

ORIGINAL ARTICLE

Preliminary Assessment of Adherence to CURB-65 Criteria And National Antimicrobial Guideline for the Treatment of Inpatients with Community-Acquired Pneumonia in a Tertiary Care Hospital in Kelantan, Malaysia.

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Abstract

Community-acquired pneumonia (CAP) is a common infection that can affect an individual at any point in life and needs to be treated accordingly. Therefore, the current study was conducted to evaluate the adherence to CURB-65 criteria and National Antimicrobial Guideline (NAG) 2019 when determining hospitalization and prescribing empirical antibiotic therapy for adult CAP patients in the inpatient setting. A retrospective, cross-sectional study was carried out from 1 October 2022 to 31 December 2022 in medical wards of Hospital Raja Perempuan Zainab II, Kelantan. Eligible subjects were identified upon hospitalization, from the ward census data using convenience sampling. Then, relevant information was obtained from the Patient Management System (SPP) and Pharmacy Information System (PhIS). Descriptive statistics were utilized using Statistical Package for the Social Sciences (SPSS) version 20.0. A total of 122 patients were recruited with the mean (SD) age was 58.2 (19.8) years old. They were predominantly female (n=92, 75.4%) of Malay ethnicity (n=118, 96.7%). A mere 52 (42.6%) admissions of CAP patients into medical wards were adherent to CURB-65 criteria while the remaining hospitalizations were not adherent (n=70, 57.4%). It was found that intravenous (IV) amoxicillin/clavulanate plus azithromycin was mostly prescribed as the empirical antibiotic therapy (n=75, 61.5%). Based on the prescribing pattern, only 62 (50.8%) CAP patients were prescribed antibiotics according to NAG 2019 whilst the rest were not adherent (n=60, 49.2%). The two types of nonadherences detected were prescribing different choices of antibiotics (n=46, 37.7%) and endorsing the durations of antibiotics other than those stated in NAG 2019 (n=14, 11.5%). The present findings revealed that the adherence to CURB-65 criteria and NAG 2019 was unsatisfactory and should be improved. Further investigation is necessary to gain further insight into the appropriate antibiotic use and antimicrobial resistance.

Keywords: *Adherence; community-acquired pneumonia; CURB-65; national antibiotic guideline; empirical antibiotics.*

Introduction

Community-acquired pneumonia (CAP) is a common infection that can affect an individual at any point in life [1]. It is one of the main causes of morbidity, imposing a great burden on health services in many countries. While many CAP cases can be successfully managed as outpatients, around 15% require hospital admission [2].

A large number of pathogens are associated with CAP and the usual etiologies are *Streptococcus pneumoniae* and *Mycoplasma pneumoniae* [3]. In Malaysia, CAP is also commonly caused by *Chlamydomphila pneumoniae* [2]. CAP is often misdiagnosed and inappropriately treated as it can initially present as a relatively mild illness. Therefore, some countries have come up with a standard guideline to help physicians provide effective treatment for CAP patients [3].

The National Antimicrobial Guideline (NAG) was developed by the Ministry of Health Malaysia in 2008, with the latest edition being published in 2019. It advocates proper antibiotic usage by healthcare professionals, thereby helping to reduce antimicrobial resistance and healthcare costs. NAG 2019 also mentions the use of CURB-65 criteria for identifying patients with severe CAP at high risk of mortality [4]. The practical clinical prediction rule was validated and proposed in 2003 by Lim et al. It is simple to use and based on the five clinical features of age, confusion, urea, respiratory rate, and blood pressure [5].

A patient with a score of zero or one should be managed in the outpatient setting unless they have comorbidities or face difficult social circumstances. Those with a score higher than one can be considered for hospitalization. CURB-65 criteria should always be used as a support and not to replace the clinical judgment of a prescriber when treating CAP patients [4].

NAG 2019 recommends the preferred antibiotic therapy for adult patients with CAP in the inpatient setting to be intravenous (IV) amoxicillin/clavulanate 1.2 g q8h for 5 to 7 days, along with IV or per oral (PO) azithromycin 500 mg q24h for 3 to 5 days. As for the alternative

treatment, it was suggested to give IV ceftriaxone 2 g q24h for 5 to 7 days with IV or PO azithromycin 500 mg q24h for 3 to 5 days. Meanwhile, oral or IV levofloxacin 500 to 750 mg q24h for 5 to 7 days should be strictly reserved for patients with penicillin allergy due to its higher risk of adverse events [4].

According to a previous local study conducted in the state of Kedah, the antibiotic therapy prescribed for patients with CAP was consistent with the recommendations in NAG 2019. They found that the most frequently prescribed antibiotic was IV amoxicillin/clavulanate. Additionally, the majority of the patients were evaluated using the CURB-65 criteria to determine the severity of pneumonia and subsequent treatment [6].

