intensive care unit (ICU) admission (1, 2). Although 2–20% of CAP patients require ICU admission (3-6), the mortality rates can be as high as 20–50% (7, 8). These patients commonly have impaired host defenses, co-morbidities and different applied invasive procedures (9).

The knowledge of the pathogenic patterns that cause severe CAP is crucial for selection of antibiotic therapy. The different reported rates for the polymicrobial etiology of CAP range considerably between 5.7 and 38.4% (10-13).

Many studies have investigated CAP co-morbidities and prognostic factors (14-21), and guidelines have been proposed by several medical societies to define the proper management of patients with CAP (22-24).

This prospective study was conducted in order to assess clinical characteristics, etiology, predictors of mortality as well as the outcome for severe CAP patients admitted to the ICU and to compare our results with other studies.

Patients and methods

Patients

The present study was conducted in the general ICU of Fayoum University Hospital and the respiratory ICU of El-Minia University Hospital from November 2013 to September 2015. The study included 95 consecutive patients admitted to the ICU for

severe CAP after giving consent from the patients or their relatives. All ages and both sexes were included.

CAP was diagnosed by presense of acute lower respiratory tract illness (cough and at least one of the other lower respiratory tract symptoms, e.g., dyspnea or chest pain) with evidence of systemic illness (temperature more than 38 °C and/or fever, sweating, shivers, aches) along with demonstrable consolidation or new radiographic shadowing on chest radiography with no other explanation (1).

Patients with severe CAP were diagnosed when one major criterion or three minor criteria of the Infectious Disease Society of America/American Thoracic Society (IDSA/ATS) guidelines were met (1). The major criteria include either the presence of septic shock or a need for mechanical ventilation. The 9 minor criteria include: respiratory rate ≥ 30 breaths/min, $\text{PaO}_2/\text{FiO}_2 \leq 250$, confusion and/or disorientation, hypotension requiring aggressive fluid resuscitation, multilobar infiltrates by radiography, presence of uremia ($\text{BUN} \geq 20$ mg/dl), leukopenia ($\text{WBC count} < 4000$ cells/mm³), thrombocytopenia (platelet count $< 100,000$ platelets/mm³) and hypothermia (temperature < 36 °C).

Diagnosis of septic shock was defined as severe sepsis associated with sustained hypotension with a systolic blood pressure less than 90 mmHg despite intravenous fluids or the need for vasopressors (22).

Exclusion criteria were one or more of the following : missing patient data, length of ICU stay of less than 24 hours, management by cardiopulmonary resuscitation on hospital admission and unestablished diagnosis of CAP.

Data collection:

All patients were examined within 24 hours of admission and subjected to the following:

- Full medical history as taken from all patients or their relatives with special emphasis to: age, sex, current smoking status and other co-morbidities including chronic chest diseases as COPD, diabetes mellitus, chronic cardiac diseases, chronic renal failure,

chronic neurological diseases, chronic liver diseases, neoplasm, immunosuppressive drugs and steroids.

- Signs and symptoms of CAP at ICU admission
- Vital signs on ICU admission at ICU admission
- Chest radiograph features at ICU admission
- Laboratory data (CBC, CRP, PT, PC, serum sodium, potassium, urea, creatinine, AST and ALT) and arterial blood gases on admission and daily during ICU stay.
- Microbial identification procedures: bacterial and fungal cultures of sputum and deep tracheal aspirate, blood cultures as well as nasopharyngeal swabs for virus PCR (in selected cases)
- Mechanical ventilation (MV) requirement on ICU admission and during the hospital stay and duration of MV.
- Duration of ICU stay
- Overall in-ICU mortality
- **APACHE II score:** All patients were evaluated according to the acute physiology and chronic health evaluation (APACHE II) scoring system at the time of admission (25). The APACHE II score contains three components: age, acute physiologic score (APS), and chronic health. The total APACHE II score ranges from 0 to 71 and the higher scores imply a less favorable outcome. The acute physiologic score includes Glasgow Coma Score (GCS) as well as other physiologic variables. The 11 physiologic variables in the acute physiologic score contribute up to 4 points for each parameter. The patient's Glasgow Coma Score can add a further 15 points. Patients with severe organ system insufficiency and immuno-compromised patients receive 5 points for chronic health..
- **CURB-65 score:** All patients were evaluated on admission according to CURB-65 score which is a clinical prediction score which has been recommended by the British Thoracic Society for the assessment of severity of pneumonia and validated for predicting mortality in community-acquired pneumonia (26). The score is an

