Original Article

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Investigation on hospital-acquired pneumonia and the association between hospital-acquired pneumonia and chronic comorbidity at the Department of General Internal Medicine, University Medical Center Hochiminh City

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Abstract

Hospital-acquired pneumonia (HAP) is the most common cause of death among nosocomial infections. Controlling for risk factors, especially comorbid conditions plays an important role in the prevention and management of HAP. The Chronic Disease Score (CDS) has been widely used as a tool for comorbidity measurement of chronic diseases. However, little is known about the use of CDS in estimating the impact of comorbidity on infectious conditions. This descriptive cross-sectional study aims at describing the charateristics of HAP patients, the use of antibiotics and identifying the association between chronic comorbidities using CDS and treatment outcome among patients with HAP. The study population included 213 patients diagnosed with HAP admitted to the Department of General Internal Medicine, University Medical Center Hochiminh city from October 1st 2014 to March 31st 2015. The mean CDS score was 4.9, ranging from 0 to 15. The most common pathogen associated with early-onset pneumonia (NP) is *Streptococcus spp.* whereas *Acinetobacter spp.* is the most common pathogen found in late-onset NP. Third generation cephalosporins and quinolones were markedly resistant. The combination of two antibiotics accounted for 65.3% of cases treated with antibiotic empiric therapy. Multivariable logistic regression analysis identified that cancer (OR = 4.95; 95% CI 1.46-16.76), CDS score (OR = 0.832; 95% CI 0.71 - 0.97), age from 45 to 64 (OR = 14.09; 95% CI 6.77 - 21.96), age 65 and above (OR = 15.13; 95% CI 7.87-15.92) and mechanical ventilation (OR = 5.05; 95% CI 1.23 - 20.60) were associated with failure in treatment outcome.

Keyword: chronic disease score, comorbidity, hospital-acquired pneumonia

1. INTRODUCTION

Hospital-acquired pneumonia (HAP) is the second most common nosocomial infection and is associated with high morbidity and mortality. HAP carries a crude mortality rate of 30% to 70%, increases hospital stay by an average of 7 to 9 days and produces an excess cost of more than $40,000 per patient[1]. Antibiotic resistance among major pathogens of HAP has become a global challenge. In recent reports on nosocomial infection in Vietnam, *Klebsiella spp.* was found to be resistant to third generation cephalosporins (90%) and vancomycin resistance in *Staphylococcus aureus* resistance to vancomycin was also reported[2,3,4].

In addition to the rational use of antibiotics, controlling for risk factors, especially comorbid conditions plays an important role in the prevention and management of HAP. Several tools for comorbidity measurement have been developed using hospital administrative or pharmacy databases. The Chronic Disease Score (CDS), a pharmacy-based indicator, has been widely used as an effective tool to measure comorbid conditions of chronic diseases. CDS

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has been validated for use as a predictor of physician-rated disease status, self-rated health status, hospitalization, and mortality[5,6]. However, little is known about the use of CDS in estimating the impact of comorbidity on infectious conditions. This study aims at providing updated information on the use of antibiotic therapy on the treatment of HAP and identifying the association between chronic comorbidities using CDS and treatment outcome among patients with HAP.

2. MATERIAL AND METHODS

2.1. Study population

Data was obtained from all patients aged 18 and over with diagnosis of HAP at discharge at the Department of General Internal Medicine, University Medical Center Hochiminh City between October 1st 2014 and March 31st 2015. Exclusion criteria included pregnancy, immunodeficiency and fungal pneumonia. A total number of 213 medical profiles of patients that met the selection criteria were taken into analysis.

2.2. Methods

A descriptive cross-sectional study was conducted to provide descriptive information on the characteristics, risk factor, comorbidities and antimicrobial treatment of HAP patients. Microbiologic diagnosis was provided by the Department of Microbiology, University Medical center. Sensitivity to antibiotics was determined using disk diffusion test based on the protocol of Clinical and Laboratory Standards Institute (CLSI, 2014). Multivariable logistic regression was used to identify factors statistically associated with treatment outcome (success/failure). All statistical analysis was performed using SPSS 22.0 software package.

3. RESULTS

Characteristics of the population

Patients aged 65 and above accounted for 74.2% of the study population whereas only 7.5% were youger than 45 years old. The majority of cases were early-onset (66.2 %), diagnosed on day 4.5 ± 2.9 from admission. The average length of stay was 13 days.