Several studies also have reported that following treatment guidelines and adhering to them improves treatment outcomes. In the long run, it can reduce morbidity, death, and healthcare expenditures [7]. That being said, differences between prescribed treatments and actual management techniques by physicians are frequently noticed [8]. This highlights the necessity to evaluate our clinical practices in Hospital Raja Perempuan Zainab II, Kelantan. Therefore, this article discussed the adherence to CURB-65 criteria and NAG 2019 when determining hospitalization and prescribing empirical antibiotic therapy for adult patients with CAP in the inpatient setting.

Methods

Design and study population

A retrospective, cross-sectional study was conducted from 1 October 2022 to 31 December 2022. The inclusion criteria were all adult patients aged 18 years old and above, diagnosed with CAP and admitted into the medical wards in Hospital Raja Perempuan Zainab II from 1 October 2022 to 31 December 2022. Additionally, they must be able to speak and write in Malay or English, as the consent forms were provided in both languages.

Cases with incomplete data were excluded from the study.

Data collection

The eligible subjects were determined upon hospitalization from the ward census data using convenience sampling. Then, relevant information such as demographic and clinical characteristics, as well as medication details and CURB-65 criteria, were obtained from the Patient Management System (SPP) and Pharmacy Information System (PhIS) using a data collection form.

Data were collected on day one of CAP diagnosis. Once the diagnosis was confirmed, demographic information such as age, gender, marital status, and occupation was gathered. Clinical characteristics and vital signs such as body temperature, respiratory rate, blood pressure, heart rate, partial oxygen saturation (SpO₂), comorbidities, and drug allergy status were also collected.

The first antibiotics administered after the diagnosis of CAP were considered empirical antibiotic therapy. When the antibiotics were prescribed according to NAG 2019 (including frequency, dose, and duration), they were deemed as adhering to the guideline. These would comprise the preferred and alternative treatment based on NAG 2019, such as in cases of penicillin allergy. Dosage adjustments for patients with renal or hepatic impairment were considered and included in the data collection.

As for CURB-65 criteria, it is an assessment used to categorize severity and to determine hospital admission. The score can be calculated based on the following five criteria: confusion, blood urea nitrogen of >7 mmol/L (19 mg/dL), respiratory rate of >30 breaths per minute, blood pressure <90 mmHg systolic or <60 mmHg diastolic, and age of >65 years old. The patient with a score of either zero or one should be managed as an outpatient, while one with a score of two and above should be considered for admission [4]. If the correct score was used to decide on a patient's

hospitalization, it was considered as adherent to CURB-65 criteria.

The sample size (n) was calculated using the single proportion formula [9]:

$$n = \frac{Z_{\alpha/2}^2 \times p(1 - p)}{d^2}$$

By inserting the value of reliability coefficient for 95% confidence ($Z_{\alpha/2}$) of 1.96, expected proportion in population based on a previous study (p) of 0.93 [10], precision (d) of 0.05, and 20% of dropout, the total number of subjects were 122 patients.

Statistical analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0 [11]. Descriptive statistics were utilized to explain the patients' demographic and clinical characteristics, the pattern of antibiotics prescribed for patients with CAP, as well as adherence to CURB-65 criteria and NAG 2019. All numerical data were expressed as mean (SD) while categorical data were presented as frequency and percentage.

Ethical approval

The study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki and the Malaysian Guideline for Good Clinical Practice. It was registered with the National Medical Research Register (NMRR), Ministry of Health Malaysia with NMRR ID-22-01855-HCA (IIR) and ethically approved by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. The permission to conduct the study at the medical wards in Hospital Raja Perempuan Zainab II was obtained from the head of the medical department and the hospital director. All study activities were carried out after ethical approval was granted by MREC. The participant information sheets and consent forms were given to the eligible subjects and data collection was performed once the patients voluntarily agreed. To ensure their confidentiality, all subjects were kept anonymous. All information from the data collection form were entered into a computer that was password

protected using anonymous identifiers. Upon completion of the study, the data were copied to a USB flash drive before they were erased from the computer. Currently, the study data are stored in a locked office of the investigators, maintained for a minimum of three years after the completion of the study and will be destroyed after that period of storage.

Results

Demographic and clinical characteristics of CAP patients

A total of 122 patients were recruited into the study. Their mean (SD) age was 58.2 (19.8) years old and were predominantly female (n=92, 75.4%) of Malay ethnicity (n=118, 96.7%). As for the vital signs, the patients were mainly afebrile (n=78, 63.9%) and had blood pressures of >140/>90 mmHg (n=58, 47.5%). Their mean (SD) respiratory rate was 26.3 (5.7) breaths/minute, mean (SD) heart rate was 101.2 (20.5) while mean (SD) SpO₂ was 93.8 (6.6) %. Other clinical characteristics revealed that the patients mostly had comorbidities (n=101, 82.8%) and no known drug allergy (n=120, 98.4%) (Table 1).