acronym for the measured risk factors which include: Confusion of new onset, Blood Urea nitrogen >7 mmol/l (19 mg/dL), Respiratory rate ≥ 30 breaths/minute, Blood pressure < 90 mmHg systolic or diastolic blood pressure ≤ 60 mmHg, Age ≥ 65 . . Each risk factor scores one point, for a maximum score of 5.

Patients were followed up until ICU discharge or demise . Type and duration of ventilatory support , development of complications during ICU stay, length of ICU stay and cause of death were recorded.

Statistical analysis

All statistical analyses were performed using SPSS statistics for Windows, version 17.0. Data were expressed as the mean \pm standard deviation for continuous variables and the number with percentage for categorical data. Comparisons between two categorical variables were made with chi-square. Continuous data were tested with Student's t-test. P values below 0.05 were taken to indicate statistical significance. All of the variables attaining a value < 0.05 in the univariate analysis were included in the multiple logistic regression analysis models with a stepwise forward selection.

Results

Patient characteristics

The present study included 95 patients who had a definitive diagnosis of severe CAP requiring ICU admission. The main baseline patient characteristics and underlying conditions are listed in table 1. Male sex represented 68.4 % of the patients and the mean age was 56.0 ± 12.7 years. Smokers constituted 38.4% of the male patients (25 patients) whereas no female patient had gave a smoking history. Seventy five patients (78.9%) had one or more comorbidities. The most frequent associated comorbidity was COPD (26.3%), cardiac disease (23.2%), and diabetes mellitus (17.5%). Initial vital signs, laboratory values are listed in table (1). The mean CURB-65 score on admission was 3.2 ± 1.2 (mean \pm SD), and the mean APACHE II score was 22.4 ± 7.2 (mean \pm SD). Twenty five (26.3 %) patients were presented with shock. Bilateral or multilobar infiltrate was present in 46 patients (52.6 %). Sixty one (64.2 %) patients required mechanical

ventilation additional 14 patients required mechanical ventilation later on during the ICU stay [total 75 (78.9 %)]. The overall mortality was 44.2 % (42 patients).

Table (1): Patient characteristics and underlying conditions

| | |
|--|------------------|
| Patients (n: 95) | |
| Males (n &% related to all patients) | 65 (59.6 %) |
| Smokers (n &% related to males) | 25 (38.4%) |
| Females: (n &% related to all patients) | 30 (40.4%) |
| Smokers : (n &% related to females) | None |
| Age (years) (mean \pm SD) | 59.0 \pm 16.8 |
| Comorbidity: (n: 75) (78.9%) | |
| COPD (n &%) | 25 (26.3 %) |
| Cardiac disease (n &%) | 22 (23.2 %) |
| Diabetes mellitus (n &%) | 16 (16.8 %) |
| Neoplasm (n &%) | 10 (10.5 %) |
| Immunosuppression (n &%) | 12 (12.6 %) |
| Steroids (n &%) | 15 (15.8 %) |
| Neurological diseases (n &%) | 7 (7.4 %) |
| Liver diseases (n &%) | 5 (5.3 %) |
| Chronic renal failure (n &%) | 5 (5.3 %) |
| Prognostic scores | |
| APACHE II score (mean \pm SD) | 22.4 \pm 7.2 |
| CURB-65 score (mean \pm SD) | 3.2 \pm 1.2 |
| Vital signs on ICU admission | |
| HR (beats/m) (mean \pm SD) | 129.2 \pm 19.2 |
| Temperature °C (mean \pm SD) | 38.2 \pm 0.8 |
| SBP mmHg (mean \pm SD) | 91.2 \pm 21.3 |
| DBP mmHg (mean \pm SD) | 50.3 \pm 12.6 |

