ASSESSMENT OF TREATMENT OUTCOMES AND SOME RISK FACTORS FOR MORTALITY OF COMMUNITY-ACQUIRED PNEUMONIA CAUSED BY *STAPHYLOCOCCUS AUREUS* IN THE ELDERLY POPULATION

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ABSTRACT

Objectives: Community-acquired pneumonia is a notable contributor to mortality from infectious diseases on a worldwide scale, especially in the older population. Staphylococcus aureus is a prevalent infection known to cause severe pneumonia, often leading to a high incidence of complications and fatality. The study's objective was to assess the treatment outcomes and some factors associated with mortality rates of Staphylococcus aureus pneumonia in older people. ***Subjects and method:*** A cross-sectional study was conducted with 93 patients diagnosed with Staphylococcus aureus pneumonia admitted to Can Tho Central General Hospital from April 2021 to May 2023. ***Results:*** The research results showed clinical outcomes including 30-day all-cause death rates and pneumonia-related complications were slightly higher in the age group over 60 compared to those aged 60 and under, but the difference was not statistically significant. After performing multivariate analysis, it was found that heart failure (OR = 5.68, 95% CI: 1.01-32.1, p = 0.049) and central nervous system disease (OR = 5.26, 95% CI: 1.32-20.9, p = 0.018) were found to be independent factors that increased the mortality rate in individuals aged over 60. ***Conclusion:*** Clinical practitioners should evaluate and manage comorbidities regarding heart failure and central nervous system diseases during treatment of Staphylococcus aureus pneumonia due to its elevated fatality rate, especially in old patients.

Keywords: *Staphylococcus aureus (S. aureus), community-acquired pneumonia (CAP), elderly patient, mortality.*

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I. INTRODUCTION

Community-acquired pneumonia (CAP) is a leading cause of mortality from infection worldwide and is significantly associated with morbidity and mortality rates, especially in the elderly and children [2]. Estimated rates of CAP vary globally from 1.5 to 14 cases per 1000 person-years [9]. In Vietnam, in 2014, the incidence rate of pneumonia in our country was 561 per 100,000 people, ranking second after hypertension, and the mortality rate due to pneumonia was 1.32 per 100,000 people, ranking first among causes of death [1]. Among the causes of pneumonia, *Staphylococcus aureus* (especially methicillin-resistant pathogens - MRSA) has emerged as a pathogen causing severe pneumonia with many complications and a high mortality rate, which can reach 56% for necrotizing pneumonia [4]. Furthermore, pneumonia caused by *S. aureus* has been shown to have a 30-day mortality rate more than 4 times higher (41% versus 9.5%, p=0.001) and a hospitalization time more than 2 times higher (24.2% versus 12.8%, p=0.001) compared to the classic pathogen causing pneumonia, *Streptococcus pneumoniae* [6]. Regarding prognosis, old age is a risk factor for increasing the incidence of MRSA [12], and is also a factor

associated with a high mortality rate due to pneumonia [3]. In Vietnam, there have been some studies on pneumonia caused by *S. aureus*, but no studies have been conducted on the elderly population. Based on this reality, we conducted the study "Assessment of treatment outcomes and some risk factors for mortality of community-acquired pneumonia caused by *Staphylococcus aureus* in the elderly population".

II. SUBJECTS AND METHODS

2.1.Research subjects

Patients was diagnosed with *S. aureus* pneumonia and treated at Can Tho Central General Hospital and Can Tho University of Medicine and Pharmacy Hospital from April 2021 to May 2023.

Inclusion criteria:

- Patients ≥ 18 years old.
- Patients with a diagnosis of *S. aureus* pneumonia meet all 3 of the following criteria:

+ Symptoms and signs: at least one of the signs, such as temperature > 38ºC or < 36ºC, have ruled out other causes; leukocytosis (≥ 12 x 10^9/L) or leukopenia (≤ 4 x 10^9/L); Consciousness disorders in elderly patients have ruled out other causes. At the same time, at least two of the following signs such as purulent sputum or change in sputum properties or increased sputum secretion or increased need for sputum aspiration; cough or increased coughing or shortness of breath or rapid breathing; crackles or wheezes sounds on lung examination, worsening of gas exchange including hypoxemia, increased need for oxygen supply, or increased need for mechanical ventilation.

