IJID Regions 14 (2025) 100505

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

Clinical, antibiotic resistance features, and treatment outcomes of Vietnamese patients with community-acquired sepsis caused by *Klebsiella pneumoniae*

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ARTICLE INFO

Keywords:
Community-acquired sepsis
Septic shock
Organ dysfunction
Klebsiella pneumoniae

ABSTRACT

Objectives: This study describes the clinical and paraclinical features, antibiotic resistance levels, and treatment outcomes of *Klebsiella pneumoniae* septicemia acquired in the Vietnamese community.
Methods: A cross-sectional descriptive study was conducted on 102 patients with community-acquired sepsis caused by *K. pneumoniae* from July 2018 to July 2023.
Results: *K. pneumoniae*–induced community sepsis had a septic shock rate of 13.7% and a death rate of 10.8%. Organ dysfunction rate in the patients with septic shock were higher than the patients without septic shock. The procalcitonin, creatinine, and platelet indexes increased more than in the septic shock group. *K. pneumoniae* strains were resistant to cephalosporins and quinolones (8-10%) and ampicillin (87%). Late hospitalization raises the risk of mortality by ~3.5 times, and combination therapy with more than two kinds of antibiotics increases the risk of death by ~1.8 times. The mortality rates were 9.1% and 63.6% after 4-6 and 2-3 weeks of therapy, respectively. Of the 11 patients who died, 90.9% died of septic shock, whereas 9.1% died of sepsis.
Conclusions: *K. pneumoniae*–induced community sepsis resulted in 13.7% septic shock, and 10.8% of the patients died. There was 87% *K. pneumoniae* resistance to ampicillin. Organ dysfunction and late hospitalization were associated with septic shock and death.

Introduction

Klebsiella pneumoniae is a common gram-negative bacterium of the Enterobacteriaceae family [1]. Bacterial species from the genus *Klebsiella* may infect humans, with *Klebsiella pneumoniae* accounting for 70% of cases [2]. *K. pneumoniae* causes numerous clinical diseases, including bacterial infection, such as sepsis, urinary tract infection, liver abscess, meningitis, soft tissue inflammation, and pneumonia in healthy people. The most serious infection caused by *K. pneumoniae* is hemorrhage, which can result in catastrophic effects such as multi-organ failure, septic shock, and high mortality rate [3]. In 2017, around 48.9 million cases of sepsis were reported. There were approximately 11 million deaths or sepsis caused 19.7% of all deaths worldwide [4].

K. pneumoniae is a common hospital-acquired infection, although it may also be acquired in the community [5]. In addition to pneumonia and urinary tract infections, sepsis caused by *K. pneumoniae* is becoming more prevalent, causing concern in the population [6,7]. Over the last decade, there has been a global increase of Enterobacteriaceae strains resistant to carbapenems, even though carbapenems are one of the most important reserve antibiotic families for the treatment of severe infections that risk the patient's survival [8,9]. *K. pneumoniae* is the most prevalent CRE strain found worldwide [10,11]. The emergence and prevalence of extended-spectrum β-lactamases (ESBLs) in *K. pneumoniae* have made therapy extremely difficult, and β-lactamase resistance outbreaks have been observed in several countries [12,13]. In particular, the rise of multidrug-resistant Klebsiella bacteria is specifically associated with the increased use of next-generation antibiotics [14,15].

Regular updates on the most severe form of *K. pneumoniae* infection, sepsis, antibiotic sensitivity, and resistance of the bacteria to antibiotics, as well as treatment outcomes, will assist clinicians in better evaluating and predicting patient prognoses and providing appropriate treatment measures to save lives and reduce mortality rates. This study aimed to describe the clinical and paraclinical characteristics of Vietnamese patients with sepsis caused by *K. pneumoniae* in the community between 2018 and 2023, as well as to evaluate antibiotic susceptibility, pathogenesis, and treatment outcomes in *K. pneumoniae* septicemia cases.

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https://doi.org/10.1016/j.ijregi.2024.100505
Received 24 August 2024; Received in revised form 27 November 2024; Accepted 28 November 2024

