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Original Research Article

A Hospital Based Study to Evaluate Clinic-Epidemiological, Etiology and Outcomes of Severe Community-Acquired Pneumonia (CAP)

Nishant Kumar Singh[1], Arun Kumar[2]

[1]Senior Resident, Department of General Medicine (Emergency) IGIMS, Patna, Bihar India
[2]Senior Resident, Department of Anesthesiology and Critical Care, AIIMS, Patna, Bihar, India

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Corresponding author: Dr. Arun Kumar
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Abstract:

Aim: The aim of the present study was to investigate the epidemiology, causative agents and outcomes of severe community-acquired pneumonia (CAP).

Methods: This was a retrospective cohort study of patients with severe CAP admitted to an adult ICU for the period of 1 year. The medical records of patients with APACHE IV admission diagnosis of "viral pneumonia", "bacterial pneumonia", and "sepsis, pulmonary origin" within this period were identified. Totally 100 patients were identified to be admitted to our ICU for pneumonia.

Results: Their age ranged from 19 to 92 years old and there was male preponderance. The severity of illness is reflected by the APACHE IV score. Most of the patients had no chronic medical problems and the most common comorbidity was diabetes mellitus. Moreover, C-reactive protein level was marked elevated with mean of almost 200 mg/dL. More than three quarters of the patients required invasive mechanical ventilatory support while more than 80% needed vasopressors for hemodynamic support. About one third of them developed renal failure with institution of renal replacement therapy. However, nitric oxide and ECMO were uncommonly employed for support of such patients. Streptococcus pneumoniae was the most commonly isolated organism. It was detected by one or more of the following methods: blood culture, sputum/endotracheal aspirate/pleural fluid culture or urine antigen test. The common agents included Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter baumannii. Other bacterial organisms identified were Staphylococcus aureus, Streptococcus pyogenes and Mycobacterium tuberculosis.

Conclusion: The common etiological organisms included Streptococcus pneumoniae and Influenza A. Pneumococcal and influenza immunizations may be effective to reduce the incidence of CAP. Such vaccine should be provided to the high risk group so that it may improve the outcome of severe chest infection.

Keywords: Community-acquired pneumonia; ICU; critically-ill patients.

Introduction

Community-acquired pneumonia (CAP) is a major public health problem with high morbidity, mortality and short- and long-term sequelae. [1-4] Very old (aged ⩾80 years) patients are at increased risk of complications and death by most causes. [5] The incidence of CAP in very old patients continues to rise. [6] The immunosenescence [7], multicomorbidities [8] and frailty [9] of these patients increases their susceptibility to infectious diseases. [10,11]

Pneumonia is a major health problem, being associated with high morbidity and short and long term mortality. It is also the leading infectious disease cause of mortality among all ages worldwide. [12,13] Pneumonia in critically ill patients may present as pneumonia acquired in the community (community acquired pneumonia, CAP); pneumonia acquired in the hospital (hospital acquired pneumonia, HAP); or pneumonia related to mechanical ventilation (ventilator associated pneumonia, VAP). Severe pneumonia is associated with high short and long term mortality, and those who survive often have important sequelae such as alterations of lung function, reduction in mental and cognitive functions, weakness and reduction of motor function, and reduced functional autonomy. [14,15]

Appropriate diagnosis of severe pneumonia is crucial to improve survival of critically ill patients. Identifying a pathogen is critical for antimicrobial stewardship in critically ill patients with severe pneumonia. However, in most patients, identifying the cause is challenging, especially in those with chronic underlying disease, those who received previous antibiotic therapy, and those treated with mechanical ventilation. Prompt and adequate

antimicrobial treatment is crucial for the best outcomes in critically ill patients with severe pneumonia, and is a key focus of international guidelines for the management of pneumonia. [16-18]

Streptococcus pneumoniae remains the main pathogen responsible of CAP, regardless of age and comorbidities. [19] However, approximately 6% of CAP are caused by antibiotic-resistant pathogens. [20] Early adequate antibiotic administration is crucial in SCAP management [21]; however, the optimal strategy is still far from being established. Initial antimicrobial therapy lacking activity against the offending pathogens has been associated with greater mortality. [22] The cluster RCT from Postma et al [23] showed the same efficacy when comparing beta-lactam monotherapy with beta-lactam plus macrolide or quinolone. The constant debate regarding the superiority of β-lactam plus macrolide compared to β-lactam plus fluoroquinolones in SCAP is still open. [24]

The aim of the present study was to investigate the epidemiology, causative agents and outcomes of severe community-acquired pneumonia (CAP).

Materials and Methods

This was a retrospective cohort study of patients with severe CAP admitted to an adult ICU in AIIMS, Patna, Bihar, India for the period of 1 year. The medical records of patients with APACHE IV admission diagnosis of "viral pneumonia", "bacterial pneumonia", and "sepsis, pulmonary origin" within this period were identified. Totally 100 patients were identified to be admitted to our ICU for pneumonia. Community acquired pneumonia was defined as any chest infection diagnosed within the first 48 hours of hospitalization and infections occurring later were considered nosocomial.