| | |
|---|-------------------|
| PaO ₂ /FiO ₂ (mean \pm SD) | 152.4 \pm 90.2 |
| Laboratory data on ICU admission | |
| Hemoglobin (g/dl) (mean \pm SD) | 11.2 \pm 2.1 |
| Total Leukocyte count (x 10 ⁹ /L) (mean \pm SD) | 13.6 \pm 4.6 |
| Platelets (x 10 ⁹ /L) (mean \pm SD) | 210.2 \pm 123.4 |
| CRP (mg/dl) (mean \pm SD) | 160.2 \pm 90.3 |
| Serum sodium (mmol/l) (mean \pm SD) | 141.1 \pm 4.2 |
| Serum potassium (mmol/l) (mean \pm SD) | 3.6 \pm 1.1 |
| Serum urea (mg/dl) (mean \pm SD) | 28.1 \pm 10.4 |
| Serum Creatinine (mg/dl) (mean \pm SD) | 1.3 \pm 0.6 |
| Bilateral multilobar infiltrate in CXR (n &%) | 46 (48.4 %) |
| Patients with initial MV required (n &%) | 61 (64.2 %) |
| Patients with MV required (initially and during ICU stay) (n &%) | 75 (78.9 %) |
| Duration of MV (day) (mean \pm SD) | 11.7 \pm 6.2 |
| Shock at admission (mean \pm SD) | 25 (26.3 %) |
| Length of ICU stay (day) (mean \pm SD) | 12.2 \pm 18.2 |
| Microbial identification (n &%) | 56 (58.9 %) |
| Positive blood culture (n &%) | 18 (18.9 %) |
| Overall mortality (n &%) | 42 (44.2 %) |

Prognostic factors

The overall mortality rate was 44.2 % among studied patients. Comparison between non-survivors and survivors was studied regarding patient characteristics and different parameters on admission including vital signs and laboratory findings.

The non-survivors had a significantly higher mean age than the survivors. They had also significantly higher APACHE II and CURG-65 scores, hear rate, lower systolic and diastolic blood pressure on admission than the survivor group. The non-survivors

showed also significantly lower PaO₂/FiO₂ and lower mean platelet count than survivors. The mean total leucocytic count, CRP, blood urea and serum creatinine were significantly higher in non-survivors compared to survivors. The duration of MV was significantly higher in non-survivors. All non-survivors required MV compared to 62.3% of survivors.

Table (2): Comparison between surviving and non-surviving patients with severe CAP

| | Non-survivors (n:42) | Survivors (n:53) | p-value |
|--|-----------------------------|-------------------------|----------------|
| Age (year) | 63.2 ± 10.5 | 52.5 ± 12.9 | 0.01 |
| Vital signs on admission | | | |
| HR (beats/m) | 135.4 ± 32.1 | 115.2 ± 21.0 | 0.09 |
| Temperature °C | 38.6 ± 1.0 | 37.9 ± 0.7 | 0.5 |
| SBP mmHg | 85.5 ± 19.2 | 97.2 ± 18.1 | 0.01 |
| DBP mmHg | 45.9 ± 9.7 | 53.9 ± 11.1 | 0.01 |
| APACHE II score | 26.1 ± 6.9 | 18.5 ± 3.7 | 0.001 |
| CURB-65 score | 3.7 ± 1.2 | 2.3 ± 1.2 | 0.005 |
| Lab investigation on admission | | | |
| PaO ₂ /FiO ₂ | 128.4 ± 67.2 | 182.2 ± 69.2 | 0.04 |
| Hemoglobin g/dl | 11.1 ± 2.3 | 10.2 ± 2.2 | 0.1 |
| Total Leukocyte count (x 10 ⁹ /L) | 15.9 ± 6.4 | 11.4 ± 3.1 | 0.01 |
| Platelets (x 10 ⁹ /L) | 171.5 ± 67.2 | 248.4 ± 48.4 | 0.01 |
| CRP mg/l | 158.1 ± 50.9 | 103.1 ± 24.2 | 0.01 |
| Serum sodium (mmol/l) | 140.5 ± 3.7 | 139.2 ± 2.6 | 0.2 |
| Serum potassium (mmol/l) | 3.8 ± 1.2 | 3.7 ± 1.1 | 0.6 |
| Serum urea (mg/dl) | 44.8 ± 11.8 | 29.1 ± 7.5 | 0.02 |
| Serum creatinine (mg/dl) | 2.9 ± 1.3 | 1.2 ± 1.1 | 0.01 |
| Duration MV (day) | 15.2 ± 7.9 | 7.2 ± 3.4 | 0.01 |
| Length of ICU stay (day) | 13.9 ± 5.7 | 14.2 ± 4.6 | 0.5 |