+ Imaging evidence: new or progressive lesions do not disappear quickly on chest imaging tests (straight chest X-ray, chest computed tomography, chest magnetic resonance imaging) and can be infiltration, consolidation, cavitation, and air bubbles.

+ Microbiological evidence: one of the criteria is a culture of blood and/or pleural fluid or respiratory secretions isolated from *S. aureus*.

- Patients with a diagnosis of *S. aureus* pneumonia were divided into two groups:

+ Case group: patient > 60 years old.

+ Control group: patients ≤ 60 years old.

Exclusion criteria:

- The patient's blood culture, pleural fluid culture, and respiratory secretion culture results were of other bacteria and/or co-infection with *S. aureus*.
- Death within 48 hours of diagnosis of pneumonia.
- The patient refused to continue participating in the study.

2.2.Research methods

2.2.1.Study design

A case-control study. Data were extracted and collected from medical records.

2.2.2.Sample size

The sample was conveniently chosen, selecting all patients with *S. aureus* pneumonia who met the criteria for hospitalization during the study period based on the data collection form. A total of 93 eligible patients were recruited and followed until the end of the study, comprising 57 old patients (study group) and 36 younger patients (control group).

2.2.3.Study contents

Demographic and clinical characteristics: age (years, mean, ≤ 60/> 60), gender (male/female), co-morbidities including hypertension, coronary artery disease, heart failure, diabetes, chronic obstructive pulmonary disease [COPD], renal failure, liver disease, central nervous system [CNS]

disease, cancer (yes/no per one), Charlson comorbidities index [CCI] (mean, < 3/≥ 3), methicillin-resistant *S. aureus* [MRSA] (yes/no).

Primary clinical outcome: 30-day all-cause mortality (alive/death) was defined as all-cause death in the hospital or at home from the time of diagnosis of *S. aureus* pneumonia.

Secondary clinical outcomes: respiratory failure (yes/no), acute respiratory distress syndrome [ARDS] (yes/no), septic shock (yes/no), acute kidney injury (yes/no), length of hospital stay (days, median), duration of intensive care unit [ICU] stay (days, median) and time to event (days, median).

Analyze the association between demographic and clinical characteristics with the 30-day all-cause mortality event of the older group.

***2.2.4.*Statistical analysis**

The data were analyzed by Statistical Package for the Social Sciences (SPSS) software 26.0.

2.3.Research ethic

The board of directors of Can Tho Central General Hospital as well as the ethics committee for biomedical research at Can Tho University of Medicine and Pharmacy approved this study with decision number 421/QĐ-ĐHYD dated May 4, 2020.

III. RESULTS

Our study was conducted on 93 patients with *Staphylococcus aureus* pneumonia and divided into 2 age groups. Specifically, there were 57 subjects aged > 60 years and 36 subjects aged ≤ 60 years. The baseline demographic and clinical characteristics of the 2 groups are presented in Table 1.

Table 1. ***Baseline demographic and clinical characteristics by age group***

Characteristics	> 60 (n = 57)	≤ 60 (n = 36)	All patients (n = 93)	P-value
Age, mean (SD)	74 ± 8,83	48,84 ± 12,37	64,41 ± 16	**<0,001†**
Gender (female), n (%)	26 (45,6)	14 (38,9)	40 (43)	0,523*
Hypertension (yes), n (%)	40 (70,2)	23 (63,9)	63 (67,7)	0,528*
CAD (yes), n (%)	12 (21,1)	5 (13,9)	17 (18,3)	0,384*
Heart failure (yes), n (%)	12 (21,1)	4 (11,1)	16 (17,2)	0,216*
Diabetes	19 (33,3)	10 (27,8)	29 (31,2)	0,573*
COPD (yes), n (%)	10 (17,5)	0 (0)	10 (10,8)	**0,006****
Renal failure (yes), n (%)	9 (15,8)	8 (22,2)	17 (18,3)	0,434*
Liver disease (yes), n (%)	2 (3,5)	2 (5,6)	4 (4,3)	0,639**
CNS disease (yes), n (%)	19 (33,3)	11 (30,6)	30 (32,3)	0,411*
Cancer (yes), n (%)	1 (1,8)	3 (8,3)	4 (4,3)	0,295**
CCI, mean (SD)	4,78 ± 1,62	2,27 ± 1,5	3,82 ± 1,99	**<0,001†**
CCI group (≥ 3), n (%)	56 (98,2)	15 (41,7)	71 (76,3)	**<0,001 ***
MRSA (yes), n (%)	48 (84,2)	28 (77,8)	76 (81,7)	0,434*

*Chi-squared test, **Fisher's Exact Test, †Independent Samples T-Test.