Also, patients were commonly admitted to ICU within 24 hours after the diagnosis of CAP was made. Therefore, those patients admitted to ICU 3 days after hospitalization were excluded as such infection might be hospital-acquired. The medical records of the patients were reviewed for data collection.

Data Collected

The following patient data were extracted from the medical records: (I) demographic data, including age, sex, date of hospital and ICU admission, (II) comorbidities which are defined in the Chronic Health Evalution component of the APACHE IV model, including chronic obstructive airway disease, congestive heart failure, cirrhosis, chronic renal failure, diabetes mellitus, metastatic carcinoma, hematological malignancy and long term steroid therapy and (III) the APACHE IV scores.

All patients had microbiological investigations upon admission to ICU and the etiological diagnosis of CAP was determined for each patient as far as possible. Bacteria or viruses were identified by isolation and culture from blood, pleural fluid, sputum and endotracheal aspirate. Influenza A and B, parainfluenza, adenovirus, respiratory syncytial virus, Coxsackie virus, rhinovirus and human metapneumovirus antigens were detected in nasopharyngeal or endotracheal aspirate by immunofluorescence or real time PCR. Urinary samples were collected to test for Legionella and pneumococcal antigen. Paired serology for respiratory viruses, Mycoplasma and Chlamydia pneumoniae was collected on admission to ICU and 4 weeks later. Positive serological test was defined as a fourfold increase in antibody levels.

Staphylococcus aureus was considered as the etiological organism only if no other infective agents were isolated. When Staphylococcus aureus was grown from sputum or endotracheal aspirate, it was regarded as colonizers if other infective organisms were identified to cause the pneumonia.

Laboratory data within the first 24 hours of ICU admission, including white cell count, platelet count, C-reactive protein, creatinine level and bilirubin level were obtained from the medical records. The clinical notes were also reviewed for use of invasive mechanical ventilation, vasopressor drugs, renal replacement therapy and other advanced modes of ventilatory support, including inhaled nitric oxide (NO) and ECMO within 48 hours of ICU admission. Outcomes of patients, in terms of mortality and length of stay, in ICU and hospital were also extracted from the medical records.

Statistical Analysis

Discrete variables were expressed as counts (percentage) and continuous variables as means ± SD. Univariate analyses were performed to detect association of outcomes with the demographic and clinical characteristics of the patients. Moreover, the causative agents of the infection were analysed. Differences between groups were assessed using the chi-square test and the Fisher exact test for categorical variable and the Student t test or Mann-Whitney U test for continuous variables. Multivariate regression analysis was used to assess the impact of independent variables on complications and outcomes. We performed multivariate logistic regression analysis to identify factors independently associated with in-hospital mortality, with the multivariate model constructed

by using both stepwise-selection and backward elimination technique.

Results

Table 1: Baseline demographics and clinical characteristics of patients

Variables	All patients (N=100)	Survivors (N=70)	Non-survivors (N=30)	P
Demographics				
Age, mean (SD)	58.4 (15.5)	56.4 (16.4)	62.8 (13.0)	0.000
Male gender, n (%)	202 (67.34)	130 (65)	72 (72)	0.207
Underlying conditions, n (%)				
COPD	4	3	1	0.136
CHF	5	3	2	0.322
Cirrhosis	1	1	0	0.558
CRF	6	2	4	0.959
DM	32	18	14	0.738
Metastatic carcinoma	3	1	2	0.182
Hematological malignancy	3	1	2	0.136
Long term steroid therapy	10	3	7	0.088
Clinical features, mean (SD)				
APACHE IV score	91.6 (32.6)	62 (28.2)	114.6 (32.64)	0.000
WBC, ×109/L	18.4 (12.8)	16.0 (9.2)	19.7 (17.5)	0.280
Platelet count, ×109/L	136.8 (85.5)	152.6 (82.5)	108.3 (80.5)	0.000
Prothrombin time, sec	18.2 (12.1)	16.7 (11.3)	20.9 (13.2)	0.003
Urea, mmol/L	15.8 (11.5)	14.0 (10.6)	19.2 (12.4)	0.000
Bilirubin, µmol/L	24.7 (31.9)	20.1 (23.8)	33.4 (41.9)	0.001
C-reactive protein, mg/L	196.8 (118.4)	192.1 (117.2)	205.9 (120.6)	0.290
Treatments, n (%)				
Mechanical ventilation	94	60	34	0.004
Shock requiring vasopressor	80	55	25	0.001
Renal replacement therapy	35	20	15	0.000
Inhaled NO	10	4	6	0.010
ECMO	12	8	4	0.670

Their age ranged from 19 to 92 years old and there was male preponderance. The severity of illness is reflected by the APACHE IV score. Most of the patients had no chronic medical problems and the most common comorbidity was diabetes mellitus. Moreover, C-reactive protein level was marked elevated with mean of almost 200 mg/dL. More than three quarters of the patients required invasive mechanical ventilatory support while more than 80% needed vasopressors for hemodynamic support. About one third of them developed renal failure with institution of renal replacement therapy. However, nitric oxide and ECMO were uncommonly employed for support of such patients.

