Comparison of bacteremic pneumonia caused by *Escherichia coli* and *Klebsiella pneumoniae*

A retrospective study

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ABSTRACT

الأهداف: لمقارنة تشخيص الالتهاب الرئوي الجرثومي الناتج عن مسببات الأمراض الكلبسيلة الرئوية (K. pneumoniae) والإشريكية القولونية (E. coli).

المنهجية: أجري تحليل بأثر رجعي على البيانات السريرية لـ 162 مريضاً مصابين بالالتهاب الرئوي الجرثومي الناجم عن الكلبسيلة الرئوية أو الإشريكية القولونية خلال الفترة من 2019–2016م. وكانت النتيجة الأولية للتحليل هي معدل وفيات المرضى لمدة 30 يومًا.

النتائج: اشتملت الدراسة على 82 مريضاً في مجموعة الالتهاب الرئوي الجرثومي الإشريكية القولونية (E. coli–BP) و 80 مريضاً في مجموعة الالتهاب الرئوي الجرثومي (KP–BP). كان معدل الوفيات لمدة 30 يومًا 43.75% (العدد=35/80) في مجموعة KP–BP و21.95% (العدد=18/82) في مجموعة E. coli–BP، القيمة الإحصائية (p<0.001). بعد تعديل المتغيرات المشتته في 4 نماذج متميزة، أجرينا تحديد نسب الخطر للنتيجة الأولية في KP–BP لتكون 0.70 تحت مستوى ثقة 95% (فترة الثقة= 1.02–0.44) في النموذج 1، 0.72 فترة الثقة= 1.14–0.46 في النموذج 2، 0.99 فترة الثقة= 1.73–0.57 في النموذج 3، و1.22 فترة الثقة= 2.18–0.69 في النموذج 4.

الخلاصة: المرضى الذين تم تشخيصهم بـKP–BP اظهروا تشخيصًا مشابهًا لتلك التي تم تشخيصها بـ E. coli–BP. بالنسبة للمرضى الذين يعانون من KP–BP، كان خطر الوفاة أعلى بكثير من الذين كانوا في وحدة العناية المركزة، أو أصيبوا بسلالات مقاومة للكاربابينيم، أو لديهم درجة عالية في تقييم فشل الأعضاء المتسلسل. في المرضى الذين يعانون من E. coli–BP، ارتبطت درجة جرثومة الدم في Pitt بقوة بمعدل الوفيات لمدة 30 يومًا.

Objectives: To compare the prognosis of bacteremic pneumonia caused by *Klebsiella pneumoniae* (*K. pneumoniae*) and *Escherichia coli* (*E. coli*) pathogens.

Methods: A retrospective analysis was carried out on the clinical data of 162 patients who were diagnosed with bacterial pneumonia caused by either *K. pneumoniae* or *E. coli* between 2016-2019. The primary outcome of the analysis was the patients' 30-day mortality rate.

Results: There were 82 patients in the *E. coli* bacteremic pneumonia (*E. coli*-BP) group and 80 patients in the *K. pneumoniae* bacteremic pneumonia (KP-BP) group. The 30-day mortality rate was 43.75% (n=35/80) in the KP-BP group and 21.95% (n=18/82) in the *E. coli*-BP group ($p<0.001$). Following the adjustment for confounding variables in 4 distinct models, the hazard ratios for the primary outcome in KP-BP were determined to be 0.70 (95% confidence interval [CI]: [0.44-1.02]) in Model 1, 0.72 (95% CI: [0.46-1.14]) in Model 2, 0.99 (95% CI: [0.57-1.73]) in Model 3, and 1.22 (95% CI: [0.69-2.18]) in Model 4.

Conclusion: Patients diagnosed with KP-BP exhibited a similar prognosis as those diagnosed with *E. coli*-BP. For patients with KP-BP, the risk of mortality was significantly higher for those who were in the intensive care unit, were infected with carbapenem-resistant strains, or had a high sequential organ failure assessment score. In patients with *E. coli*-BP, the Pitt bacteremia score was strongly associated with the 30-day mortality rate.

Keywords: *Klebsiella pneumoniae*, *Escherichia coli*, bacteremic pneumonia, 30-day mortality, risk factors

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The global morbidity and mortality of community-acquired pneumonia (CAP) significantly affect the public health systems worldwide.[1] Nosocomial pneumonia, inclusive of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), is the predominant form of iatrogenic infection.[2] While pneumonia is primarily caused by Gram-positive bacteria, the incidence of Gram-negative bacteria-induced pneumonia is steadily increasing.[3,4]

Klebsiella pneumoniae (*K. pneumoniae*) is the main cause of CAP, HAP, and VAP, such that *K. pneumoniae* has led to a relatively large number of cases (15.4%) of CAP in Asia.[5-7] In recent years, there has been an increasing incidence of carbapenem-resistant *K. pneumoniae* (CRKP), thereby posing a substantial concern in public health.[8] *Escherichia coli* (*E. coli*) is derived from the *Enterobacteriaceae* family and is the second most prevalent bacterial cause of bacteremic pneumonia in the United States.[9] A comprehensive study revealed that *E. coli* constituted approximately 8% of culture-positive bacterial CAP cases.[10]