169 patients had at least one risk factors (79.3%), ranging from 1 to 4. Of the factors observed, the use of H_2 blockers, proton pump inhibitors (PPIs) or antacids accounted for 68.1%. Nasogastric intubation (19.7%), hemoglobin below 10 g/dl (18.8%) and mechanical ventilation (18.3%) were among the leading factors previously reported to be associated with HAP. The most frequent comorbid chronic diseases included hypertension (55.4%), lung diseases (29.1%), diabetes mellitus (28.6%) and cardiovascular diseases (27.7%).

Physical examination and laboratory investigations

Confusion (16%), hypotension (25.4%), tachycardia (33.8%) and tachypnea (6.1%) were symptoms remarkedly observed in the study population.

29 patients (13.6%) had an initial SpO_2 less than 90%, mainly due to comorbid pulmonary diseases.

Chronic diseases scores and comorbidities (CDS)

The mean CDS score of the study population was 4.9 ± 3.4, ranging from 0 to 15. Mean CDS were significantly different among 3 age groups (<45; 45-64; >=65). Mean CDS were higher in women (5.3 ± 3.2) than in men (4.5 ± 3.4). However, the difference was not statistically significant.

Almost HAP hospital profiles were observed with comorbidities (94.8%), ranging from 1 to 5. The mean number of comorbid diseases were 2.2 ± 1.1. Hypertension (55.4%), other lung diseases (29.1%), diabetes mellitus (28.6%) and other cardiovascular diseases (27.7%) were the most common group of comorbid diseases recorded.

Baseline characteristics, CDS and laboratory findings of the study population are presented in Table 1.

Table 1. Baseline characteristics, CDS and laboratory findings of the study population

Variables	Values †
Male (%)	48.8
Age (years)	77 (16-98)
Early-onset NP (%)	66.2
Length of stay (days)	13 (2-100)
Risk factor (%)	79.3
H2 blocker, PPIs or antacid therapy	68.1
Nasogastric intubation	19.7
Haemoglobin <10 g/dl	18.8
Mechanical ventilation	18.3
Smoking	10.8
Malnutrition	8.0
Chest surgery	0.9
Comorbidity (%)	94.8
Hypertension	55.4
Lung diseases	29.1
Diabetes mellitus	28.6
Other cardiovascular diseases*	27.7
Chronic kidney disease	18.3
Cerebrovascular disease	16.4
Liver disease	16.4
Peptic ulcer disease	15.5
Malignancy	12.7
Alzheimer	1.9
Number of comorbidities	2.2 ± 1.1
CDS	4.9 ± 3.4
SpO2, %	94
SpO2 < 90%, n (%)	29 (13.6)
Haemoglobin, g/dl	11.82 ± 2.148
Haematocrit, %	35.39 ± 6.446
Platelets, /10-9 litter	271.65 ± 122.745
Leucocytes, /10-9 litter	11.69
C-reactive protein, mg/l	335
Glucose, mg/dl	120
Serum creatinine, mg/dl	0.88
Urea, mg/dl	36

* include ischaemic heart disease, heart failure
† Values outside reference range were in bold

• Bacterial pathogens

Of 213 hospital profiles analyzed, antimicrobial testing was indicated in 151 cases (70.9%) and 77 cases were found with positive test results. Specimens tested included sputum (74.0%), bronchoalveolar lavage fluid (13.0%) and blood (13.0%).

There were no significant differences in the total numbers of pathogen found in early-onset and late-onset HAP cases but the distribution varied among the two pneumonia categories. *Streptococcus spp.* (16.2%) was the most common pathogen in early-onset NP while *Acinetobacter spp* was the most common pathogen (14.0%) in late-onset cases (Table 2). All the patients infected with *S. aureus* in this study also had comorbid diabetes mellitus**.**

Table 2. Distribution of microorganisms isolated from patients with HAP in the study population

Microorganisms	Early-onset NP	Late-onset NP	Total
Gram-positive microorganisms, n (%)			
Streptococcus spp.	16 (16.2)	9 (9.1)	25 (25.3)
Staphylococcus aureus	2 (2.0)	2 (2.0)	4 (4.0)
Staphylococcus coagulase (-)	-	2 (2.0)	2 (2.0)
Gram-negative microorganisms, n (%)			
Acinetobacter spp.	8 (8.1)	14 (14.0)	22 (22.2)
Klebsiella spp.	5 (5.1)	7 (7.1)	12 (12.2)
Pseudomonas aeruginosa	6 (6.1)	7 (7.1)	13 (13.1)
Escherichia coli	5 (5.1)	5 (5.0)	10 (10.1)