Assessment of different risk parameters and risk ratios for in-ICU mortality among patients with severe CAP:

Different risk parameters for predicting in-ICU mortality were studied by univariate analysis and risk ratios for these parameters were calculated (table 3). Parameters which carried significantly higher risk ratios for mortality predication included patients requirement for MV required (RR:25.5), PaO₂/FiO₂ < 250 (RR:11.2) CURB-65 score \geq 3 (RR:10.7), Bilateral or multilobar infiltrate in chest x ray (RR: 8.9) and age > 65 years (RR:7.13). Other risks included APACHE II score > 20 (RR:5.76), serum urea > 30 mg/dL (RR:5.33), serum creatinine >1.0 mg/dL (RR:3.5), shock at admission (RR:4.65), polymicrobial identification (RR:4.44), current Smoking (RR: 3.15), total leucocyte counts < 4 or > 11 x 10⁹/) (RR:3.55) and presence of \geq two comorbidities (RR:1.93). On the other hand, CURB-65 score 2 and presence of no or only one comorbidity on admission showed more significant favorable outcome (RR: 0.08, 0.34 0.42 respectively). Off the 62 patients who initially required MV on admission, only 22 survived and mortality was 62.9% among those patients.

Table (3): Univariate analysis for different risk parameters for in-ICU mortality among patients with severe CAP

| | Number and percentage in all patients (95) | Number and percentage in non-survivors (n:42) | Number and percentage in survivors (n: 53) | Relative risk | 95% CI | p-value |
|--------------------------------------|--|---|--|---------------|-----------|---------|
| Age > 65 years | 46 (48.4%) | 31 (73.8 %) | 15 (28.3%) | 7.13 | 6.19-8.29 | 0.001 |
| Male sex | 65 (68.4%) | 32 (76.2 %) | 33 (62.3 %) | 1.94 | 1.52-2.64 | 0.01 |
| No associated comorbidity | 20 (21.1%) | 5 (11.9%) | 15 (28.3%) | 0.34 | 0.29-0.41 | 0.01 |
| Presence of one comorbidity | 52 (53.7%) | 18 (42.9 %) | 34 (64.2 %) | 0.42 | 0.12-0.71 | 0.04 |
| Presence of \geq two comorbidities | 23 (24.2%) | 13 (46.4 %) | 10 (18.9 %) | 1.93 | 1.22-2.53 | 0.01 |
| COPD | 25 (26.3%) | 15 (35.7%) | 10 (18.9%) | 2.39 | 2.01-2.82 | 0.01 |
| Current Smoking | 30 (31.6%) | 19 (45.2%) | 11 (20.8%) | 3.15 | 2.94-3.35 | 0.01 |
| APACHE II score > 20 | 28 (29.5%) | 13 (30.9 %) | 15 (28.3 %) | 5.76 | 4.17-6.14 | 0.006 |
| CURB-65 score \geq 3 | 41 (43.2%) | 31 (73.8 %) | 11 (20.8 %) | 10.7 | 9.11-12.7 | 0.001 |