Recently, the emergence of multidrug-resistant Gram-negative bacteria has emerged as a significant concern, particularly among individuals receiving hospital care. Consequently, an increasing body of research has been dedicated to examining the epidemiology, risk factors, and clinical outcomes associated with pneumonia caused by Gram-negative bacteria. Although some studies have characterized pneumonia caused by these 2 pathogens individually, it was observed that hospital-acquired bacteremic pneumonia (HABP) attributed to *K. pneumoniae* exhibited a markedly elevated mortality rate in comparison to *E. coli*.[7,10-12] However, comprehensive comparative studies are still lacking. Hence, a study was carried out to analyze the characteristics of patients with *K. pneumoniae* bacteremic pneumonia (KP-BP) and those with *E. coli* bacteremic pneumonia (*E. coli*-BP) to compare the outcomes and to identify the predictors of the 30-day mortality rate in the 2 groups, which complemented a previous small cohort study.[12]

Methods. A comprehensive retrospective cohort study was carried out at the Affiliated Hospital of Nanchang University, Jiangxi, China, a tertiary healthcare facility with a bed capacity of 2400. The study focused on various factors and outcomes related to bacteremic pneumonia caused by *K. pneumoniae* and *E. coli*. Enrollment was limited to patients admitted to the hospital between January 2016 and December 2019, and these patients had to be diagnosed with a specific type of pneumonia. Based on the consensus criteria, patients exhibiting typical signs and symptoms of pneumonia along with a demonstrable infiltrate were diagnosed with pneumonia.[13,14] Blood samples were obtained from adult patients aged 18 years old or older within 24 hours of being diagnosed with pneumonia. The inclusion criteria for the study required patients to have at least one positive blood culture for *K. pneumoniae* or *E. coli*. Exclusion from the study included deaths occurring within 48 hours of admission, polymicrobial infections, pregnant women, patients with incomplete data, and infections other than pneumonia (**Figure 1**). In patients with multiple episodes of KP-BP or *E. coli*-BP during hospitalization, only the first episode was considered. The present study was approved by the research ethics committee of the Second Affiliated Hospital of Nanchang University, Jiangxi, China. Given the retrospective nature of the study, the requirement for informed consent was waived.

Community-acquired pneumonia was defined as the contraction of community-onset pneumonia within 48 hours of hospitalization. The diagnostic criteria for CAP included the presence of the following symptoms: i) the manifestation of a recently acquired cough, production of sputum, or deterioration of pre-existing respiratory symptoms, accompanied by or without the presence of purulent sputum, chest discomfort, difficulty in breathing, and coughing up blood; ii) fever; iii) evidence of pulmonary solid lesions or audible wet rhonchi; iv) peripheral blood leukocyte counts exceeding 10 x 109/L or falling below 4 x 109/L, with or without the presence of immature white blood cells; v) chest imaging demonstrates the identification of emerging patchy infiltrative shadows, lobar or segmental solid shadows, ground glass shadows, or interstitial changes, with or without the presence of pleural effusion.[13] In contrast, HAP was diagnosed if it occurred after 48 hours of hospitalization (including VAP).[14] The determination of sepsis was established according to the diagnostic criteria outlined in Sepsis-3, a publication by the American Society of Critical Care Medicine (SCCM)/European Society of Critical Care Medicine (ESICM) from 2016.[15] These criteria encompassed 2 key components: i) the detection or existence of an infection and ii) a sequential organ failure assessment (SOFA) score equal to or exceeding 2. Polymicrobial infection was defined as 2 or more bacterial species in respiratory or blood cultures collected within 48 hours