Adherence to CURB-65 criteria among CAP patients

A mere 52 (42.6%) admissions of CAP patients to the ward were adherent to CURB-65 criteria which meant they had scores of two and above. The remaining hospitalizations (n=70, 57.4%) were not adherent as the patients had scores of either zero or one (Table 2).

Pattern of the empirical antibiotics prescribed for CAP patients

The most frequently prescribed antibiotic was IV amoxicillin/clavulanate plus azithromycin (n=75, 61.5%), followed by IV amoxicillin/clavulanate alone (n=38, 31.1%), IV ceftazidime plus azithromycin (n=5, 4.1%). Only one patient was prescribed with each antibiotic regime of IV ceftriaxone alone, IV ceftriaxone plus

azithromycin, IV cefuroxime plus azithromycin, and IV piperacillin/tazobactam (Table 3).

Adherence of empirical antibiotics to NAG 2019 for CAP patients

Only 62 (50.8%) CAP patients were prescribed empirical antibiotics according to NAG 2019 while the rest (n=60, 49.2%) were not adherent. The two types of nonadherences detected were prescribing different choices of antibiotics (n=46, 37.7%) and endorsing the durations of antibiotics other than those stated in NAG 2019 (n=14, 11.5%) (Table 4).

Discussion

CAP is a common respiratory disease that causes death worldwide. It is a potentially life-threatening illness, especially in older adults and those with comorbidity [12].

Our current study population had a mean age of almost 60 years old, approaching the elderly population, with the majority being female patients. Through our literature review, we found a few previous studies conducted on the same topic but focused on geriatric patients [6], [13-14]. Additionally, a local study was also carried out in a state in the Northern region of Malaysia. Consequently, the demographic data in these previous studies were different from ours, with an older mean (SD) age of 73.5 (6.2) years old and a predominantly male gender distribution. Most of them were of Malay ethnicity and presented with underlying comorbidities such as hypertension, diabetes mellitus, and chronic obstructive pulmonary disease (COPD) [6]. It is common for patients with comorbidities to contract CAP, especially those having diabetes mellitus. This is pointed out by a systematic review, which suggests that people with type 2 diabetes are at greater risk for infections and may be associated with an increased risk of CAP [15].

CAP is a common diagnosis, contributing substantially to healthcare costs, mostly for patients who require hospitalization [12]. In the assessment and management of CAP, disease

severity assessment is crucial, guiding therapeutic options such as the need for hospital or intensive care (ICU) admission, suitability for discharge home, the extent of diagnostic investigations, and choice and route of antibiotic administration [16-17]. National guidelines recommend assessing patients using the CURB-65 criteria, as it helps physicians in classification of patients and facilitates the selection of appropriate antibiotic therapy as part of subsequent treatment. The use of the tool has been demonstrated to improve care for patients with CAP by providing independent predictors of disease severity [18-19]. However, our findings revealed that less than half of the admitted CAP patients in the ward adhered to CURB-65 criteria. The result contradicted the finding by Shakeel et al. (2021), whereby the majority of their patients (93%) were evaluated using the CURB-65 criteria [6]. However, other researches abroad documented the poor usage of CURB-65 criteria for the decision of hospital admissions [8], [16], [20]. A study in Ethiopia showed that the CURB-65 tool was never used to determine CAP severity [8] while in the Gaza Strip, only 11% of patients were documented with all five parameters of the CURB-65 criteria [16]. Moreover, an interventional project had to be carried out to improve the utilization of CURB-65 criteria in four regional hospitals in Denmark [20]. Failing to use a CAP severity score such as CURB-65 criteria could impact healthcare finances, as it may result in unnecessary hospitalizations of CAP patients [6]. CAP has been associated with many pathogens however, the most significant pathogen remains *Streptococcus pneumoniae*. Thus, any empirical antibiotic therapy for CAP must be effective against the organism with consideration of local antibacterial resistance [21-22]. The antibiotics of choice are usually from the groups of β -lactams such as penicillin and cephalosporin and macrolides such as azithromycin [3], [23]. Combination antibiotic therapy achieves a better outcome compared with monotherapy, in terms of reducing mortality significantly [3], [23-24]. This is because including a macrolide in the antibiotic

regimen for CAP offers wide coverage of atypical pneumonia, polymicrobial pneumonia, or resistant *S. pneumoniae*. Additionally, macrolides exhibit properties beyond antimicrobial activity, including anti-inflammatory effects [24]. The same principle was outlined in NAG 2019 whereby the suggested antibiotic therapy for CAP in the inpatient setting is the combination of IV amoxicillin/clavulanate or IV ceftriaxone and IV or PO azithromycin [4].