• Antibiotic resistance

P. aeruginosa showed high resistance rates to quinolones and meropenem (46.2% and 77.0%, respectively). Antibiotics that remained highly effective to *P. aeruginosae* were colistin (100% sensitive) and piperacillin/tazobactam (92.3% sensitive). Resistance rates of *Acinetobacter spp*. to commonly used antibiotic were above 40.0%; colistin, imipenem and cefoperazon/sulbactam still remained effective to *Acinetobacter spp*. ESBL-producers exhibited low susceptibility to first-line antibiotics such as meropenem (12.5%), piperacillin/tazobactam (22.2%) (Appendix).

Antibiotic therapy in treatment of hospital-acquired pneumonia

Antibiotics were indicated to all 213 cases in the study population with a total of 642 antibiotics. The average duration of antimicrobial treatment was 11 days. Figure 1 shows the distribution of patients based on the number of antibiotics administered, table 3 enlists the frequency and proportion of each antibiotic group.

The most frequently prescribed antibiotics, which represented 76.7% of all antibiotic prescriptions, were quinolones (37.3%), carbapenems (21.3%) and third-generation cephalosporins (18.2%). Only 9 out of 213 patients received aminoglycosides (1.4%), possibly due to the advanced age and decline in renal function of the study population.

Third generation cephalosporins (11.3%) and quinolones (9.4%) were the most commonly antibiotics empirically used in cases of monotherapy. The combination of two antibiotics was indicated in 139 cases (65.3%) including quinolone plus cephalosporin (28.2%) and quinolone plus carbapenem (17.8%). Only 15 patients (7.0%) were administered with three antibiotics.

Table 3. Frequency and proportion of prescribed antibiotics

Antibiotic group	Frequency	Proportion
β-lactam		
Penicillin	15	2.3%
Antipseudomonal Penicillin	35	5.4%
Cephalosporin	117	18.2%
Carbapenem	137	21.3%
Aminoglycoside	9	1.4%
Quinolone	239	37.3%
Glycopeptide	31	4.9%
Others	59	9.2%
Total	642	100%

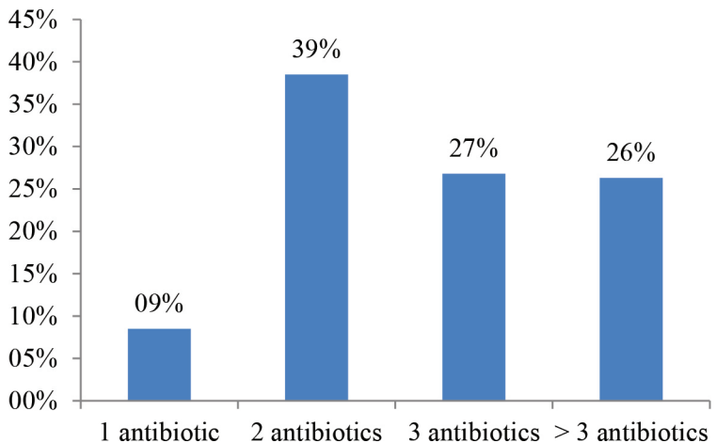

Figure 1. Distribution of the study population based on the number of antibiotics administered

Association between chronic comorbidities and other risk factors with treatment outcome

There were 148 cases (69.5%) with successful treatment outcome. The association between treatment outcome (success/failure) with chronic comorbidities (type of comorbidity, number of comorbidities, chronic disease score) and other factors including age, sex, previously reported risk factors, onset of HAP, number of antibiotics administered was identified by multivariable logistic regression. Result from the analysis showed that cancer (OR = 4.95; 95% CI 1.46-16.76), CDS score (OR = 0.832; 95% CI 0.71 - 0.97), age from 45 to 64 (OR = 14.09; 95% CI 6.77 - 21.96), age 65 and above (OR = 15.13; 95% CI 7.87-15.92) and mechanical ventilation (OR = 5.05; 95% CI 1.23-20.60) were associated with failure in treatment outcome.

3. DISCUSSION

The mean length of stay observed in the study population was 13 days. The mean length of stay of unsuccessful cases tended to be shorter than successful cases due to the fact that patients usually requested to be transferred

to another hospital as soon as progressive deterioration was noted.