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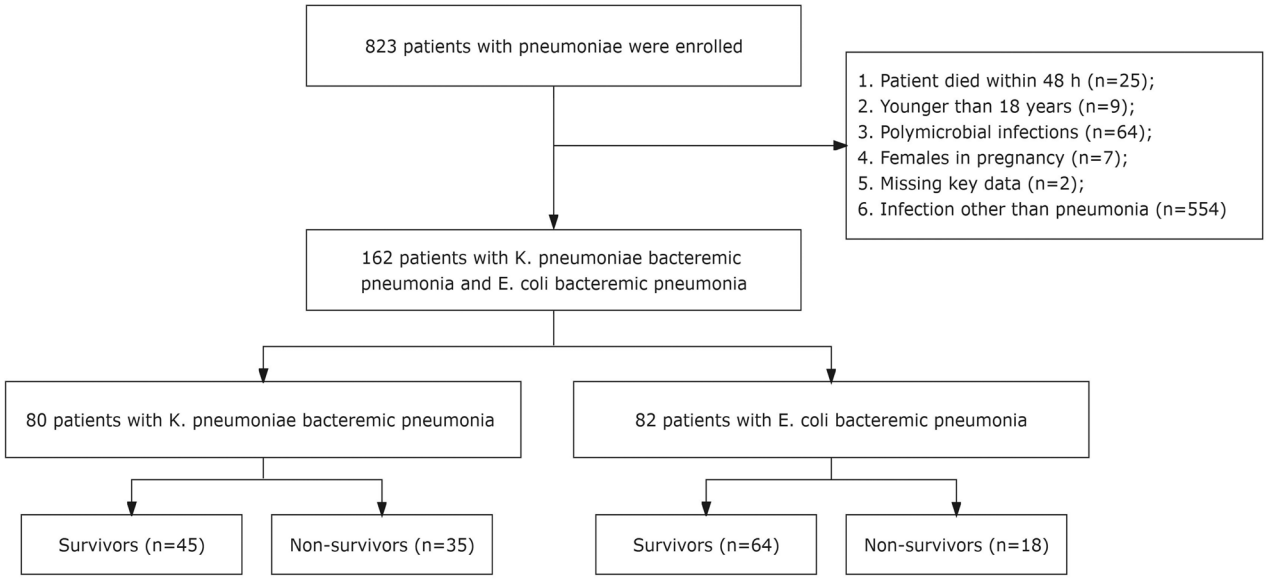

Figure 1 - Flow chart of patients selected. *K. pneumoniae*: *Klebsiella pneumoniae*, *E. coli*: *Escherichia coli*.

of admission. Immunosuppression was defined to include various forms, such as the administration of oral steroids or other immune system-suppressing medications, organ transplantation, the presence of HIV infection, and chemotherapy for cancer.[16] If the chosen antibiotic displayed no efficacy against the isolated strain in the laboratory test, antibiotic treatment was deemed ineffective. Empirical therapy was defined as antimicrobial treatment administered before drug susceptibility testing. Appropriate empirical therapy referred to an active agent that was started within 24 hours of pneumonia diagnosis, while inappropriate therapy was defined as antibiotic treatment without any active agent. Failure of antimicrobial therapy was characterized by the persistence or progression of signs and symptoms of infection. The primary outcome chosen for this study was the mortality rate within 30 days.

The hospital information system (HIS) and laboratory information system (LIS) were used to collect clinical data and laboratory results. The collected data included the following: i) demographics, such as age and gender; ii) type of pneumonia (community-acquired or nosocomial); iii) department of hospitalization (namely, Internal Medicine Department); iv) invasive procedures (surgery, tracheotomy, and trachea cannula); v) bacterial type (extended-spectrum β-lactamases [ESBL]-producing strains, carbapenemase-resistant strains, and others); vi) underlying disease (immunocompromisation, cerebral vascular disease, hypertension, and others); vii) laboratory values, including C-reaction protein (CRP; BC-5390, Shenzhen, China) and procalcitonin (PCT; Burgess Hill, Roche Diagnostic, UK); viii) illness severity; ix) the strategy for antibiotic use and clinical outcomes; and x) the test outcomes for drug sensitivity. The comorbidity was assessed using the age-adjusted Charlson comorbidity index (aCCI) on the day of admission, while disease severity upon admission was evaluated through the SOFA and Pitt bacteremia scores.

Bacterial identification was carried out using the VITEK® 2 system (Bio-Merieux, Inc., France) or the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF/MS) system (bioMérieux, Germany). Antibiotic susceptibility testing of the isolates was carried out using a Kirby-Bauer test (HD-L100, Xiamen, China) and the Vitek 2 compact system. Additionally, minimal inhibitory concentrations (MICs) were determined through microdilution testing following the criteria established by the Clinical and Laboratory Standards Institute (CLSI), and ESBL production was detected using the combined disc method (ceftriaxone alone and ceftriaxone-clavulan).[17]

Statistical analysis. Data that followed a normal distribution were reported as mean ± standard deviation (SD). Data that deviated from a normal distribution were reported as the median and interquartile range (IQR). One-way analysis of variance was carried out to compare normally distributed data. Alternative statistical methods were employed if the data did not conform to a normal distribution, such as the Mann-Whitney-U test. Count data were presented as numbers

and precentages (%), while group comparisons were analyzed using either the Chi-square test or Fisher's exact test. Furthermore, the study carried out by KP-BP utilized the Cox proportional hazards model to assess the 30-day mortality rate. The analysis involved calculating hazard ratios (HR) and 95% confidence intervals (CI). These estimated HR and CI were employed to evaluate the influence of different factors on the 30-day mortality rate. To mitigate the impact of confounding factors, this study established 4 distinct modules. Model 1 was adjusted for demographic factors such as age and gender, as well as variables related to the inpatient department and invasive procedures. Model 2 included additional adjustments for bacterial type, while Model 3 further accounted for underlying diseases and severity scores. In contrast, Model 4 incorporated adjustments for specific empiric therapies and treatment outcomes. Lastly, the risk factors for the 30-day mortality rate in patients with KP-BP and *E. coli*-BP were assessed using univariate and multivariate Cox regression analyses. Variables with a *p*-value of <0.10 in univariate analysis were included in the multivariate analysis.