This explains why the most frequently prescribed antibiotics for hospitalized CAP patients were IV amoxicillin/clavulanate and IV or PO azithromycin as depicted in our findings. However, the adherence of empirical antibiotics to NAG 2019 among our study population was low considering only slightly over half of them were prescribed accordingly. Some of the patients were endorsed with monotherapy of IV amoxicillin/clavulanate or IV ceftriaxone while the rest were administered with other cephalosporins (ceftazidime and cefuroxime) and penicillin/ β -lactamase inhibitor (piperacillin/tazobactam). Apart from prescribing the different choices of antibiotics, the durations of antibiotic therapy administered to the patients were also different than stated in NAG 2019. These findings contradicted both reports from the local studies conducted at Hospital Kulim, Kedah and Hospital Jerantut, Pahang that noted a prescribing pattern with high adherence towards NAG [6], [10]. Shakeel et al. (2021) reported that IV amoxicillin/clavulanate was the most prescribed antibiotic for non-severe pneumonia, while the combinations of β -lactam/ β -lactamase inhibitors with macrolide were the most common antibiotic prescribed for severe CAP either in patients with or without comorbidities [6]. Vijayasamy et al. (2021) also noted that most of the IV antibiotics prescribed for hospitalized patients with various infections adhered to NAG (n=349, 92.8%) with IV amoxicillin/clavulanate (n=183, 48.5%) being the most frequently used antibiotic in their study population [10]. The inconsistent results were likely due to our study had a stricter methodology. Only empirical

antibiotic therapy precisely conforming to the antibiotic regimen in NAG 2019 was accepted as adherent. Monotherapy, other choices of antibiotics, and different durations of treatment were considered non-adherent even though there is documented evidence suggesting they can work against organisms causing CAP [25].

We acknowledged the limitations of our study which included the following reasons; firstly, the results were based on one point in time retrospective observation within the three-month data collection period. Secondly, the number of patients recruited was relatively small in a single-center setting. Thirdly, the justification and appropriateness of prescribing different antibiotics and durations were not assessed. Finally, the etiological diagnosis of the culprit organism was not able to be determined at the time of assessment.

Conclusion

Overall, this article discusses adherence to CURB-65 criteria and NAG 2019 when treating adult CAP patients admitted to the medical wards in Hospital Raja Perempuan Zainab II. The present findings revealed that the adherence to CURB-65 criteria and NAG 2019 was unsatisfactory and should be improved. This is because determining hospital admission based on the former is crucial while prescribing empirical

antibiotic therapy according to the latter is critical to ensure that CAP patients receive optimum quality of care. Further investigation is necessary to gain additional insight into appropriate antibiotic use and antimicrobial resistance.

Conflict of interest

The authors declare that no conflict of interest may arise from the research publication.

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Table 1. The demographic and clinical characteristics of patients with CAP (n=122).

Characteristics	Mean (SD)	n (%)
<i>Age (years old)</i>	58.2 (19.8)	
<i>Gender</i>		
Male		30 (24.6)
Female		92 (75.4)
<i>Ethnicity</i>		
Malay		118 (96.7)
Non-Malay		4 (3.3)
<i>Temperature</i>		
Febrile		44 (36.1)
Afebrile		78 (63.9)
<i>Respiratory rate (breaths/minute)</i>	26.3 (5.7)	
<i>Blood pressure (mmHg)</i>		
<120/<80		25 (20.5)
120-139/80-89		39 (32.0)
>140/>90		58 (47.5)
<i>Heart rate (beats/minute)</i>	101.2 (20.5)	
<i>SpO₂ (%)</i>	93.8 (6.6)	
<i>Comorbidities</i>		
No		21 (17.2)
Yes		101 (82.8)
<i>Drug allergy status</i>		
No		120 (98.4)
Yes		2 (1.6)

Table 2. Adherence to CURB-65 criteria (n=122).

Adherence	n (%)
Adherent	52 (42.6)
Not adherent	70 (57.4)

Table 3. Pattern of the first empirical antibiotics prescribed for CAP patients (n=122).

Antibiotics	n (%)
IV amoxicillin/clavulanate	38 (31.1)
IV amoxicillin/clavulanate + IV or PO azithromycin	75 (61.5)
IV ceftriaxone	1 (0.8)
IV ceftriaxone + IV or PO azithromycin	1 (0.8)
IV ceftazidime + IV or PO azithromycin	5 (4.1)
IV cefuroxime + IV or PO azithromycin	1 (0.8)
IV piperacillin/tazobactam	1 (0.8)

Table 4. Adherence of empirical antibiotics to NAG 2019 for CAP patients (n=122).

Adherence	n (%)
Adherent	62 (50.8)
Not adherent	60 (49.2)
Different choices of antibiotics	46 (37.7)
Other durations of antibiotics	14 (11.5)

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