Methods

Population

This study was conducted between July 2018 and July 2023. Patients were recruited from two specialized hospitals of infectious diseases in Vietnam: the National Hospital of Tropical Diseases (NHTD) in Ha Noi and the National Hospital of Tropical Diseases in Dong Anh. The inclusion criteria were as follows (according to the Vietnamese Ministry of Health's guideline for diagnosis and treatment of infectious diseases) [16]: (i) having two of four criteria of systemic inflammatory response syndrome (temperature >38°C or <36°C, heart rate >90 beats/min, respiratory rate >20 cycles/min, or $PaCO_2$ <32 mm Hg [spontaneous breathing], BC >12,000/mm^3 or <4000/mm^3, or >10% premature BC), (ii) having clinical symptoms suggestive of sepsis (with an initial focus of infection) points, there are signs of bacteria entering the blood: fever, rapid pulse, fatigue, lethargy, and reticuloendothelial system symptoms such as enlarged liver and spleen lymph nodes and swollen lymph nodes near the initial infection site, with or without signs of metastatic infection), and (iii) positive blood culture results for *K. pneumoniae* within the first 48 hours of admission and antibiogram results. The exclusion criteria were as follows: (i) positive blood culture findings for two microbiological sources, (ii) patients who dropped out of therapy or were moved to the hospital without monitoring treatment results, and (iii) patients 18 years of age. We used the convenience sampling method; all eligible patients were included in the study.

Study design

This was a cross-sectional descriptive study. From July 2018 and July 2023, we collected data on all sepsis patients in the community who had positive blood cultures for *K. pneumoniae* within 48 hours of hospitalization. Patients with sepsis caused by *K. pneumoniae* who visited the hospital for any other treatment in the previous 14 days were excluded from the study. Sepsis was diagnosed and treated based on the patient's clinical symptoms and test results, with the treating physician determining the treatment strategy. In this study, two groups of patients with septic shock and without septic shock were separated to identify variables associated with the chance of developing septic shock, as well as two groups of patients who survived and died to identify factors related to treatment outcomes in patients. The Sanford Guide was used to establish single and combination antibiotic doses.

Definitions

Patient with community-acquired sepsis were identified after meeting all clinical and paraclinical criteria and being treated in accordance with the Ministry of Health of Vietnam's 2015 recommendations and revised international definitions of sepsis and septic shock [17–20].

Sepsis was defined using the following criteria: (i) having two or more of four criteria of systemic inflammatory response syndrome (temperature >38°C or <36°C, heart rate >90 beats/min, respiratory rate >20 cycles/min, or $PaCO_2$ <32 mm Hg [spontaneous breathing], white blood cells >12 G/l or <4 G/l, immature white blood cell rate >10%, thrombocytopenia <100 G/l, coagulation disorder international normalized ratio >1.5, or activated partial thromboplastin time >60 seconds) or have clinical symptoms suggestive of sepsis (there is an initial focus of infection; there are signs of bacteria entering the blood: fever, rapid pulse, fatigue, lethargy, symptoms of the reticuloendothelial system such as enlarged liver and spleen lymph nodes and swollen lymph nodes around the initial infection site, with or without evidence of metastatic infection) and (ii) blood culture results positive for microbial etiology.

Septic shock was identified using the following criteria: sepsis, systolic blood pressure <90 mm Hg, systolic blood pressure decline >40 mm Hg from baseline, or average blood pressure <70 mm Hg.

Conducted study

Patients with suspected sepsis who had typical clinical symptoms of sepsis at admission, such as fever, skin rash or skin congestion, and subcutaneous edema or hemorrhage, as well as other symptoms such as digestive, respiratory, cardiovascular, neurological, and urinary symptoms, were included in the study. Blood cultures, biochemistry, hematology, and imaging tests were ordered immediately upon admission. Only patients with positive *K. pneumoniae* blood culture findings within 48 hours of admission were eligible to participate in the study. According to the guidelines of the Ministry of Health of Vietnam [17], patients chosen for the study were inspected, tested, and treated until they recovered, were discharged, or died. Individual records and codes were used to maintain study information for each patient, as specified in a pre-designed form.

Study indicators included (i) clinical: underlying diseases, time of disease progression before admission, characteristics of fever symptoms (onset, nature, amplitude), functional symptoms, clinical symptoms (abdominal pain, difficulty breathing, cough, meningeal syndrome, mental disorders, painful urination, boils, or aps), organ dysfunction (digestive, respiratory, neurological, cardiovascular, urinary tract), rate of septic shock, time of septic shock, combination of antibiotics in treatment, fever resolution time, treatment duration, and treatment results; (ii) laboratory: anemia, white blood cell changes, platelet changes, coagulation status changes (%prothrombin time, activated partial thromboplastin time, fibrinogen), liver enzyme levels (aspartate transaminase/alanine transaminase), bilirubin, albumin, sodium, potassium, blood urea, creatinine, changes in infection markers (C-reactive protein, procalcitonin [PCT]), and antibiotic resistance (reduced antibiotic susceptibility rate of *K. pneumoniae*); and (iii) imaging diagnosis: pneumonia, pleural effusion, lung abscess, liver abscess, peritoneal fluid, hepatomegaly or splenomegaly, heart failure, pericardial fluid, and mitral valve vegetation.