| | | | | | | |
|--|------------|--------------|-------------|------|-------------|-------------|
| CURB-65 score 2 | 53 (55.8%) | 11 (26.2%) | 42 (79.2%) | 0.08 | 0.065-0.092 | 0.001 |
| Total leucocyte counts < 4 or > 11 x 10⁹/l | 85 (89.5%) | 40 (95.2 %) | 45 (84.9 %) | 3.55 | 3.07-5.13 | 0.01 |
| PaO₂/FiO₂ < 250 | 51 (53.7%) | 36 (85.8 %) | 15 (28.3 %) | 11.2 | 10.9-12.6 | 0.001 |
| Na < 135 mmol/l | 23 (24.2%) | 11 (26.2 %) | 12 (22.6 %) | 1.21 | 0.83-1.93 | 0.45 |
| Serum urea > 30 mg/dL | 20 (21.1%) | 15 (35.7 %) | 5 (9.4 %) | 5.33 | 4.34-6.21 | 0.01 |
| Serum creatinine >1.0 mg/dL | 19 (20.0%) | 13 (31%) | 6 (11.%) | 3.5 | 3.1-4.2 | 0.01 |
| Shock at admission | 25 (26.3%) | 19 (45.2 %) | 6 (11.3 %) | 4.65 | 3.91-5.28 | 0.001 |
| Bilateral or multilobar infiltrate in CXR | 46 (48.4%) | 32 (76.2 %) | 14 (26.4 %) | 8.9 | 8.14-9.24 | 0.01 |
| Microbial identification | 56 (58.9%) | 30 (71.4 %) | 26 (49.0 %) | 1.76 | 1.2-2.10 | 0.43 |
| Polymicrobial identification | 29 (30.5%) | 20 (47.6%) | 9 (17%) | 4.44 | 3.9-5.12 | 0.01 |
| Positive blood culture | 18 (18.9%) | 8 (19.0 %) | 10 (18.9 %) | 1.01 | 0.95-1.25 | 0.5 |
| Patients with initial MV required | 61 (64.2%) | 39 (92.8 %) | 22 (41.5 %) | 4.23 | 3.94-5.01 | 0.01 |
| Patients with MV required | 75 (78.9%) | 42 (100.0 %) | 33 (62.3 %) | 25.5 | 22.2-27.4 | 0.001 |
| Length of ICU stay > 10 days | 73 (76.8%) | 32 (76.2 %) | 41 (77.4 %) | 0.94 | 0.09-1.06 | 0.59 |

Microbial identification

Microbiological identification could be obtained in 56 cases (58.9%). Polymicrobial affection could be documented in 29 cases (30.2% of all cases and 51.8% of patients with positive microbial cultures). Blood cultures were positive in 10 (17.5 %) of the cases. The most frequently isolated etiological agents were streptococcus pneumoniae (58.9%) and staphylococcus aureus (42.8 % of patients) followed by pseudomonas aeruginosa (19.6%) and klebsiella pneumoniae (17.8%) . Other less common isolated microbial agents were escherichia coli (7.1%), influenza A (5.4%) and candida (5.4%) (table 4). A positive blood culture was obtained in 18 cases (18.9 % of

patients), the majority was streptococcus pneumoniae (50%) and staphylococcus aureus (39%) (table 4).

Table (4): Microorganisms isolated from the clinical culture specimens

| Causative organisms | Number and percentage * | Positive blood Culture (N&%) |
|-------------------------------|--------------------------------|---|
| Identified | 56 (58.9 %) | 18 (18.9 %)** |
| Streptococcus species | 30 (53.5 %) | 9 (50%)*** |
| Staphylococcus aureus | 24 (42.8 %) | 7 (39.0%)*** |
| Pseudomonas aeruginosa | 11 (19.6 %) | 1 (5.5%)*** |
| Klebsiella pneumoniae | 10 (17.8 %) | 1 (5.5 %)*** |
| Escherichia coli | 4 (7.1 %) | None |
| Influenza A | 3 (5.4 %) | None |
| Candida | 3 (5.4 %) | None |

*Number and percentage in relation to total number of identified organisms in 56 positive cultures (total 85 in 56 cases in which 29 cultures with polymicrobial identification).