Compared to the ≤ 60 years age group, the > 60 years age group had a higher prevalence of COPD (17.5% vs. 0%, p = 0.006). Additionally, the older age group also exhibited a higher average Charlson Comorbidity Index (CCI) compared to the younger group (2.27 ± 1.5 vs. 4.78 ± 1.62, p < 0.001). Moreover, the older patient cohort tended to have comorbidities such

as hypertension, cardiovascular diseases, heart failure, diabetes mellitus, and central nervous system disease. However, the differences were not statistically significant (p > 0.05).

Table 2. ***Clinical outcomes of pneumonia patients by age group***

Characteristics	> 60 (n = 57)	≤ 60 (n = 36)	All patients (n = 93)	P-value
Primary outcome				
30-day all-cause mortality (death), n (%)	25 (43,9)	15 (41,7)	40 (43)	0,835*
Secondary outcomes				
Respiratory failure (yes), n (%)	46 (80,7)	30 (83,3)	76 (81,7)	0,749*
ARDS (yes), n (%)	15 (26,3)	5 (13,9)	20 (21,5)	0,155*
Septic shock (yes), n (%)	14 (24,6)	9 (25)	23 (24,7)	0,962*
Acute kidney injury (yes), n (%)	8 (14)	3 (8,3)	11 (11,8)	0,520**
Length of hospital stay, median (Q1-Q3)	12 (8-21)	10,5 (7-17)	12 (7-20)	0,362†
Duration of ICU stay, median (Q1-Q3)	10 (3-15)	6,5 (2,5-9,5)	7 (3-12)	0,502†
Time to event, median (Q1-Q3)	30 (10-30)	30 (7-30)	30 (10-30)	0,824

*Chi-squared test, †Mann–Whitney U test.

Regarding the primary outcome assessment, the 30-day all-cause mortality rate in the >60 years age group compared to the ≤60 years age group did not exhibit statistically significant differences (43.9% vs. 41.7%, p = 0.835). Upon analysis of secondary outcomes, it was observed that the >60 years age group tended to have more extended hospital stays, longer ICU stays, a higher incidence of ARDS and acute kidney injury, and an equivalent incidence of septic shock and respiratory failure compared to the ≤60 years age group. However, the differences in these secondary outcomes were not statistically significant between the two age groups (p > 0.05).

Table 3. ***Univariate and multivariate analyses of associated factors for 30-day all-cause mortality in elderly S. aureus pneumonia patients***

Factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age (+1 year)	0,94 (0,88-1,01)	0,069		
Gender (female)	1,19 (0,42-3,39)	0,749		
Hypertension (yes)	1,17 (0,37-3,69)	0,790		
CAD (yes)	2,1 (0,58-7,65)	0,261	2,04 (0,37-11,06)	0,411
Heart failure (yes)	5,44 (1,29-23)	**0,021**	5,68 (1,01-32,1)	**0,049**
Diabetes	1,7 (0,56-5,17)	0,347	2,67 (0,7-10,16)	0,150
COPD (yes)	0,49 (0,11-2,12)	0,337		

Factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Renal failure (yes)	1,75 (0,42-7,35)	0,445	1,72 (0,31-9,66)	0,539
Liver disease (yes)	1,29 (0,08-21,73)	0,859		
CNS disease (yes)	3,3 (1,05-10,39)	**0,042**	5,26 (1,32-20,9)	**0,018**
Cancer (yes)	-	-		
CCI (+1)	1,31 (0,91-1,9)	0,153		
CCI group (≥ 3)	-	-		
MRSA (yes)	1,69 (0,38-7,57)	0,491		

The univariate analysis results indicate that heart failure and CNS disease involvement are two factors associated with increased mortality rates in the older patient group with community-acquired pneumonia caused by *S. aureus*, with odds ratios (OR) of 5.44 (95% CI: 1.29-23; p = 0.021) and 3.3 (95% CI: 1.05-10.39; p = 0.042), respectively. Similarly, the multivariate analysis also identified heart failure (OR = 5.68, 95% CI: 1.01-32.1, p = 0.049) and CNS disease (OR = 5.26, 95% CI: 1.32-20.9, p = 0.018) as factors increasing the risk of 30-day all-cause mortality in this patient group. Factors such as cardiovascular disease, diabetes mellitus, and renal failure also increased the risk of 30-day all-cause mortality in multivariate analysis, although the differences were not statistically significant (p > 0.05).