The Statistical Package for the Social Sciences, version 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. A *p*-value of <0.05 was considered significant.

Results. A comprehensive study carried out over 48 months included a total of 162 patients diagnosed with bacteremic pneumonia. Among these patients, 80 (49.4%) were identified as KP-BP patients, while the remaining 82 (50.6%) were classified as *E. coli*-BP patients (Figure 1). In this study, sputum cultures were not established. The collected patient information included their demographic and clinical features (Table 1). The 162 patients included 95 (58.6%) men and 67 (41.4%) women with a mean age of 60.97±16.15 years, and hospital-acquired pneumonia was found in 72.22% of patients. A total of 53 (32.7%) isolates produced ESBLs, and 30 (18.5%) were resistant to carbapenem antibiotics. The median aCCI score was 4 (IQR: 2-5). Most of the patients included in this study were severe cases with a median SOFA score of 5 (IQR: 3-8), and 122 (75.31%) patients had sepsis during hospitalization. Empiric carbapenem therapy was initiated in 64 (39.5%) patients. A total of 49 (30.3%) patients received at least 3 antibiotics during their hospitalization, and 32.72% of patients received inappropriate empirical treatment. The 30-day mortality rate was 32.7% for all patients. Most patients with *E. coli*-BP were primarily admitted to the surgical department, had ESBL-producing strains, and received empiric third-generation cephalosporin therapy. Furthermore, a lower proportion of *E. coli*-BP patients were male, admitted to the ICU, received an indwelling urinary catheter, tracheotomy, trachea cannula, had carbapenemase-resistant strains, diabetes mellitus, sepsis, and received empiric carbapenem therapy. The Pitt and SOFA scores were significantly higher in KP-BP patients than in *E. coli*-BP patients ($p<0.05$). Compared with the *E. coli*-BP group, higher 14-day treatment failure and 30-day mortality rates were observed in the KP-BP group ($p<0.05$).

Drug susceptibility was tested for 80 isolates of *K. pneumoniae* and 82 isolates of *E. coli* (Table 2). *Escherichia coli*-BP isolates exhibited higher susceptibility rates for amikacin, aztreonam, cefoxitin, cefixime, imipenem, and piperacillin than KP-BP isolates, but the susceptibility rate for levofloxacin was lower ($p<0.05$).

The study observed a 30-day mortality rate of 43.75% (n=35/80) in the KP-BP group, which was significantly higher compared to the 21.95% (n=18/82) mortality rate in the *E. coli*-BP group ($p=0.003$). To evaluate potential predictors of 30-day mortality in both groups, 4 multivariate Cox regression models were developed (Table 3). After adjustments for demographic factors (namely, age and gender) and other variables (namely, inpatient department and invasive procedures), the HR for the 30-day mortality rate of KP-BP to *E. coli*-BP was reported to be 0.70 (95% CI: [0.44-1.02], $p=0.059$; Model i). Additional analyses were carried out to account for the type of bacteria involved, and the HR remained statistically insignificant (HR=0.72, 95% CI: [0.46-1.14], $p=0.163$; Model ii). Furthermore, similar findings were observed after adjustments for underlying diseases (such as cerebral vascular disease and diabetes mellitus) and scores related to severity of illness (Pitt score and SOFA score) (HR=0.99, 95% CI: [0.57-1.73], $p=0.975$; Model iii), as well as after further adjustments for empiric therapy (namely, third-generation cephalosporins and carbapenems) and 14-day treatment failure (HR=1.22, 95% CI: [0.69-2.18], $p=0.493$; Model 4).

The baseline clinical characteristics of the survival and non-survival groups are displayed in Table 4. Additionally, univariable and multivariable Cox regression analyses were carried out to ascertain the risk factors for 30-day mortality (Table 5). In the KP-BP group, univariate analysis revealed that factors such as ICU stay, venous catheterization, tracheotomy, trachea cannula, carbapenem-resistant strains, Pitt score, SOFA score, and inappropriate empirical therapy were significantly associated with an increased 30-day mortality rate. The multivariate Cox regression analysis

Table 1 - Clinical characteristics of patients with *Klebsiella pneumoniae* and *Escherichia coli* bacteremic pneumonia.