Blood culture, bacterial identification, and antibiotic sensitivity test

The blood of patients suspected of having sepsis was cultured in a Bactec Plus Aerobic/F Culture Vial (Becton Dickinson, USA) and incubated using the Bactec 9050/9120 system (Bactec Dickinson, USA). Blood culture bottles positive for bacteria were subcultured and isolated with blood and chocolate media. The recovered bacteria were subsequently Gram-stained and identified with the BioMerieux VITEK 2 Compact System (Marcy I'Etoile, France). To evaluate the antibiotic susceptibility of all clinical isolates of *K. pneumoniae*, the paper circle diffusion technique was used at the Bacterial Laboratory (NHTD) to determine the antibiotic MICs. The antibiotic in the paper circle was diffused into Meuller–Hinton agar containing *K. pneumoniae*, and the diameter of the sterile zone around the paper circle demonstrated *K. pneumoniae*'s susceptibility to the antibiotic. The antibiotic susceptibility test findings were interpreted using the diameter of the sterile zone surrounding the paper circle and the break point in the Clinical and Laboratory Standards Institute (CLSI) document. According to CLSI 2023, susceptibility levels can be classified as susceptible (S), intermediate (I), and resistant (R) based on the diameter of the inhibition zone and the break point in the documentation guiding the interpretation of antibiogram results [21].

Data analysis

The data were analyzed using SPSS software (version 20.0). Categorical variables were reported using frequencies and percentages. To identify the prognosis signs of septic shock, patients were separated into two groups: septic shock and non-septic shock. We examined the study indicators based on the rate of organ dysfunction; duration of infection before admission; and changes in biochemical, hematologic, and imaging indicators throughout the study. The algorithms were: (i) calculating the

mean value, SD, maximum value, minimum value, median, interquartile range, and standard test for quantitative variables; (ii) comparing percentages with qualitative variables; (iii) comparing proportions of qualitative variables using the chi-square test and Fisher's exact test. A $P \leq 0.05$ indicates statistical significance. Antibiotic resistance indicators in *K. pneumoniae* were cited using the CLSI 2023 guidelines [21]. The values of the test indicators at the higher (or lower) threshold or the ideal threshold value were established in accordance with the guidelines of CLSI 2023 recommendations, as well as the Ministry of Health of Vietnam.

Ethical considerations

The ethics committee of the NHTD approved the study design (document no: 14/HĐĐĐ-NĐTƯ). Before participating in the study, written informed consent was obtained from all patients or the patient's parent/guardians if the patient was under 18 years of age.

Results

The average age of 102 Vietnamese patients with sepsis caused by *K. pneumoniae* in the community was 54 years. The highest proportion of patients were aged 40-64 (65.7%), ≥65 (25.5%), and 18-39 (8.8%) years. There were 84.3% men and 15.7% women. A total of 66.7% of patients resided in rural regions, compared with 33.3% who lived in urban areas. Diabetes (46.1%), cirrhosis and hepatitis virus infection (29.4%), hypertension (25.5%), urinary diseases (7.8%), and other diseases (23%) were among the documented comorbidities. A total of 57.8%, 32.4%, and 9.8% of patients had *K. pneumoniae* infection in the community 3 days before admission, 4-7 days before hospitalization, and 8-13 days before hospitalization, respectively. Septic shock was reported in 13.7% of patients, whereas 86.3% did not have sepsis shock. After therapy, 10.8% of patients died, whereas 89.2% survived (Table 1).

Organ dysfunction in patients with community-acquired sepsis caused by *K. pneumoniae* was most frequent in the digestive, respiratory, cardiovascular, urinary, and neurologic systems. The patient's skin and soft tissue also showed signs of pimples, abscesses, tissue infection, open wounds, and other traumas. The septic shock group had the highest rates of cough/sputum (35.7%), shortness of breath (28.6%), reduced lung ventilation (42.9%), and lung rales (14.3%) compared with the non-septic shock group, which had rates of 11.4%, 1.1%, 10.2%, and 5.7%, respectively (Table 2). Furthermore, pimples, abscesses, and tissue infections occurred at a rate of 21.4% and 4.5% in the septic shock and non-septic shock groups, respectively. Dysfunctions in the respiratory, cardiovascular, neurologic, and urinary organs did not differ significantly between the septic shock and non-septic shock groups ($P > 0.05$; Table 2).