III. DISCUSSION

Our study was conducted on 93 patients with community-acquired pneumonia caused by *S. aureus*, divided into two age groups: > 60 and ≤6 0. The study results showed no statistically significant difference in the primary outcome of 30-day all-cause mortality and secondary outcomes. When evaluating risk factors for the primary outcome in the > 60-year-old group, we found that heart failure and CNS disease were associated with increased 30-day all-cause mortality rates in univariate and multivariate analyses. Other factors such as cardiovascular disease, diabetes mellitus, and renal failure also increased the mortality rate in this patient group, although the differences were not statistically significant.

Regarding clinical characteristics, the older patient group tended to have a higher prevalence of underlying diseases including COPD, hypertension, cardiovascular diseases, heart failure, and diabetes mellitus, compared to the ≤ 60-year-old group. This result aligns with classical literature indicating that older age carries a higher risk of developing chronic non-communicable diseases. These findings underscore the significant burden of illness within this demographic group.

Regarding treatment outcomes, there was no difference in mortality rates between the > 60 and ≤ 60 years old patient groups. However, when evaluating secondary outcomes, the older patient group had more extended hospital stays, longer ICU treatment durations, a higher incidence of

ARDS and acute kidney injury, and an equivalent incidence of septic shock and respiratory failure compared to the ≤ 60-year-old group. It is evident from our results that both primary and secondary outcomes occur relatively frequently, which is consistent with the severe clinical course of pneumonia caused by *S. aureus* compared to classical pneumococcal pathogens as demonstrated in various parameters such as PSI, pleural effusion, altered mental status, BUN, leukocytosis, and impaired oxygen exchange as seen in the study by Thabet et al [15]. Additionally, advanced age has long been established as a risk factor for mortality in pneumonia in general [3] and increases the likelihood of MRSA infection [12], thus contributing to a higher risk of complications and adverse outcomes, specifically in *S. aureus* pneumonia [4].

In assessing 30-day all-cause mortality in elderly patients with *S. aureus* pneumonia, we found that underlying conditions such as heart failure and CNS disease are risk factors associated with increased incidence of this primary outcome. Additionally, comorbidities, including cardiovascular disease, diabetes mellitus, renal failure, and MRSA infection, also contribute to increased mortality risk, although the observed differences were not statistically significant. Indeed, several previous studies have indicated that MRSA does not directly contribute to 30-day mortality outcomes after adjusting for concurrent comorbidities [8], [10]. Moreover, heart failure has been demonstrated to exacerbate pneumonia severity, and pneumonia itself can precipitate heart failure exacerbations, thus leading to higher mortality rates, as evidenced in various studies [7], [11], [13].

In severe cases of pneumonia caused by *S. aureus* complicated by sepsis, heart failure has also been shown to be a factor that increases the mortality rate [14]. Similarly, CNS disease has been proven to worsen the prognosis of pneumonia patients by impairing respiratory protective mechanisms, increasing the risk of prolonged hospitalization, reducing cough reflexes, reducing gag reflexes, and increasing the risk of sputum retention [5].

Our study has several limitations, particularly concerning sample size. Indeed, the number of patients followed up to record 30-day mortality outcomes is relatively small to provide accurate estimates of prognostic factors. Additionally, many results suggest associations but do not reach statistical significance.

IV. CONCLUSION

In conclusion, our study compared *Staphylococcus aureus* pneumonia between patients over 60 and those aged 60 or younger, finding no difference in the 30-day mortality rate. Evaluation of secondary outcomes such as prolonged hospitalization, prolonged ICU treatment, ARDS, and acute kidney injury showed higher occurrences in the over-60 age group, although not statistically significant. Specifically, regarding the primary outcome of 30-day all-cause mortality in the > 60 age group, heart failure and CNS disease were found as significant risk factors in both univariate and multivariate analyses.

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