Table 2: Distribution of causative pathogens of community-acquired pneumonia by diagnostic tests

Pathogens	**Number (%)**	**Blood culture**	**Urine antigen**	**Culture from sputum/ tracheal aspirate/pleural fluid**	**Nasopharyngeal/ tracheal antigen/PCR**	**Serological test**
Bacterial						
Strep. pneumoniae	15 (15)	4	12	7	–	–
Gram -ve bacilli	18 (18)	5	–	15	–	–
Staph. aureus	8 (8)	–	–	7	–	–
Strep. pyogenes	2 (2)	1	–	2	–	–
Mycobacteria	2 (2)	–	–	2	–	–
Atypical pneumonia						
Legionella pneumophila	2 (2)	–	2	–	–	2
Mycoplasma pneumoniae	1 (1)	–	–	–	–	1

Chlamydia pneumoniae	1 (1)	–	–	–	–	1
Viral		–	–	–	–	–
Influenza A	12 (12)	–	–	–	10	5
Influenza B	2 (2)	–	–	–	2	1
Parainfluenza	3 (3)	–	–	–	2	1
RSV	2 (2)	–	–	–	2	1
Adenovirus	1 (1)	–	–	–	1	–
Coxsackie A	1 (1)	–	–	–	1	–
Human metapneumovirus	1 (1)	–	–	–	1	–
Rhinovirus	1 (1)	–	–	–	1	–

Streptococcus pneumoniae was the most commonly isolated organism. It was detected by one or more of the following methods: blood culture, sputum/endotracheal aspirate/pleural fluid culture or urine antigen test. The common agents included Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter baumannii. Other bacterial organisms identified were Staphylococcus aureus, Streptococcus pyogenes and Mycobacterium tuberculosis.

Table 3: Multivariate analysis of factors associated with hospital survival

Variables	Odds ratio (95% CI)	P
Age	0.92 (0.95, 0.98)	0.000
Presence of metastatic carcinoma	0.044 (0.00, 0.52)	0.012
Renal replacement therapy	0.42 (0.28, 0.78)	0.002
Platelet count	1.007 (1.005, 1.012)	0.000
Nitric oxide therapy	0.36 (0.17, 0.89)	0.022

In order to identify independent prognostic factors, we performed multivariate analysis that included significant variables from the univariate analysis. Because the APACHE score was calculated from some of the independent variables, it was not included in the final model. Significant factors identified to be associated with mortality included age, platelet count, presence of metastatic carcinoma, need of renal replacement therapy and use of nitric oxide therapy.

Discussion

During recent decades, the number of patients requiring intensive care management due to severe community-acquired pneumonia (SCAP) has increased globally, especially among the elderly, patients with comorbidities and the immunocompromised.[6] A large population based surveillance study on hospitalized CAP patients found that 21% of patients required intensive care unit (ICU) admission, with 26% of them needing mechanical ventilation. [25] SCAP hospital mortality is still high, ranging from 25% to more than 50%. [26,27]

Their age ranged from 19 to 92 years old and there was male preponderance. The severity of illness is reflected by the APACHE IV score. Most of the patients had no chronic medical problems and the most common comorbidity was diabetes mellitus. Moreover, C-reactive protein level was marked elevated with mean of almost 200 mg/dL. More than three quarters of the patients required invasive mechanical ventilatory support while more than 80% needed vasopressors for hemodynamic support. About one third of them developed renal failure with institution of renal replacement therapy. However, nitric oxide and ECMO were uncommonly employed for support of such patients. Streptococcus pneumoniae was the most commonly isolated organism. It was detected by one or more of the following methods: blood culture, sputum/endotracheal aspirate/pleural fluid culture or urine antigen test. The common agents included Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter baumannii. Other bacterial organisms identified were Staphylococcus aureus, Streptococcus pyogenes and Mycobacterium tuberculosis. Atypical pathogens, including Legionella pneumoniae, Mycoplasma and Chlamydia, were identified as the second most common causes of CAP in several studies [28-31] but it was not found in the present cohort. Most of the studies were conducted in the Western countries and geographical variation may account for such difference. Viral pneumonia is becoming more important especially during influenza epidemics. [32-34] The most common agent is influenza A and other respiratory viruses include influenza B, parainfluenza, rhinovirus, respiratory syncytial virus, Coxsackie virus, human metapneumovirus and adenovirus.

In order to identify independent prognostic factors, we performed multivariate analysis that included significant variables from the univariate analysis.

Because the APACHE score was calculated from some of the independent variables, it was not included in the final model. Significant factors identified to be associated with mortality included age, platelet count, presence of metastatic carcinoma, need of renal replacement therapy and use of nitric oxide therapy. In our study, pneumococcus and influenza were major causes of severe CAP. It was suggested that people infected by influenza may be prone to bacterial chest infection. [35-37] Therefore, pneumococcal and influenza vaccination may be an effective means to reduce hospitalisation and death due to chest infection.

Conclusion

The common etiological organisms included Streptococcus pneumoniae and Influenza A. Pneumococcal and influenza immunizations may be effective to reduce the incidence of CAP. Such vaccine should be provided to the high risk group so that it may improve the outcome of severe chest infection.

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