Variables	All (n=162)	Bacteremic pneumonia		*P*-values
		K. pneumoniae (n=80)	*E. coli* (n=82)	
Age, mean±SD (years)	60.97±16.15	59.85±16.89	62.06±15.42	0.482
Gender				
Male	95 (58.6)	56 (70.0)	39 (47.6)	0.004
Female	67 (41.4)	24 (30.0)	43 (52.4)	
Acquisition				
Hospital-acquired	117 (72.2)	60 (75.0)	57 (69.5)	0.436
Community-acquired	45 (27.8)	20 (25.0)	25 (30.5)	
Inpatient Department				
Internal medicine	79 (48.8)	38 (47.5)	41 (50.0)	0.750
Surgery ward	35 (21.6)	10 (12.5)	25 (30.5)	0.005
ICU	33 (20.4)	27 (33.7)	6 (7.3)	<0.001
Invasive procedures				
Surgery	39 (24.1)	16 (20.0)	23 (28.0)	0.660
Venous catheterization	26 (16.0)	16 (20.0)	10 (12.2)	0.176
Wound drainage tube	12 (7.4)	5 (6.2)	7 (8.5)	0.578
Indwelling urinary catheter	22 (13.6)	16 (20.0)	6 (7.3)	0.018
Bone marrow aspiration	22 (13.6)	10 (12.5)	12 (14.6)	0.692
Lumbar puncture	9 (5.6)	6 (7.5)	3 (3.7)	0.469
Thoracentesis	6 (3.7)	4 (5.0)	2 (2.4)	0.655
Tracheotomy	45 (27.8)	34 (42.5)	11 (13.4)	<0.001
Trachea cannula	39 (24.1)	30 (37.5)	9 (11.0)	<0.001
Bacterial type				
ESBL-producing strains	53 (32.7)	12 (15.0)	41 (50.0)	<0.001
Carbapenem-resistant strains	30 (18.5)	29 (36.2)	1 (1.2)	<0.001
Underlying disease				
Immune compromise	44 (27.2)	27 (33.7)	17 (20.7)	0.063
Cerebral vascular disease	51 (31.5)	31 (38.7)	20 (24.4)	0.049
Hypertension	60 (37.0)	30 (37.5)	30 (36.6)	0.904
Diabetes mellitus	25 (15.4)	19 (23.7)	6 (7.3)	0.004
Pleural effusion	34 (21.0)	15 (18.7)	19 (23.2)	0.490
Hypoproteinaemia	45 (27.8)	24 (30.0)	21 (25.6)	0.533
Leukaemia	25 (15.4)	14 (17.5)	11 (13.4)	0.472
Sepsis	122 (75.3)	74 (92.5)	48 (58.5)	<0.001
Laboratory values, median (IQR)				
CRP (mg/L)	92.61 (48.36-148.58)	98.42 (59.51-153.73)	77.13 (27.35-147.42)	0.093
PCT (ng/ml)	2.72 (0.94-11.21)	3.96 (1.02-11.96)	1.90 (0.78-10.91)	0.116
Disease severity, median (IQR)				
Pitt score	1.0 (2.0-5.0)	3.0 (1.0-6.0)	1.0 (0.0-2.0)	<0.001
SOFA score	5.0 (3.0-8.0)	5.0 (4.0-9.0)	3.0 (1.0-6.0)	<0.001
aCCI score	4.0 (2.0-5.0)	4.0 (2.5-6.0)	4.0 (2.0-5.0)	0.962
Empiric therapy				
Third-generation cephalosporins	14 (8.6)	3 (3.7)	11 (13.4)	0.029
BLBLI	54 (33.3)	23 (28.7)	31 (37.8)	0.222
Carbapenems	64 (39.5)	41 (51.2)	23 (28.0)	0.003
Aminoglycoside	4 (2.5)	3 (3.7)	1 (1.2)	>0.999
Inappropriate empirical therapy	53 (32.7)	32 (40.0)	21 (25.6)	0.051
Antibiotics ≥3 during hospitalization	49 (30.2)	27 (33.7)	22 (26.8)	0.338
Outcomes				
14-day treatment failure	75 (46.3)	50 (62.5)	25 (30.5)	<0.001
30-day mortality	53 (32.7)	35 (43.7)	18 (21.9)	0.003
Length of hospital stay in days, median(IQR)	21.0 (13.0-31.0)	24.0 (14.0-34.0)	18.0 (12.0-25.0)	0.097

Values are presented as numbers and precentages (%), mean ± standard deviation (SD), or median and interquartile range (IQR). *K. pneumoniae*: *Klebsiella pneumoniae*, *E. coli*: *Escherichia coli*, ICU: intensive care unit, ESBL: extended-spectrum β-lactamase, CRP: C-reaction protein, PCT: procalcitonin, Pitt: Pitt bacteremia score, SOFA: sequential organ failure assessment, aCCI: age-adjusted Charlson comorbidity index, BLBLI: β-lactam-β-lactamase inhibitor

Table 2 - Antimicrobial resistance of *Klebsiella pneumoniae* and *Escherichia coli* isolated from 2 groups.

