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ORIGINAL ARTICLE

Clinical, epidemiological, and etiological profile of inpatients with community-acquired pneumonia in a public hospital in the interior of Brazil

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ABSTRACT

Objective: To describe the patient profile, mortality rates, the accuracy of prognostic scores, and mortality-associated factors in patients with community-acquired pneumonia (CAP) in a general hospital in Brazil. **Methods:** This was a cohort study involving patients with a clinical and laboratory diagnosis of CAP and requiring admission to a public hospital in the interior of Brazil between March 2014 and April 2015. We performed multivariate analysis using a Poisson regression model with robust variance to identify factors associated with in-hospital mortality. **Results:** We included 304 patients. Approximately 70% of the patients were classified as severely ill on the basis of the severity criteria used. The mortality rate was 15.5%, and the ICU admission rate was 29.3%. After multivariate analysis, the factors associated with in-hospital mortality were need for mechanical ventilation (**OR:** 3.60; 95% **CI:** 1.85-7.47); a Charlson Comorbidity Index score > 3 (**OR:** 1.30; 95% **CI:** 1.18-1.43); and a mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years (CURB-65) score > 2 (**OR:** 1.46; 95% **CI:** 1.09-1.98). The mean time from patient arrival at the emergency room to initiation of antibiotic therapy was 10 h. **Conclusions:** The in-hospital mortality rate of 15.5% and the need for ICU admission in almost one third of the patients reflect the major impact of CAP on patients and the health care system. Individuals with a high burden of comorbidities, a high CURB-65 score, and a need for mechanical ventilation had a worse prognosis. Measures to reduce the time to initiation of antibiotic therapy may result in better outcomes in this group of patients.

Keywords: Community-acquired infections; Pneumonia; Hospital mortality; Risk factors.

INTRODUCTION

Community-acquired pneumonia (CAP) is one of the leading causes of death from infectious diseases worldwide.[1] It is a public health problem and is a cause of morbidity and mortality in all age groups.[2] Mortality rates vary according to the population and context studied, ranging from 1%, in outpatients, to 50%, in inpatients.[3,4] High mortality rates are more common in developing countries, such as Brazil, Argentina, and India.[5,6] CAP is responsible for high costs in public and private health care facilities, whether in outpatient clinics, emergency rooms, or hospital wards.[7,8] In Brazil, data from the Brazilian Unified Health Care System show that pneumonia was the second leading cause of hospitalization in 2017, accounting for approximately 14% of all hospitalizations.[9]

Although CAP is a high-incidence disease, with multiple studies having been conducted on risk factors and available therapies, several issues regarding CAP remain controversial.[10] Using guidelines for the treatment of pneumonia has been shown to reduce hospital stays, mortality rates, and complications rates.[11-13] However, a recent study conducted in Brazil showed that slightly more than half of the patients admitted to a university hospital were treated in accordance with current guidelines.[14] With regard to assessment of disease severity, studies have shown that using clinical judgment alone can either underestimate or overestimate the severity of the clinical presentation. This strategy can lead to unnecessary hospitalizations, as well as to interventions that are less aggressive than those required in more severe cases, culminating in negative outcomes.[15-17] Nevertheless, a study published in 2015 showed that most physicians in Brazil use clinical judgment alone to assess disease severity in patients with CAP.[14]

It is possible to suspect that the aforementioned discrepancies are partly due to the fact that the major guidelines and severity scores are based on large international studies, and, despite the high reported incidence of CAP in Brazil, little is known about local microbiological patterns and disease severity at the regional level.[18] Therefore, we conducted a cohort study involving patients with CAP admitted to a hospital in the interior of Brazil over a one-year period, in order to describe the patient profile, mortality rates, the accuracy

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of prognostic scores, and factors associated with in-hospital mortality in these patients.

