SEVERE COMMUNITY-ACQUIRED PNEUMONIA IN SINGAPORE

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ABSTRACT

Background: *There has been no previous study documenting the aetiology and prognosis of severe community-acquired pneumonia in Singapore. Patients with severe community-acquired pneumonia (SCAP) needing admission to a medical intensive care unit in Singapore were studied retrospectively.*

Methods: *All patients admitted to the medical intensive care unit at National University Hospital from June 1991 to February 1993 with a diagnosis of community-acquired pneumonia were entered into the study. All patients had blood cultures, sputum cultures, serologies for Legionella and mycoplasma drawn on admission. APACHE II scores were determined prospectively.*

Results: *Fifty-nine consecutive cases from June 1991 to February 1993 were identified with a mean age of 61 (SD 17) years. Nearly all the cases needed mechanical ventilation (90%) and overall mortality was 63%. An aetiological agent was identified in the majority of cases (68%), with Klebsiella pneumoniae being the most common agent (9 cases, 15%). Haemophilus influenzae and Streptococcus pneumoniae were identified in 8% (5 cases) and 5% (3 cases) of cases respectively. Pseudomonas pseudomallei was identified in 4 cases (7%) with a 100% mortality. Overall, gram-negative organisms were identified in 47% of cases. APACHE II was significantly higher in non-survivors. Age, creatinine levels, and the presence of bacteraemia were not prognostic features.*

Conclusion: *SCAP in Singapore carries a high mortality with the predominance of gram-negative organisms. Empiric antibiotics should include gram-positive and gram-negative coverage with specific coverage for Pseudomonas pseudomallei.*

Keywords: *severe community-acquired pneumonia, Singapore, Pseudomona pseudomallei*

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INTRODUCTION

Community-acquired pneumonia remains a common disease and a common cause for hospital admission. Many studies have documented the pathogens involved, and the associated factors for mortality[1-8]. Severe community-acquired pneumonia (SCAP) is the extreme end of the spectrum that requires admission to an intensive care unit, and the frequent use of mechanical ventilation. In these situations, the pathogens involved may be different[9]. Furthermore, geographical differences may be important, and may impact upon the initial choice of empirical antibiotics. We have therefore performed a retrospective study of SCAP in our hospital. This represents the first such study in Singapore.

METHODS

We retrospectively studied all the patients admitted to the 6-bedded medical intensive care unit (MICU) at the National University Hospital, Singapore with a diagnosis of community-acquired pneumonia from June 1991 to February 1993. Patients were admitted to MICU because they needed mechanical ventilation or were potential candidates for ventilatory support. Community-acquired pneumonia was defined as an acute lower respiratory tract infection (cough with purulent sputum, and fever) which started before hospital admission and the presence of chest infiltrates on the chest radiograph compatible with acute pneumonia.

All patients had routine sputum and blood cultures taken on admission before the commencement of empirical antibiotics, as well as serology of *Legionella pneumophila* and *Mycoplasma pneumoniae*. Positive sputum cultures with excessive epithelial cells were disregarded, as they were considered to represent upper airway contamination. The APACHE II score for the first 24 hours was calculated[10]. Hospital outcome was recorded along with any underlying diseases, and the overall length of ventilatory support was determined.

Clinical management was determined by the individual attending physician, including the choice of antibiotics, and the need for mechanical ventilation.

STATISTICS

Results were presented as mean ± standard deviation. Unpaired t-test, or chi-squared with continuity correction was used for statistical analysis. A 'p' value of less than 0.05 was taken as significant.

RESULTS

Fifty-nine cases were identified during the study period. There were 32 males (54%) and 27 females (46%). The mean age was 61 years (±17 years, range 15 to 86 years). Their average length of stay in the MICU was 9.5 days (median 5 days, range 1 to 106 days). Nearly all the cases needed mechanical ventilation (90%), and they were ventilated for a mean duration of 7.5 days (±15 days). Other diseases that were present included diabetes mellitus (29%), chronic obstructive airway disease (26%), and immunocompromised state (underlying malignancy or solid organ transplant) (7%).