Antimicrobials	*Klebsiella pneumoniae* (n=80)			*Escherichia coli* (n=82)			*P*-value*
	S	I	R	S	I	R	
Amikacin	64 (80.0)	-	16 (20.0)	81 (98.8)	-	1 (1.2)	<0.001
Aztreonam	41 (51.2)	-	39 (48.7)	56 (68.3)	-	26 (31.7)	0.027
Ciprofloxacin	33 (41.2)	4 (5.0)	43 (53.7)	33 (40.2)	5 (6.1)	44 (53.7)	0.896
Gentamicin	57 (71.2)	-	23 (28.7)	49 (59.8)	-	33 (40.2)	0.124
Ceftriaxone	40 (50.0)	-	40 (50.0)	37 (45.1)	-	45 (54.9)	0.534
Cefoxitin	46 (57.5)	2 (2.5)	32 (40.0)	62 (75.6)	5 (6.1)	15 (18.3)	0.015
Cefixime	44 (55.0)	-	36 (45.0)	67 (81.7)	-	15 (18.3)	<0.001
Tobramycin	56 (70.0)	5 (6.2)	19 (23.7)	45 (54.9)	29 (36.4)	8 (9.8)	0.328
Imipenem	51 (63.7)	-	29 (36.2)	81 (98.8)	-	1 (1.2)	<0.001
Levofloxacin	34 (42.5)	9 (11.2)	37 (46.2)	16 (19.5)	33 (40.2)	33 (40.2)	0.002
Piperacillin	48 (60.0)	3 (3.7)	29 (36.2)	76 (92.7)	5 (6.1)	1 (1.2)	<0.001

Values are presented as numbers and precentages (%). *Comparison of antimicrobial susceptibility between 2 groups. S: susceptible, I: intermediate-resistant, R: resistant

Table 3 - Hazard ratio for 30-day mortality according to *Klebsiella pneumoniae* bacteremic pneumonia and *Escherichia coli* bacteremic pneumonia.

30-day mortality	Events (total)	HR (95% CI)			
		Model 1	Model 2	Model 3	Model 4
KP-BP	35 (43.7)	0.70 (0.44-1.02)	0.72 (0.46-1.14)	0.99 (0.57-1.73)	1.22 (0.69-2.18)
E. coli-BP	18 (21.9)	Ref	Ref	Ref	Ref
P-values	0.003	0.059	0.163	0.975	0.493

Values are presented as numbers and precentages (%) or , hazard ratio (HR) and 95% confidence interval (CI). Model 1: adjusted for age, gender, inpatient department (surgery ward and ICU), and invasive procedures (indwelling urinary catheter, tracheotomy, trachea cannula). Model 2: further adjusted for bacterial type. Model 3: further adjusted for underlying disease (cerebral vascular disease, diabetes mellitus, and sepsis), pitt score, and SOFA score. Model 4: further adjusted for empiric therapy (third-generation cephalosporins and carbapenems) and 14-day treatment failure. KP-BP: *Klebsiella pneumoniae* bacteremic pneumonia, E. coli-BP: *Escherichia coli* bacteremic pneumonia

revealed that ICU stay (adjusted HR=2.88, 95% CI: [1.42-5.82], p=0.003), carbapenem-resistant strains (adjusted HR=2.61, 95% CI: [1.28-5.32], p=0.008), and SOFA score (adjusted HR=1.16, 95% CI: [1.09-1.25], p<0.001) were identified as independent predictors of the 30-day mortality rate in patients with KP-BP (Table 5).

In the *E. coli*-BP group, univariate analysis revealed a significant association between tracheotomy, trachea cannula, sepsis, Pitt score, and SOFA score with an increased 30-day mortality rate. However, multivariate analysis revealed that only the Pitt score remained a significant risk factor for the 30-day mortality rate (adjusted HR=1.99, 95% CI: [1.49-2.65], p<0.001; Table 5).

Discussion. This study analyzed the clinical characteristics and antimicrobial susceptibility of KP-BP and *E. coli*-BP between January 2016 and December 2019. The 2 groups demonstrated several differences, revealing that men were more at risk of *K. pneumoniae* pneumonia than women. Epidemiological studies indicate that KP pneumonia is more common in middle-aged and old men. Similar results were obtained by Chen et al.[7] However, the gender discrepancy might be explained by the relatively small number of cases. Compared with *E. coli*-BP, patients with KP-BP had a more severe primary condition, higher rates of ICU admission, invasive procedures, and carbapenem resistance. Overall, patients with KP-BP had a higher 30-day mortality rate (43.75% vs. 21.95%, p=0.003) than *E. coli*-BP patients.

Escherichia coli and *K. pneumoniae* are prevalent *Enterobacteriaceae* causing pneumonia in hospital and community settings. Their high morbidity and mortality rates have gained the attention of clinicians worldwide.[17-19] In 2 studies of liver abscesses caused by *K. pneumoniae* and *E. coli*, investigators reported significantly higher Pitt bacteremia scores and disease severity in *K. pneumoniae* infection than in the *E. coli*

Table 4 - Characteristics of 30-day survivors and non-survivors.