METHODS

Study population

The present study was conducted in a secondary-care general hospital, with 130 beds, located in the city of Montenegro, Brazil. The hospital provides care via the Brazilian Unified Health Care System to approximately 160,000 people, many of whom reside in one of 19 surrounding municipalities. In 2015, respiratory infections represented the leading cause of admission to the hospital, and the rate of in-hospital mortality was 10.2%.[19]

Study design

We screened for patients who were 14 years of age or older, had respiratory symptoms, and were referred for hospital admission between May 2014 and April 2015. Patient inclusion in the cohort at baseline was based on a clinical and radiographic diagnosis of CAP and a referral by the attending physician for hospitalization. We excluded patients with nosocomial pneumonia—characterized by hospitalization for 2 or more days in the past three months—residents of nursing or retirement homes; those who received intravenous antibiotics, chemotherapy, or scar treatment in the past 30 days; and those undergoing renal replacement therapy. Patients were assessed using the following severity scores: Charlson Comorbidity Index (CCI); mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years (CURB-65) score; and Pneumonia Severity Index (PSI), on the basis of data documented in the cohort's medical records collected at baseline. We assessed the clinical course of patients during in-hospital follow-up and determined clinical outcomes at the time of hospital discharge.

Cases of pneumonia were defined in accordance with the criteria established by the Centers for Disease Control and Prevention,[20] on the basis of chest X-rays with at least one of the following findings: new or progressive and persistent infiltrate, consolidation, and/or cavitation; and at least one of the following signs or symptoms: fever (> 38 °C) with no other cause detected; leukopenia (< 4,000 leukocytes/mm^3) or leukocytosis (≥ 12,000 leukocytes /mm^3); and, for adults aged 70 years or older, a change in mental state with no other cause identified. In addition, there should be at least two of the following findings: new onset of purulent sputum or change in character of sputum; increased respiratory secretions; increased frequency of aspiration; onset or worsening of cough, dyspnea, or tachypnea; bronchial breath sounds; worsening of gas exchange (e.g., oxygen desaturation, with a PaO_2/FiO_2 ratio ≤ 240); increased need for oxygen; or need for mechanical ventilation.

The study was approved by the Porto Alegre *Hospital de Clínicas* Research Ethics Committee (Protocol GPPG no. 150168), which is accredited by the Office of Human Research Protections as an institutional review board, and researchers signed a data use agreement protecting the confidentiality of medical records.

Study variables

Clinical, laboratory, and radiological data for the first 24 h following the emergency room visit were obtained from a review of medical records, and included the following variables: age; gender; place of residence; RR; arterial blood pressure; axillary temperature; HR; presence of mental confusion; SpO_2; comorbidities (as documented by the attending physician); history of hospitalization; chest X-ray findings (as assessed by a radiologist); and laboratory tests ordered in the emergency room. Laboratory tests included arterial blood gas analysis, urea, serum creatinine, blood glucose, sodium, and blood count. We recorded the antibiotics administered during hospitalization, as well as total length of hospital stay, length of ICU stay, and need for mechanical ventilation. The primary outcome was all-cause in-hospital mortality, as documented in the medical records and confirmed by review of hospital discharge summaries or death certificates, as appropriate. All patients had medical records, and their discharge summaries were completed by the attending physician within 48 h of discharge.

It is important to emphasize that patient management, treatment choice, and outcomes suffered no interference from this study, because it was an observational study and we had no contact with either the patients or the attending physicians, who were responsible for all clinical decisions. In the hospital, there is a care protocol for the treatment of pneumonia, and inpatients are treated by a physician team, which was composed of five members at the time of the study.

Data analysis

Data were entered into an Excel® database by two different individuals and subsequently compared to identify possible typographical errors. Continuous variables are expressed as mean and standard deviation; categorical variables are expressed as frequency and proportion. The bivariate analysis between clinical characteristics and mortality was performed by using the Student's t-test (for means and standard deviations) or Pearson's chi-square test (for proportions). ROC curve analysis was performed to evaluate the prognostic indices. A Poisson regression model with robust variance was used to assess the relationship between the variables and the primary outcome (in-hospital mortality). Analyses with a two-tailed p value < 0.05 were considered statistically significant.