Biochemical testing revealed that the rate of increase in the infection marker C-reactive protein across the two groups of patients with and without shock was substantially identical (78.6% vs 78.4%, respectively). However, the rates of increase in PCT and creatinine in patients with shock were 100% and 50%, respectively, compared with 43.2% and 8.0% in patients without shock. There was a significant difference between the two patient groups ($P < 0.05$; Table 3). Hematologic indexes also revealed that 65.9% and 35.7% of patients without shock had an elevated white blood cell index, whereas 35.7% and 13.6% of patients with shock had thrombocytopenia (Table 3). Diagnostic imaging results revealed a pneumonia rate of 70.5% in patients without shock, which was higher than the rate in patients with septic shock (14.3%). In comparison, the proportion of patients without shock who had liver abscesses were just 45.5% and 64.3% in the shock group. In addition, there was no statistically significant difference in the frequency of prehospital sepsis ≤3 days, 4-7 days, and 8-13 days in the two groups of patients with and without septic shock ($P > 0.05$) (Table 3).

Table 1
Demographic and epidemiologic characteristics of patients with bacteremia caused by *K. pneumoniae*.

Characteristics	Number of patients (n = 102)	%
Age (years)		
18-39	9	8.8
40-64	67	65.7
≥ 65	26	25.5
Median (interquartile range)	(Minimum: 18, maximum: 36, median: 54)	
Gender		
Male	86	84.3
Female	16	15.7
Geographic distribution		
Rural	68	66.7
Urban	34	33.3
Co-morbidities		
Diabetes	47	46.1
Cirrhosis, viral hepatitis	30	29.4
Hypertension	26	25.5
Urinary diseases	8	7.8
Gout	5	4.9
Cancer	3	2.9
Chronic obstructive pulmonary disease/bronchial asthma	2	1.9
Others	13	12.7
Duration of infection before admission (days)		
≤3	59	57.8
4-7	33	32.4
8-13	10	9.8
Septic shock		
Patient with septic shock	14	13.7
Patient with no septic shock	88	86.3
Treatment outcome		
Survival	91	89.2
Death	11	10.8

Table 2
Clinical symptoms in patients with sepsis caused by *K. pneumoniae*.

Clinical symptoms	Patients with septic shock	Patients without septic shock	*P-value*
Digest			
Nausea, vomiting	2 (16.7 %)	7 (8.0%)	0.343[a]
Loose stools	0	7 (8.0%)	0.589[a]
Stomach ache	2 (16.7%)	29 (37.2%)	0.206[a]
Jaundice	1 (7.1%)	14 (15.9%)	0.687[a]
Enlarged liver/spleen	3 (21.4%)	15 (17%)	0.709[a]
Ascites	3 (21.4%)	10 (11.4%)	0.381[a]
Respiratory			
Cough/sputum	**5 (35.7%)**	**10 (11.4%)**	**0.032**[a]
Shortness of breath	**4 (28.6%)**	**1 (1.1%)**	**0.001**[a]
Reduced lung ventilation	**6 (42.9%)**	**9 (10.2%)**	**0.006**[a]
Lung rales	2 (14.3%)	5 (5.7%)	0.245[a]
Nerve			
Headache	1 (7.1%)	10(11.4%)	1.00[a]
Disorders of consciousness	2 (14.3%)	11 (12.5%)	1.00[a]
Meningeal syndrome	1 (7.1%)	9 (10.2%)	1.000[a]
Localized nerve damage	0	3 (3.4%)	1.000[a]
Urinary			
Painful/dribbling urination	0	4 (4.5%)	1.00[a]
Hematuria	1 (7.1%)	0	0.137[a]
Urinary retention/difficult urination	0	2 (2.3%)	1.00[a]
Low back pain - pelvic area	0	3 (3.4%)	1.00[a]
Skin and soft tissue			
Pimples, abscesses, tissue infection	3 (21.4%)	4 (4.5%)	0.052[a]
Open wound	0	1 (1.1%)	1.00[a]
Other injuries	0	2 (2.3%)	1.00[a]
Cardiovascular			
Angina pectoris	0	1 (1.1%)	1.00[a]
Anxiety and palpitations	1 (7.1%)	0	0.137[a]
Peripheral vascular occlusion	0	1 (1.1%)	1.00[a]

[a] Fisher's exact test.

Table 3
Comparison of some biochemical, hematologic, imaging characteristics and treatment time between the group of patients with septic shock and without shock.

Indices	Patients with septic shock	Patients without septic shock	*P-value*
Biochemistry			
C-reactive protein >100 mg/l	11(78.6)	69(78.4)	0.480[a]
Procalcitonin >10 ng/ml	**14(100)**	**38(43.2)**	**0.004**[a]
Creatinine >120 µmol/l	**7(50.0)**	**7(8.0)**	**0.000**[a]
Hematology			
White blood cells > 10 G/l	**5(35.7)**	**58(65.9)**	**0.04**[b]
Platelet <150 G/l	**5(35.7)**	**12(13.6)**	**0.048**[b]
Diagnostic imaging			
Pneumonia	**2(14.3)**	**62(70.5)**	**0.000**[b]
Liver abscess	9(64.3)	40(45.5)	0.153[a]
Duration of infection before admission (days)			
≤3	8 (57.1)	51 (58%)	0.954[b]
4-7	4(28.6%)	29 (33.0%)	1.00[a]
8-13	2(14.3%)	8 (9.1%)	0.624[a]

[a] Fisher's exact test; [b]chi-square test.