Variables	Bacteremic pneumonia					
	K. pneumoniae (n=80)			*E. coli* (n=82)		
	Survivors (n=45)	Non-survivors (n=35)	*P*-values	Survivors (n=64)	Non-survivors (n=18)	*P*-values
Age, mean±SD (years)	58.31±16.43	61.83±17.51	0.386	62.31±14.66	61.17±18.30	0.949
Gender						
Male	33 (73.3)	23 (65.7)	0.461	28 (43.7)	11 (61.1)	0.289
Female	12 (26.7)	12 (34.3)		36 (56.2)	7 (38.9)	
Acquisitions						
Hospital-acquired	31 (68.9)	29 (82.9)	0.152	43 (67.2)	14 (77.8)	0.389
Community-acquired	14 (31.1)	6 (17.1)		21 (32.8)	4 (22.2)	
Inpatient departments						
Internal medicine	25 (55.6)	13 (37.1)	0.005	31 (48.4)	10 (55.5)	0.594
Surgery ward	8 (17.8)	2 (5.7)	0.201	20 (31.2)	5 (27.8)	0.777
ICU	8 (17.8)	19 (54.3)	0.001	4 (6.2)	2 (11.1)	0.851
Invasive procedures						
Surgery	12 (26.7)	4 (11.4)	0.091	18 (28.1)	5 (27.8)	0.977
Venous catheterization	4 (8.9)	12 (34.3)	0.005	6 (9.4)	4 (22.2)	0.287
Wound drainage tube	2 (4.4)	3 (8.6)	0.771	6 (9.4)	1 (5.6)	0.972
Indwelling urinary catheter	10 (22.2)	6 (17.1)	0.573	4 (6.2)	6 (33.3)	0.002
Bone marrow aspiration	6 (13.3)	4 (11.4)	0.798	7 (10.9)	5 (27.8)	0.159
Lumbar puncture	5 (11.1)	1 (2.9)	0.336	2 (3.1)	1 (5.6)	0.627
Thoracentesis	2 (4.4)	2 (5.7)	0.796	2 (3.1)	0 (0.0)	>0.999
Tracheotomy	11 (24.4)	23 (65.7)	<0.001	4 (6.2)	7 (38.9)	0.001
Trachea cannula	11 (24.4)	19 (54.3)	<0.001	4 (6.2)	5 (27.8)	0.031
Bacterial types						
ESBL-producing strains	6 (13.3)	6 (17.1)	0.636	29 (45.3)	12 (66.7)	0.109
Carbapenem-resistant strains	10 (22.2)	19 (42.2)	0.003	1 (1.6)	0 (0.0)	>0.999
Underlying diseases						
Immune compromise	14 (31.1)	13 (37.1)	0.571	13 (20.3)	4 (22.2)	0.860
Cerebral vascular disease	12 (26.7)	19 (54.3)	0.012	16 (25.0)	4 (22.2)	0.808
Hypertension	18 (40.0)	12 (34.3)	0.600	25 (39.1)	5 (27.8)	0.380
Diabetes mellitus	13 (28.9)	6 (17.1)	0.221	4 (6.2)	2 (11.1)	0.484
Pleural effusion	7 (15.6)	8 (22.9)	0.407	14 (21.9)	5 (27.8)	0.600
Hypoproteinaemia	8 (17.8)	16 (45.7)	0.007	15 (23.4)	6 (33.3)	0.236
Leukaemia	5 (11.1)	9 (25.7)	0.088	6 (9.4)	5 (27.8)	0.103
Sepsis	40 (88.9)	34 (97.1)	0.336	33 (51.6)	15 (83.3)	0.016
Laboratory values, median (IQR)						
CRP (mg/L)	106.83 (69.40-156.75)	79.13 (45.33-141.97)	0.198	78.09 (23.45-145.15)	77.13 (47.66-165.76)	0.521
PCT (ng/ml)	2.84 (1.06--12.90)	4.86 (0.94-11.54)	0.956	1.89 (0.77-8.32)	4.26 (0.76-28.61)	0.445
Disease severity, median (IQR)						
Pitt score	2.0 (1.0-3.0)	5.0 (2.0-8.0)	<0.001	0.0 (1.0-1.0)	4.5 (2.0-6.5)	<0.001
SOFA score	5.0 (3.0-5.0)	9.0 (5.0-14.0)	<0.001	3.0 (1.0-4.0)	7.5 (3.5-12.5)	<0.001
aCCI score	3.0 (2.0-5.0)	4.0 (3.0-6.0)	0.047	4.0 (2.0-5.0)	4.0 (2.50-5.0)	0.688
Empiric therapy						
Third-generation cephalosporins	3 (6.7)	0 (0.0)	0.335	8 (12.5)	3 (16.7)	0.947
BLBLI	14 (31.1)	9 (25.7)	0.597	27 (42.2)	4 (22.2)	0.123
Carbapenems	21 (46.7)	20 (57.1)	0.352	17 (26.6)	6 (33.3)	0.572
Aminoglycoside	2 (4.4)	1 (2.9)	>0.999	1 (1.6)	0 (0.0)	>0.999
Inappropriate empirical therapy	13 (28.9)	19 (54.3)	0.021	13 (20.3)	8 (44.4)	0.077
Antibiotics ≥3 during hospitalization	11 (24.4)	16 (45.7)	0.046	15 (23.4)	7 (38.9)	0.314
14-day treatment failure	18 (40.0)	32 (91.4)	<0.001	8 (12.5)	17 (94.4)	<0.001
Length of hospital stay, median (IQR) (day)	25.0 (17.0-35.5)	22.0 (10.0-31.0)	0.111	19.0 (11.0-28.0)	14.5 (11.5-28.0)	0.354
Time interval between IEAT and AAT, median (IQR) (day)	4.0 (3.0-5.0)	3.0 (3.0-4.0)	0.055	5.0 (4.0-5.0)	5.0 (4.0-6.0)	0.056