All analyses were performed with the Statistical Package for the Social Sciences, version 17.0 (SPSS Inc., Chicago, IL, USA) and the R software, version 4.0-1 (The R Foundation for Statistical Computing, Vienna, Austria).[21-24]

RESULTS

Between March 2014 and April 2015, we assessed 459 patients with respiratory infection, 155 of whom did

not meet the diagnostic criteria for CAP, and, therefore, 304 patients were included in the final analysis (Figure 1). Of those, 171 (56%) were male, and the mean age was 67.1 ± 17.2 years. Most participants (69%) resided in the city of Montenegro. Of the patients in the final sample, 150 (49%) had asthma or COPD (previous lung disease), and 155 (51%) were smokers. The mean CCI score was 4.9 ± 3.1. The characteristics of the patients are presented in Table 1.

The mean CURB-65 score was 2.2 ± 1.1, and 71% of the patients were considered to have severe CAP (CURB-65 scores ≥ 2). The mean PSI score was 3.8 ± 1.3, and 74% of the patients were considered to have severe CAP (PSI scores > 3). The two indices showed good ability to predict in-hospital mortality, with areas under the ROC curve being 0.73 for the CURB-65 score (95% CI: 0.66-0.80; p < 0.001) and 0.75 for the PSI (95% CI: 0.68-0.82; p < 0.001); there was no statistically significant difference between the indices (p = 0.65), as shown in Figure 2.

The mean time from patient arrival at the emergency room to initiation of antibiotic therapy was 10.4 ± 7.7 h. Blood or sputum samples were collected for culture from 101 patients (33%), and the infectious agent was isolated in 53 patients (17%). The most commonly isolated agent was *Streptococcus pneumoniae* (in 36% of positive cultures). The most commonly used antibiotic regimen was amoxicillin plus clavulanate, in 219 patients (72%), followed by azithromycin, in 200 (66%).

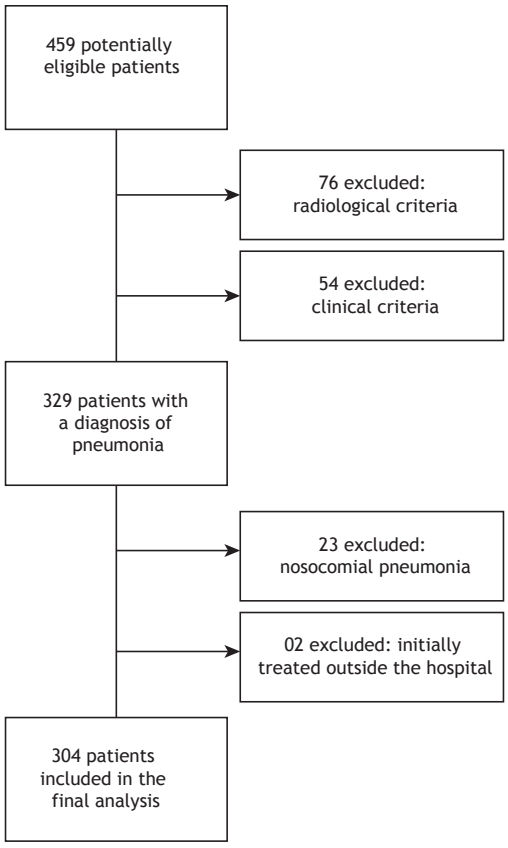

Figure 1. Flow chart of patient inclusion in the study.

We found that 191 (63%) of the patients required a change in the antibiotic regimen during hospitalization. The most common change was the addition of azithromycin to the antimicrobial regimen, on the basis of clinical assessment by the attending physician. During the in-hospital follow-up period, 47 (15.5%) of the patients died, 89 (29.3%) required ICU treatment, and 98 (32.2%) underwent mechanical ventilation. The mean length of hospital stay was 7.2 ± 7.3 days (median, 5 days).