The mortality rate was 63% (37 deaths), with the majority (61%) dying within 48 hours of MICU admission. Most of them (81%) died from refractory hypotension. Mean APACHE II score was 19 (range 0 to 30) and the APACHE II score was significantly higher in those who died, while other factors failed to show a difference (Table I).

A pathogen was identified in the majority of cases (68%),

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Table I – Differences between survivors and non-survivors.

	Survivors	Non-survivors	p-value
APACHE II score	14.5±6 (range 0 to 30)	22±9	0.001[a]
Age (year)	60.7 ± 18 (range 19 to 86)	61.2 ± 16	0.907[a]
Creatinine > 139 mmol/L	4 (7%)	17 (29%)	0.0061[b]
Bacteraemia	2 (3%)	6 (10%)	0.704[b]

[a] p-value from unpaired t-test
[b] p-value from chi-squared with continuity correction

Table II – Types of pathogens identified

Organisms	Number of cases (%) (n = 59)
Klebsiella pneumoniae (8 from sputum, 1 from sputum & blood culture)	9 (15)
Haemophilus influenzae (All from sputum)	5 (8)
Staphylococcus aureus (All from sputum)	4 (7)
Pseudomonas pseudomallei (1 from sputum, 1 from blood culture, 2 from both sputum and blood culture)	4 (7)
Streptococcal pneumoniae (1 from sputum, 2 from blood culture)	3 (5)
Pseudomonas aeruginosa (2 from sputum, 1 from both sputum and blood culture)	3 (5)
Legionella pneumophila (Diagnosed from serology)	2 (3)
Mycoplasma pneumoniae (Acid-fast positive, and culture positive)	1 (2)
Other gram-negatives (5 from sputum, 1 from BAL[a], 1 from both sputum and blood culture)	7 (12)
Group D streptococcal non-faecal (From sputum)	1 (2)
Unidentified	19 (32)
Total	59 (100%)

[a] BAL - bronchoalveolar lavage

with the predominance of gram-negative organisms (47%) (Table II). Fourteen per cent were bacteraemic. Gram-positive organisms were isolated in 14% of cases. It is important to note that all 4 cases with identified *Pseudomonas pseudomallei*, died from refractory hypotension.

DISCUSSION

The striking findings from our study were the unusually high incidence of gram negative pathogens (47%), and the presence of *Pseudomonas pseudomallei*. *Klebsiella pneumoniae* was the most common pathogen (15%), while *Streptococcus pneumoniae* was identified in only 5% of cases. Other severe community-acquired pneumonia studies have placed the incidence of *Streptococcus pneumoniae* at between 10% and 45%, and almost always as the most common pathogen[11-21]. In our hospital, *Streptococcus pneumoniae* was identified as the second most common pathogen (12%) for community-acquired pneumonia over a study period of 6 months[8]. It was interesting to note that *Mycobacterium tuberculosis* was the most common pathogen identified in that study. In that study, pneumococcal antigen assay (Wellcome, ZL 22) was used in addition to culture methods. We may have therefore underestimated the true incidence of *Streptococcus pneumoniae* without employing the pneumococcal antigen assay[8,22].

The significant presence of gram-negative isolates in our study deserves note. The British study[18] had only 2 out of 60 cases (3%) with a gram-negative isolate when *Haemophilus influenzae* was excluded, while a more recent French study[21] had 15% gram-negative bacilli with the exclusion of *Haemophilus influenzae*. In two separate South African studies[16,17], a high incidence, 11% and 32%, was also found for *Klebsiella pneumoniae* as the pathogen for severe community-acquired pneumonia. A study reported from Saudi Arabia[23] identified *Pseudomonas aeruginosa* as their most common isolate (16%). Thus, the presence of gram-negative isolates in these more recent studies of SCAP serve as an important factor in the choice of empiric antibiotics.