Table 4
Characteristics of treatment of patients with bacteremia caused by *K. pneumoniae*.

Characteristics	Patient survival (n = 91)	Patient death (n = 11)	*P-value*
Antibiotic combination			
1 antibiotic	22(24.2)	3(27.3)	0.723[a]
2 antibiotics	41(45.0)	3(27.3)	0.198[a]
>2 antibiotics	**28(30.8)**	**6(54.5)**	**0.043**[a]
Duration of infection before admission (day)			
≤3	55 (60.4)	4 (36.4)	0.195[a]
4-7	29(31.9)	4(36.4)	0.744[a]
8-13	7(7.7)	3(27.3%)	0.074[a]
Treatment duration (week)			
<1	6(6.6)	3(27.3)	0.055[a]
2-3	40(43.9)	7(63.6)	0.910[b]
4-6	46(50.5)	1(9.1)	0.198[a]
Clinical status of patients			
Septic shock	**7(7.7)**	**10(90.9)**	**0.000**[a]
No septic shock	**84(92.3)**	**1(9.1)**	**0.000**[a]

[a] Fisher's exact test; [b]chi-square test.

Antibiogram test findings revealed that carbapenem antibiotics (ertapenem, imipenem, and meropenem) were effective against 92% of bacterial strains. *K. pneumoniae* was also susceptible to certain antibiotics, including piperacillin/tazobactam (92.2%), amikacin (98%), and gentamycin (98%). Approximately 8-10% of strains were resistant to cephalosporins (ceftriaxone, ceftazidime, cefotaxime, and cefepime) and quinolone (ciprofloxacin). *K. pneumoniae* strains were highly resistant to ampicillin (87%), fosfomycin, and co-trimoxazole, with over 10% resistant to fosfomycin. The overall sensitivity to other antibiotics remains strong, ranging from 80% to 90% (Figure 1). The data also revealed that multidrug-resistant *K. pneumoniae* strains accounted for just 17.6% (16 strains), with two antibiotic resistance at 7.8%, three antibiotic resistance at 1.0%, and four antibiotic resistance at 8.8%.

When different antibiotics were used to treat sepsis induced by *K. pneumoniae*, patients who received only one antibiotic had survival and mortality rates of 24.2% and 27.3%, respectively. Patients administered a combination of two antibiotics had a survival rate of 45% and a mortality rate of 27.3%. Patients treated with more than two types of antibiotics had survival and mortality rates of 30.8% and 54.5%, respectively. Survival rates for infection before hospitalization <3, 4-7, and 8-13 days were 60.4%, 31.9%, and 7.7%, respectively. The mortality rates for infection before hospitalization of <3, 4-7, and 8-13 days were 36.4%, 36.4%, and 27.3%, respectively. Patients with a treatment period of ≤3 weeks had higher mortality rate than those who survived. In the septic shock group, the mortality rate was 90.9%; however, in the non-septic shock group, it was only 9.1% (Table 4).

Discussion

Sepsis may occur at any age; however, it is more likely in elderly people owing to weakened resistance. Furthermore, elderly people may have a number of chronic diseases that contribute to the development of infection with sepsis and the consequences to septic shock [22,23]. According to Li et al. [24], the average age for sepsis caused by K. pneumoniae in the community was 61.1 years, with men accounting for 67.6% of all cases. Men are more likely to become infected, which explains their prevalence. Men are more likely than women to be addicted to stimulants and have chronic ailments. According to Ko et al. [25], the average age of the patients was 58.8 years, with men accounting for 62.0%. Melot et al. [26] reported an average patient age of 51 years and a proportion of men of 43%. Our findings also suggest that 91.2% of patients aged >40 years had sepsis, with an average age of 54 years and a proportion of men up to 84.3%. These findings are completely consistent with the trend and direction of research.

Diabetes, cirrhosis, burns, surgeries, and K. pneumoniae sepsis, which occurs frequently in people with preexisting chronic diseases, are all predisposing factors for gram-negative sepsis. In our study, 77.5% of patients had one or more comorbidities; diabetes (46.1%), cirrhosis (29.4%), and hypertension (25.5%) were the most frequent. Tsay et al. [27] showed that the rate of diabetes due to sepsis caused by K. pneumoniae in the community was 49%. Chen et al. [28] found that comorbidities included diabetes (36.7%), chronic kidney disease (32.7%), and cardiovascular disease (30.8%). Melot et al. [26] reported 38% diabetes, 14% liver disease, and 9% kidney failure. Chronic diseases differ between regions based on social variables. It impairs the immune system and the body's stress response, so when infections develop, the body is unable to fight them efficiently, leading to sepsis and septic shock.