Treatment outcome of HAP varied considerably in different studies according to the characteristics of the study population. Mortality rate is frequently used to evaluate treatment outcome of severe infectious diseases in many studies[7,8]. In this study, since almost patients requested to be discharged or transferred to another hospital when deterioration was noted, the true mortality rate could not be recorded through hospital profiles. Treatment outcome recorded was the conclusion at discharge by physicians.

The use of PPIs or drugs that can change gastric pH was found to be the predominant risk factor of HAP in this study (68.1%). In University Medical Center, the majority of postoperative or long-stay inpatients were administered H2 blockers, antacids or PPIs to prevent stress-induced gastrointestinal bleeding. The association between the increase in gastric pH and the incidence of HAP has been reported in several studies. A recent review on HAP and its management by Natalie Schellack also confirms medicines that result in an increase in the gastric pH as a pharmacological risk factor associated with HAP and ventilator-associated pneumonia[9].

Findings from this study were similar to those reported in some previous studies worldwide. According to Magret M, bacteremic pneumonia episodes were more frequent in patients with prolonged mechanical ventilation and independent risk factors for mortality[7]. A survey by Craven DE also confirmed that mechanically ventilated patients have higher incidence of pneumonia and mortality than non-ventilated patients[10]. Data from a study by Tumbarello M showed old age to be independently associated with ICU mortality in patient with *Pseudomonas* pneumonia[8] while a study by Burgos J. found that age above 50 years was a risk factor for respiratory failure in pneumococcal pneumonia[11] . Although the impact of cancer on pneumonia has not been adequately studied, some reports noted that nearly 15% of cancer patients experienced acute respiratory failure requiring admission to the intensive care unit, where their mortality rate was about 50%[12]. N. Shimazaki and colleagues also reported that underlying malignancy was a factor that affected the efficacy of vancomycin therapy on MRSA pneumonia[13].

Although the sample size was not large enough to detect a statistical significance, the data analysis suggested that patients with chronic diseases of kidney, liver, lung, heart, diabetes mellitus or with risk factors such as smoking, using H2 blockers, PPIs or antacids, feeding through nasogastric tube and having haemoglobin <10 g/dl were more likely to get failure in treatment of HAP.

However, quite opposite to initial predictions, CDS was inversely related to treatment outcome. Even though the use of Chronic Disease Score has not been reported in pneumonia, the use of Charlson Comorbidity Index (CCI) in previous studies showed a strong and positive relation between the two factors. According to Librero, length of stay significantly rose with each level of the CCI and in-hospital mortality rate in patients with higher scores increased by 4 times compared to patients without comorbidities[14]. In a survey by Lensen, comorbidity was found to contribute to death in patients with *Staphylococcus aureus* bacteremia. The CCI is a good predictor of mortality in this population[15]. The calculation of CDS was based on medications used during hospitalization. Since physicians generally focus on antibiotic therapy and discontinue unessential medicines during exacerbations of infection, the CDS score may not accurately reflect the comorbidities of the study population.

Results from the study revealed that the majority of the study population was found with chronic comorbid conditions. Cancer, mechanical ventilation, age 45 and above were found to be significantly associated with failure in overall outcome. Isolated pathogens exhibited high resistance against third generation cephalosporins and quinolones. Reduced susceptibility to aminoglycosides, carbapenems and antipseudomonal penicillins were also reported. Colistin still showed efficacy on gram negative bacteria, whereas vancomycin and linezolid were still effective on gram positive

bacteria. Quinolones, carbapenems and third generation cephalosporins were the most frequently prescribed antibiotics (accounted for 41.1%, 23.5% and 20.0%, respectively). Combination of two antibiotics was commonly chosen as initial empiric therapy (65.3%).

In addition to an adequate and timely antibiotic therapy, controlling for comorbid chronic conditions should be taken into consideration in managing infectious diseases including HAP. Mechanical ventilation should be carefully indicated based on risk/benefit assessment. Noninvasive ventilation should be considered if possible. Since there was no guideline on prevention and management of HAP at University Medical Center when data was collected, findings from the study suggested that in order to improve the outcome of HAP, a standard treatment guideline should be developed based on local microbiological patterns.

Further studies should be conducted on larger population to determine the association between comorbidity and treatment outcome as well as the possibility of using CDS as a predictive score in infectious diseases.

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