The 4 cases of melioidosis (*Pseudomonas pseudomallei* infection) were notable in our series of SCAP, although this had also been described in Thailand[24] as well as from the Northern Territories of Australia[25]. Melioidosis is endemic in Singapore[26], and is a particularly common cause of septicaemia with pneumonia in Northeastern Thailand[27]. None of our cases had any significant travel history. The chest radiographs of patients with melioidosis were not characteristics of any pattern in contrast to a series previously described from Thailand[27]. The possibility of encountering melioidosis in SCAP therefore has implications for selecting the appropriate empiric antibiotics, since the antibiotic of choice in melioidosis is ceftazidime[28], which is not the usual first line drug for SCAP. Melioidosis should be treated aggressively, as the mortality is high (42% mortality in our hospital - Lee KH, personal communication). All our 4 cases died from refractory hypotension.

Our study did not look specifically for *Chlamydia pneumoniae* as serological tests were not sent. Fang et al in their study of 359 cases of community-acquired pneumonia, identified 6.1% of their cases due to *Chlamydia pneumoniae*[3], and we could therefore be missing some of these cases. Viral infections were not specifically looked for except in the immuno-compromised hosts. Other series of severe community-acquired pneumonias have documented a small number of viral infections, ranging from 1% to 11%[11,12,15,17,18]. Future prospective studies of local SCAP should therefore include paired viral serologies and perhaps nasopharyngeal aspirate for viral isolation.

Mortality rate was 63%, which stands above all the other previously published series where the rate ranged from 22% to 53%[11-20]. The high percentage of ventilated patients (90%) in our series suggest that we had a large number of severely ill patients. APACHE II data was collected in our study and non-survivors had a higher score. This agrees with a South African study[29] who also documented a significantly higher APACHE II score in non-survivors (11.3±3.5 in survivors, 19.0±6.7 in non-survivors, p = 0.03). In another South African study, the Simplified Acute Physiology Score System (SAPS) was employed but they found no significant difference between survivors and non-survivors[16]. SAPS is a modification of the original APACHE using some of the variables employed in APACHE II[30]. It is unclear whether any specific recommendations can be made to improve mortality beyond what is currently practised (good resuscitative measures and prompt alleviation of hypoxaemia with supplemental oxygen and intubation as needed). The right antibiotics have to be administered early, and there appears to be no rise in the level of TNF α with bactericidal antibiotics[29].

Another factor contributing to the higher mortality may be the elderly population in our study, as demonstrated by a higher mean age (61 years) compared to the other series (range 45 years to 57 years)[11-20]. The high incidence of gram-negative organisms, in particular *Klebsiella pneumoniae*, may be another explanation for the higher mortality. A study from Taiwan had reported a 100% mortality in bacteraemic *Klebsiella pneumoniae* pneumonias despite receiving intensive care[31]. Fourteen percent of our cases were bacteraemic, and there was no significant difference in mortality between the bacteraemic and non-bacteraemic cases. This compares to a bacteraemic rate of 20% in a study from Barcelona[14], where there was a significant difference in mortality between bacteraemic and non-bacteraemic patients (44% vs 16%, p=0.0223). Factors associated with increased mortality include: elderly age, previous immunocompromised state, septic shock, high creatinine levels, high phosphate levels, low white cell count, low platelet count, low albumin, presence of adult respiratory distress syndrome, radiographic spread of the pneumonia after admission, bacteraemia, and *Pseudomonas aeruginosa* as a cause for pneumonia[11,14-16]. In the British Thoracic Society study on severe community-acquired pneumonias[18] however, no prognostics feature was identified.

Diabetes mellitus was present in nearly a third of our patients and may thus predispose to a higher incidence of *Staphylococcus aureus* and *Pseudomonas pseudomallei*. Other studies had a lower described incidence of diabetes mellitus (range 5% to 16%)[11,14,16,18,19].

In summary, our retrospective study of 59 cases of SCAP, defined as pneumonia requiring admission to an intensive care unit had a high mortality (63%). APACHE II was significantly higher in those who died, and gram-negative organisms were the most commonly isolated aetiological agents. Based on our data, empiric antibiotics should cover for both gram-positive and gram-negative organisms, including *Pseudomonas pseudomallei*. Thus, penicillin, cloxacillin and ceftazidime should be considered as an initial combination of empiric antibiotics for SCAP. However, our study is retrospective in nature and the data emanate from a single restructured hospital. Thus the final decision of antibiotic choices should be individualised until further multi-centred prospective studies are concluded.

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