According to medical literature, gram-negative septic shock is synonymous with hypovolemic shock. The first stage is heated shock, which causes symptoms such as increased circulatory output, increased ventilation, hot and dry skin, and so on. This stage is generally brief and soon progresses to the normal cold shock stage, which includes pale skin, a purple and cold head, limbs, and rapid and weak pulse. All the patients in our study were identified at this typical stage of cold shock. The two most common disorders at this stage are hypovolemia and tissue anemia-hypoxia. If it is not intervened immediately, it will lead to a pathological spiral; the shock will worsen, producing multi-organ dysfunction leading to rapid death. Li et al. [24] found that the rate of patients with septic shock due to K. pneumoniae in the community was 27.4%, whereas Lin et al. [29] reported a rate of 51%. Our study found a substantially lower risk of septic shock progression, with just 13.7% of cases.

Patients with sepsis may develop dysfunction in practically every system, independent of the location of the infection. The most often afflicted organs are the kidneys, liver, lungs, heart, central nervous system, and hematologic system. This multi-organ failure is a defining feature of sepsis and determines whether the patient has progressed from infection to recovery or death. In fact, the sequential organ failure assessment score is one method that may be used to assess disease severity and guide treatment. However, we did not produce this score to include in the study's findings. We only mentioned a few criteria in the sequential organ failure assessment score, such as platelets and creatinine. In this study, we found that the proportion of patients with digestive, respiratory, and neurologic failure was higher than patients with urinary and cardiovascular failure. However, when the rate of organ dysfunction between patients with septic shock and patients without septic shock was compared, there was a statistically significant difference in respiratory system dysfunction.