Univariate analysis showed that the factors associated with increased risk for in-hospital mortality were: a CCI score > 3 (OR: 7.18; 95% CI: 2.28-22.58; p < 0.001); a CURB-65 score > 2 (OR: 4.45; 95% CI: 1.64-12.02; p = 0.001); a PSI score > 3 (OR: 9.05; 95% CI: 1.27-64.14; p = 0.004); need for a change in the antibiotic regimen (OR: 2.15; 95% CI: 1.05-4.42; p = 0.02); need for mechanical ventilation (OR: 6.13; 95% CI: 3.33-11.28; p < 0.001); age > 62 years (OR: 6.73; 95% CI: 2.35-19.34; p < 0.001); and being institutionalized (OR: 2.82; 95% CI: 1.08-7.35; p = 0.03).

After multivariate analysis, the factors that remained associated with in-hospital mortality were need for mechanical ventilation (OR: 3.58; 95% CI: 1.92-6.67; p < 0.001); a CCI score > 3 (OR: 1.30; 95% CI: 1.22-1.39; p < 0.001); and a CURB-65 score > 2 (OR: 1.45; 95% CI: 1.05-2.00; p = 0.04; Table 2).

DISCUSSION

CAP continues to be one of the leading causes of death from infectious disease worldwide. Despite the large number of international studies on this subject, there are few studies describing the impact of CAP on patients and the characteristics of the disease in Brazil, especially in inpatient units. In our study, we assessed inpatients with CAP in a secondary-care hospital in Brazil over a one-year period. The observed in-hospital mortality rate of 15.5% reflects the major impact of this disease, being similar to that found in other national and international studies.[25,26] In addition, ICU admission was required in almost one third of the cases (29.3%), which increases the impact of CAP on patients and the health care system.

In our study, we found no relationship between the time of initiation of antibiotic therapy and mortality, possibly because of the long elapsed time to initiation of antibiotic therapy (a mean of 10 h) and the low proportion of patients (19%) who received antibiotic therapy within the first 4 hours. Difficulty in prompt initiation of antibiotic therapy had been reported in another study conducted in Brazil.[27] In the present study, we found that, even after the implementation of a protocol for the treatment of pneumonia, there was no success in the attempt to reduce the time to initiation of antibiotic therapy. This is probably due to a tendency to administer antibiotics at scheduled

Table 1. Characteristics of the total study sample and subgroups.[a]

Variable	Total	In-hospital mortality		p
		Yes	No	
	(N = 304)	(n = 47)	(n = 257)	
Gender				
Male	171 (56.2)	28 (16.4)	143 (83.6)	0.6
Female	133 (43.8)	19 (14.3)	114 (85.7)	
Age, years	67 ± 17.3	77.5 ± 12.7	65.2 ± 17.3	0.6
Race				0.7
White	290 (95.4)	46 (15.9)	244 (84.1)	
Non-White	14 (4.6)	1 (7.1)	13 (92.9)	
CCI score	4.9 ± 3.1	8.11± 2.8	4.3 ± 2.8	< 0.001
CURB-65 score	2.2 ± 1.1	3.0 ± 1.0	2.0 ± 1.1	< 0.001
PSI score	107.2 ± 50.6	147.3 ± 32.5	99.9 ± 50.0	< 0.001
Smoking	155 (51.0)	23 (14.8)	132 (85.2)	0.9
Dementia	65 (21.4)	23 (35.4)	42 (64.6)	< 0.001
Diabetes	46 (15.5)	8 (17.4)	132 (85.2)	0.7
Heart failure	71 (23.4)	15 (21.1)	56 (78.9)	0.14
Neoplasia	39 (12.8)	15 (38.5)	24 (61.5)	< 0.001
Renal disease	34 (11.2)	13 (38.2)	21 (61.8)	< 0.001
Chronic lung disease	150 (49.3)	23 (15.3)	127 (84.7)	1.0
Institutionalized	22 (7.2)	7 (31.8)	15 (68.2)	0.03

CCI: Charlson Comorbidity Index; CURB-65: mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years; and PSI: Pneumonia Severity Index. [a]Values expressed as n (%) or as mean ± SD.