**Number and percentage in relation to total number of studied patients (95 patients).

***Number and percentage in relation to number of identified positive blood cultures (18).

Discussion

In the present study, we prospectively determined patient's characteristics, mortality rate, mortality predictors and etiological pathogens in patients with severe CAP who required ICU admission. The overall mortality of the present study was 44.2%, which was high and similar to those of previous studies. Previous reports from the Middle East region have indicated ICU mortality rates of 37% (27,28). A meta-analysis showed an average mortality of 36.5% for CAP patients admitted to the ICU, with a range of 21.7 % to 57.3% (21). Our results showed that mortality was 62.9% among patients who had required MV initially on ICU admission .This high mortality consists with other studies which revealed higher mortality rate exceeding 60% in patients with severe CAP requiring intubation and mechanical ventilation (29, 30, 33).

It is suggested that the outcome of CAP patients in the ICU depends on the interactions between various factors such as age, genetic predisposition, comorbidities,

presence of organ failure, host defenses, microbial virulence, bacterial load, timing of ICU admission, choice of antibiotics and adjuvant therapies **(31-33)**.

The mean age of ICU admitted patients with severe CAP varies in different studies **(17, 34, 35)**. The mean age of our patients was 59.3 ± 16.8 and was significantly higher in non-survivors. In the present study, the mortality rate in patients older than 65 years was 73.8 %; which was significantly higher than those younger than 65 years who revealed 28.3% mortality ($p = 0.03$). In addition, age > 65 carried 7.13 mortality risk compared to patients with lower ages. These results are in consistent with previous studies **(29, 33, 36-43)**. These results indicate that elderly patients may have a depressed immune response to infection and may be at higher risk of acquiring over-whelming infection **[44]**.

The present study found that presence of one comorbidity had significant reduced risk of mortality and this is consistent with other previous studies **(8, 16, 40, 41)**. Patients with two or more comorbidities showed about 2 fold mortality risk particularly COPD patient who had about 3 fold mortality risk . This is consistent with other studies which found a significant impact of COPD, DM, neoplasm, immunosuppressive drugs, and chronic renal failure on mortality of severe CAP **(28, 29,)**.

Notably, our results revealed that current smokers had 3.15 fold increase of mortality (45.2% mortality in smokers compared to 20.8% survival). All smokers were males which can explain the 2 fold increase of mortality among males not the effect of gender itself. This comes in agreement with the known deleterious effect of smoking on the respiratory tract and its suppressive effects on the defense host mechanisms respiratory system.

The present study revealed that APACHE II scores were significantly higher in the non-surviving patients score and APACHE II > 20 score had carried about 6 fold mortality risk. This comes in agreement with other studies reporting higher APACHE II scores as independent predictors of mortality **(28, 41, 45, 46)**.

Our patients included 42 patients with CURB-65 score ≥ 3 and 53 with CURB-65 score 2. We found that non-surviving patients had significant higher mean CURB-65 scores and CURB-65 score ≥ 3 was associated with 73.8% mortality and carried 10.7 fold

mortality risk compared to patients with CURB-65 score 2. On the other hand, patients with CURB-65 score 2 had 26.2% mortality and carried significantly lesser mortality risk compared to patients with CURB-65 score ≥ 3 (RR: 0.08) . This comes in concordance with other reports concluded that more grave outcome in severe CAP was associated with higher CURB-65 scores **(28, 47-49)** On the other hand, Phua et al **(50)** found that IDSA/ATS minor criteria were more valuable than CURB-65 for predicting hospital mortality and ICU admission,

The present study found that $\text{PaO}_2/\text{FiO}_2$ ratio on admission was significantly higher in the surviving group and $\text{PaO}_2/\text{FiO}_2 < 250$ was encountered in 85.8 % of non-survivors who carried 11.2 fold mortality risk. In the study of Luna et al **(51)**, $\text{PaO}_2/\text{FiO}_2 < 250$, aerobic Gram-negative pathogen, chronic renal failure, Glasgow score < 15 , malignancy, and aspiration pneumonia were associated with more worse outcome. On the contrary, there were no significant differences between the survivors and non-survivors regarding $\text{PaO}_2/\text{FiO}_2 < 250$ in two studies **(29, 41)**. However, it is suggested that hypoxemia is associated with impending respiratory failure, subsequent ICU admission **(48, 52)**, and mortality **(53)** in patients with CAP, reflecting the severity of primary organ impairment in this illness.