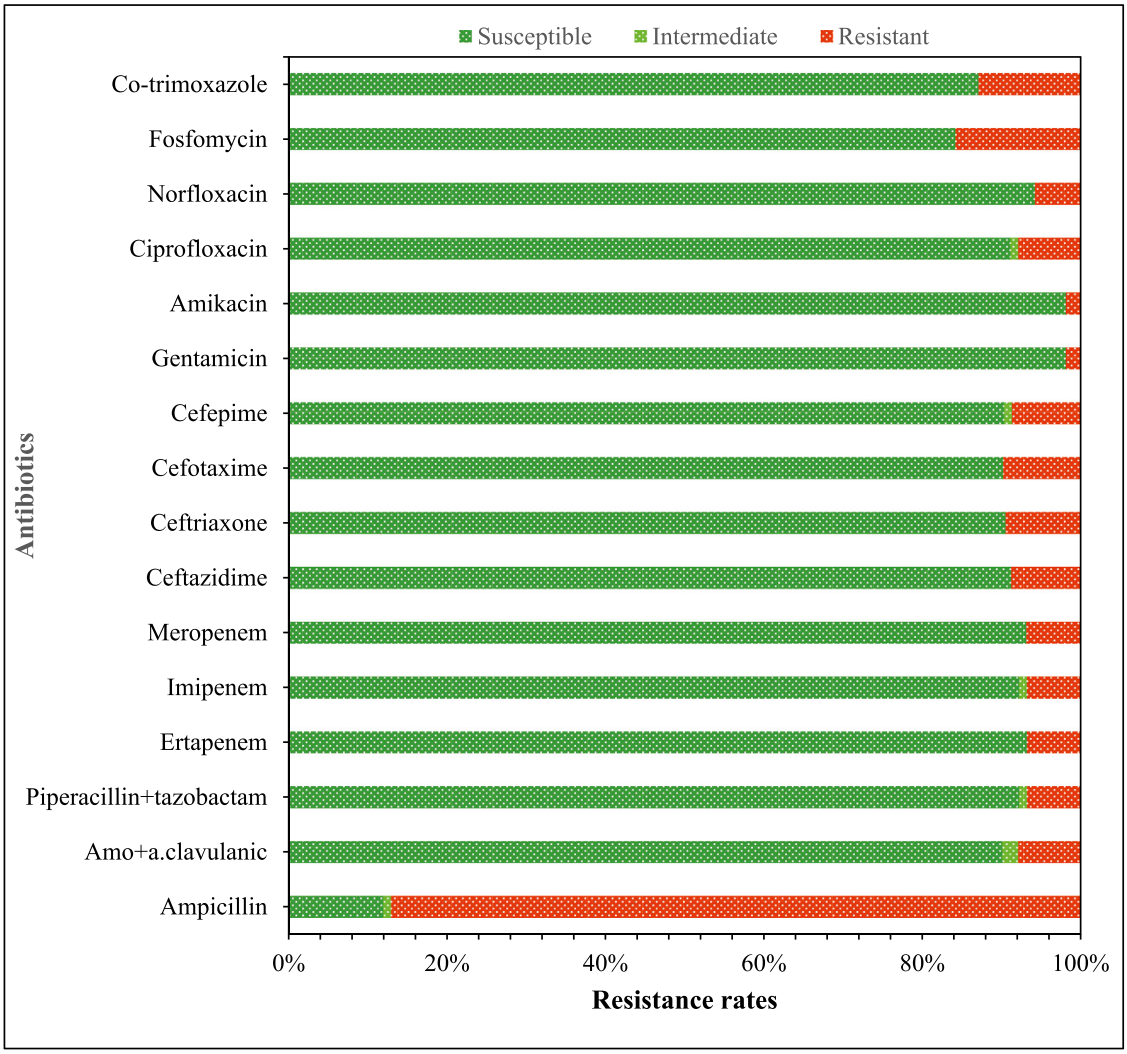

Figure 1. Antibiotic susceptibility of *K. pneumoniae* strains causing community sepsis.

Sepsis induced by gram-negative bacteria affects a number of organs, including the liver, kidney, and hematologic function. Blood clotting disorders are frequently caused by variations in platelets and clotting factors. In addition, patients with *K. pneumoniae*–induced sepsis had higher white blood cell counts, and leukopenia was associated with septic shock. Comparing the septic shock and non-septic shock group, the rate of elevated blood creatinine was significantly higher in the former. Leukopenia and thrombocytopenia were also prevalent in the patients with septic shock. The PCT index was higher in the septic shock group than in the non-septic shock group, but the pneumonia rate was much lower in this group. The PCT at the time of hospitalization is meaningful for the diagnosis, monitoring, and treatment of sepsis. Imaging diagnostics play a role in identifying primary infection foci in the lungs or detecting metastatic foci in the lungs or detect concealed infection foci throughout the body.

Our findings revealed that *K. pneumoniae* is still susceptible to most carbapenem antibiotics (meropenem, imipenem, and ertapenem), with approximately 7% of patients resistant to this group of antibiotics. All carbapenem-resistant *K. pneumoniae* in the community were associated with underlying medical conditions and risk factors for infection with resistant organisms, such as hospitalization or previous antibiotic use. *K. pneumoniae* remains highly vulnerable to other antibiotics such as piperacillin/tazobactam and amikacin, with only a small percentage of bacteria resistant to piperacillin/tazobactam (6.9%), amikacin (2.0%), and gentamycin (2.0%). Ampicillin (87%), cotrimoxazole (13.0%), and amoxicillin + clavulanic acid (8%) had highly resistance rates. The sensitivity rate to antibiotics in the third-generation cephalosporin and quinolone groups was around 80-90%; therefore, in clinical practice, it is necessary to consider the empirical use of these antibiotics when the patient is first hospitalized for treatment. The NHTD frequently updates microbiological and antibiogram data for clinicians and recommends first-line empirical antibiotics for physicians. This study, as well as several others conducted at hospitals throughout Vietnam, demonstrates that third-generation cephalosporins are still effective against this pathogen.

Our findings revealed that 102 patients with *K. pneumoniae*–related sepsis were treated with intravenous antibiotics, with 28 receiving a single antibiotic, 35 receiving a combination of two antibiotics, and 36 receiving a combination of three or more antibiotics. The empirical use of antibiotics by clinicians is also based on microbiologic data and antibiogram results from previous years. Clinicians who use numerous antibiotics must collaborate with the treating physician, clinical department leaders, clinical pharmacists, clinical microbiologists, and hospital specialists to decide whether to administer antibiotics to patients. Despite the relatively low level of antibiotic resistance in *K. pneumoniae*, clinicians in Vietnam frequently base their treatment on the patient's condition, combining antibiotics based on experience to broaden the spectrum of effect, enhance antibacterial effectiveness,

and inhibit many bacterial growth stages, thereby improving treatment effectiveness.