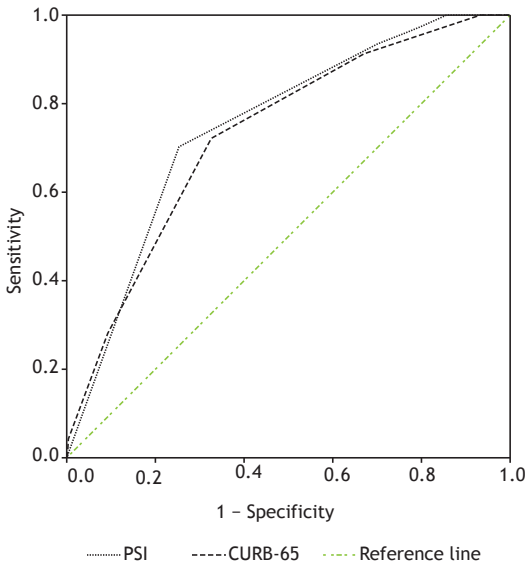

Figure 2. ROC curve of severity indices for prediction of in-hospital mortality. PSI: Pneumonia Severity Index; and CURB-65: mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years.

times that are pre-determined by routine hospital protocols. Given that early initiation of medication is associated with better outcomes, with a study reporting a reduction of up to 30% in mortality when antibiotics are administered within the first hours of admission,[28] efforts to reduce the time to treatment initiation are needed.

In a recent study, Rabello et al.[14] reported that only 40% of the physicians used a validated prognostic score to assess patients with CAP, with clinical assessment alone remaining the most commonly used way to assess disease severity. In our study, the severity scores performed well in predicting in-hospital mortality, with areas under the ROC curve being 0.73 for the CURB-65 score and 0.75 for the PSI, similarly to previous and recent international studies.[12,29] These findings reinforce that these scores are useful for use in the Brazilian population as well and justify the efforts to promote their routine use in health care facilities.

The risk factors that remained associated with mortality after logistic regression were need for mechanical ventilation, a high CCI score, and a high CURB-65 score. The CCI is considered a good predictor of mortality in several settings, being an important marker of the patient's underlying health status, since it evaluates comorbidities in relation to acute infection. Although the CCI has been validated in several settings, including in patients with COPD,[30] it has not commonly been reported as a risk factor for negative outcomes in other studies of CAP. The CURB-65 score, in addition to showing good prognostic ability, was independently associated with in-hospital mortality (OR, 1.45). It is of note that the PSI did not show significance in the logistic regression model, probably because of the overlapping of variables assessed by the CURB-65 score and the CCI. Given that the CURB-65 score is much simpler (only five variables assessed) than the PSI (twenty variables assessed) and both are similar in terms of efficacy, the routine use of the CURB-65 score is justified. Lastly, need for mechanical ventilation is widely associated with worse outcomes, probably because it is an important marker of severity.

Table 2. Factors associated with in-hospital mortality after multivariate analysis.

Factor	OR (95% CI)	p
Need for mechanical ventilation	3.60 (1.85-7.47)	< 0.001
CCI score	1.30 (1.18-1.43)	< 0.001
CURB-65 score	1.46 (1.09-1.98)	0.006

CCI: Charlson Comorbidity Index; and CURB-65: mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years.

Our study has some limitations. The major limitation is that this was a single-center study involving a relatively small number of patients. However, our study is unique, since it is one of the few involving data from the interior of Brazil and involving all patients who were hospitalized for CAP over a one-year period, which is important in this disease with a seasonal variation. No patients were lost during the in-hospital follow-up period, and the severity profile of the patients was monitored in terms of underlying diseases, by using the CCI, and in terms of acute disease, by using the PSI and the CURB-65 score.

In conclusion, the findings of our study, such as the high in-hospital mortality rate and the need for ICU admission in almost on third of the patients, emphasize the impact that CAP has on individuals and the health care system. Individuals with a high burden of comorbidities, a high CURB-65 score, and a need for mechanical ventilation had a worse prognosis. Lastly, we observed delayed initiation of antibiotic therapy, even in a hospital setting. Measures to reduce the time to initiation of antibiotic therapy may result in better outcomes in this group of patients.

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