It was found that patients who had been presented with multilobar infiltrates by CXR carried had poor outcome in the present study. Multilobar affection was encountered in 76.2% of non-survived patients compared to only 26.4% of the survived patients. Moreover, presentation with multilobar lesions was highly predictive of mortality in severe CAP carrying 8.9 fold risk. This finding is consistent with reports from other studies **(29, 40, 46, 48, 54-57)** which revealed that this finding is a very important and valuable clinical feature in the assessment of disease severity.

In our study, univariate analysis had shown that septic shock was statistically higher in non-survivors compared to survivors and was highly predictive of mortality (RR: 4.56). These results were also consistent with other different reports **(28, 34, 40, 48,)**

In the present study, serum urea and creatinine were significantly higher in the non-surviving group and serum urea > 30 mg/dL and creatinine > 1 mg/dL carried 5.3

and 3.5 increased mortality risk respectively on univariate analysis. These results are consistent with those of previous studies **(28, 40, 46, 51)**.

In the present study, the defined microbial etiology of CAP had been established in 58.9 %, which was higher than the finding of Cillóniz et al (54 %) **(55)**, Yoshimoto et al (44.4 %) **(59)** and Wilson et al (46 %) **(36) studies** and lower than Paganin et al (78.6 %) **(40)** and PROWESS (60 %) **(60) studies**.

The present study found that *Streptococcus pneumoniae* and *Staphylococcus aureus* were the most common pathogen by monomicrobial and polymicrobial isolation (58.9 % and 53.5 % respectively) followed by aerobic Gram-negative organisms (37.4%). Results reported by PROWESS study found that *Streptococcus pneumoniae* was most common at (26%), followed by *Staphylococcus aureus* (14%), aerobic Gram-negative rods as a group (15%) **(60)**. Yoshimoto et al **(59)** found that *Streptococcus pneumoniae* was the most common isolated pathogen (13.9%), followed by *Pseudomonas aeruginosa* (8.3%) and *Klebsiella pneumoniae* (6.9%). Wilson et al **(36)** found that the most frequently identified cause was *Streptococcus pneumoniae* (13.5 %), followed by influenza A (9.4 %), *Haemophilus influenzae* (5.2 %), and *Staphylococcus aureus* (4.2%).

Undoubtedly, differences in methodology and the influence of geography on etiology, can contribute to these differences in percentages of identification and isolated organisms. *Streptococcus pneumoniae* was the most common organism in our study and most of previous studies **(28, 36, 40, 49, 59, 60)**. *Staphylococcus aureus* was the second most common organism in severe CAP in our study. Khawaja et al **(46)** found that *Staphylococcus aureus* was the most common identified pathogen causing severe CAP. Its incidence has been increasing in recent years, ranging from 12% to 22%, as reported in several patient series **(8, 18, 61)**.

In conclusion, ICU patients admitted with severe CAP are associated with high mortality. The most frequently predicted high risk of mortality were requirement for MV , PaO₂/FiO₂ < 250, CURB-65 score ≥ 3, multilobar infiltrate in chest x ray, age > 65 years, APACHE II score > 20 , serum urea > 30 mg/dL, serum creatinine >1.0 mg/dL,

shock at admission, polymicrobial identification, current smoking, total leucocyte counts < 4 or $> 11 \times 10^9$) and presence of \geq two comorbidities. CURB-65 score 2 and presence of no or only one comorbidity on admission showed more favorable outcome . Microbiological identifications were obtained in 58.9% and Streptococcus pneumonia and Staphylococcus aureus were the most common isolated pathogens. Early identifying these predictors is crucial for focusing these risks for meticulous follow up and tailoring more suitable therapeutic planning. This will have the potential of improving the outcome of critically ill patients with severe CAP.

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