Susceptibility testing often determines the antibiotic treatment for *K. pneumoniae* infections. Clinical strains of *K. pneumoniae* are becoming increasingly resistant to a wide range of medicines, which is concerning. When selecting an antibiotic regimen for *K. pneumoniae* infections, it is important to consider the probability of ESBL or carbapenemase development. Infection of mild severity, host not immunocompromised, low suspicion of ESBL-producer, ceftriaxone 2 gm intravenous (IV) every 24 hours if under 60; 1 gm IV if over 60, ciprofloxacin 400 mg IV every 24 hours or 750 mg orally twice per day, or levofloxacin 750 mg orally/IV every 24 hours are additional possible alternatives. Carbapenems (imipenem, meropenem, and ertapenem) are the recommended, established treatment alternatives for severe infections caused by ESBL-producing organisms in critical care units and/or immunocompromised patients with MDR. Meropenem 1-2 gm IV every 8 hours. Resistant to ceftriaxone, ceftazidime (ESBL-generating organism), ertapenem 1 gm IV every 24 hours or meropenem 2 gm IV every 8 hours, carbapenem-resistant bacterium, most likely serine carbapenemase ceftazidime-avibactam 2.5 gm IV every 8 hours, or meropenem-vaborbactam 4.0 gm (2 gm meropenem + 2 gm vaborbactam) IV over 3 hours and given every 8 hours.

Our data demonstrated that the fever resolution time was often less than 7 days (58.8%). Most antibiotic treatments last 7-21 days and often involve a combination of two antibiotics. In Vietnam, three types of antibiotics are used to treat elderly patients and those with a variety of co-morbidity diseases such as diabetes, alcoholic cirrhosis, multiple organ damage, and septic shock. Many recommendations have been made that in cases of severe sepsis or septic shock, the combination of two antibiotics is necessary, such as carbapenem + quinolone or third-generation cephalosporin + quinolone or third-generation cephalosporin + aminosid. In Vietnam, *E. coli* and *K. pneumoniae* are the most common causes of severe sepsis with liver abscess; therefore, anaerobic bacterial superinfection is conceivable. As a result, these instances are frequently paired with metronidazole to treat anaerobic bacteria. When the culture findings are obtained, the doctor will de-escalate the infection with a suitable antibiotic based on the clinical condition and antibiotic susceptibility testing results. Patients with large abscesses that have not been aspirated or who are in septic shock have not yet had their antibiotic levels decreased or a single antibiotic used for therapy.

The majority of the patients (52.9%) stayed in the hospital for 1-3 weeks. In addition, approximately 38.2% of patients received treatment for more than 3-6 weeks. The duration of antibiotic treatment is determined by the patient's clinical response, clinical status (sepsis, septic shock, sepsis with liver abscess), and whether or not the subsequent blood culture findings are negative. Study by Yinnon found that community infections caused by *K. pneumoniae* resulted in an average hospital stay of 15 ± 22 days. In our study, the population mortality rate from *K. pneumoniae* was 10.8%, with the septic shock group having a mortality rate of almost 91%. The mortality rate in this study is lower than that reported by Verani et al. [30] (30%), Tsay et al. [27] (22.8%), Melot et al. [26] (22%), and Kang et al. [31] (16%). Our unpublished data showed that patients with sepsis caused by K. pneu*moniae* who were hospitalized late had a 1.6 times higher risk of septic shock, and the fatality rate in the late hospitalized group was 3.5 times higher than the early hospitalized group. This shows that early identification and admission for treatment are critical in limiting the development of septic shock and reducing patient death. Although there have been significant advances in emergency care and treatment of patients with sepsis and septic shock over the last decade, the mortality rate from sepsis is still quite high and remains a difficult challenge for the health care system. Vietnam is a low-to-moderate–income country with a developing economy and a high risk of infectious diseases. Antibiotic resistance, which is a major cause of treatment failure and mortality, is also widespread.

However, in this study, we attempted to use the chi-square test and Fisher's exact test algorithms to distinguish between clinical symptoms such as organ dysfunction or abnormalities in laboratory indicators, imaging diagnosis, antibiotic use, hospitalization time, and treatment outcomes. There is a noticeable difference; however, the algorithms' *P*-values frequently fail to appropriately reflect this difference owing to insufficient sample size. This is also a limitation of this study; with a larger sample size, it would be feasible to clearly demonstrate which index the difference is in.

In conclusion, patients with *K. pneumoniae*–induced sepsis in the community had a shock frequency of 13.7% and a mortality rate of 10.8%. Organ dysfunction, a higher infection index, late hospitalization, and the use of more than two combination antibiotics were all related with the development of septic shock and death. *K. pneumoniae*, which causes community sepsis, remained highly susceptible to numerous commonly used antibiotics, except for ampicillin.

Declarations of competing interest

The authors have no competing interests to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

The ethical approval of this study was waived according to our center's policy.

Author contributions

Le Van Duyet: study design, data collection, data analysis, manuscript writing, and revising. **Tran Van Giang:** data analysis, writing draft. **Nguyen Quoc Phuong:** data analysis, writing draft. **Le Thanh Dat:** data collection, data analysis. **Nguyen Kim Anh:** data collection, data analysis.

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