Values are presented as numbers and precentages (%), mean ± standard deviation (SD), or median and interquartile range (IQR). *K. pneumoniae*: *Klebsiella pneumoniae*, *E. coli*: *Escherichia coli*, ICU: intensive care unit, ESBL: extended-spectrum β-lactamase, CRP: C-reaction protein, PCT: procalcitonin, SOFA: sequential organ failure assessment, Pitt: Pitt bacteremia score, aCCI: age-adjusted Charlson comorbidity index, BLBLI: β-lactam-β-lactamase inhibitor, IEAT: inappropriate empirical antibiotic treatment, AAT: appropriate antibiotic therapy

Table 5 - Risk factors for 30-day mortality in patients with *Klebsiella pneumoniae* and *Escherichia coli* bacteremic pneumonia.

Variables	Patients with *K. pneumoniae* bacteremic pneumonia						Patients with *E. coli* bacteremic pneumonia					
	Univariate			Multivariate			Univariate			Multivariate		
	HR	95% CI	*P*-values	HR	95% CI	*P*-values	HR	95% CI	*P*-values	HR	95% CI	*P*-values
Internal medicine stay	0.58	0.29-1.19	0.136	-	-	-						
ICU stay	3.14	1.59-6.22	0.001	2.88	1.42-5.82	0.003	4.79	1.84-12.44	0.001	-	-	-
Venous catheterization	2.67	1.31-5.45	0.007	-	-	-	3.73	1.32-10.59	0.013	-	-	-
Indwelling urinary catheter							1.37	0.32-5.99	0.673	-	-	-
Tracheotomy	3.36	1.63-6.91	0.001	-	-	-	4.79	1.84-12.44	0.001	-	-	-
Trachea cannula	2.65	1.34-5.23	0.005	-	-	-	3.73	1.32-10.59	0.013	-	-	-
Carbapenem-resistant strains	2.66	1.34-5.24	0.005	2.61	1.28-5.32	0.008						
Cerebral vascular disease	1.60	0.80-3.18	0.180	-	-	-						
Sepsis							3.66	1.06-12.66	0.041	-	-	-
Hypoproteinaemia	1.64	0.82-3.27	0.163	-	-	-						
Pitt score	1.19	1.09-1.31	<0.001	-	-	-	1.49	1.29-1.72	<0.001	1.99	1.49-2.65	<0.001
SOFA score	1.18	1.11-1.26	<0.001	1.16	1.09-1.25	<0.001	1.22	1.12-1.32	<0.001	-	-	-
aCCI score	1.14	1.00-1.31	0.059	-	-	-						
Antibiotics ≥3 during hospitalization	1.35	0.69-2.67	0.384	-	-	-						
Inappropriate empirical therapy	2.35	1.19-4.64	0.014	-	-	-						

K. pneumoniae: *Klebsiella pneumoniae*, *E. coli*: *Escherichia coli*, ICU: intensive care unit, HR: hazard ratio, CI: confidence interval, SOFA: sequential organ failure assessment, Pitt: Pitt bacteremia score, aCCI: age-adjusted Charlson comorbidity index

group, supporting the results of our study.[20,21] Another study revealed that ESBL-producing *K. pneumoniae* was associated with a significantly higher 30-day mortality rate than ESBL-producing *E. coli* (33.7% vs. 17.4%). The results of the present study further supported the conclusion.[22]

Patients with *E. coli*-BP were used as a reference to identify the risk factors for the 30-day mortality rate in KP-BP. After adjustments for various confounding factors such as age and gender, ward admission, and invasive procedures, there was no significant disparity observed in the risk of mortality within 30 days between the 2 cohorts (Model 1; HR=0.70, p=0.059). Equivalent results were obtained after adjustments for additional confounders (Models 2, 3, and 4). This finding was consistent with a previous study, which also reported no significant difference in mortality between *E. coli* and *K. pneumoniae* pneumonia.[10] Although statistically nonsignificant, the 30-day mortality risk was consistently higher in KP-BP patients (Model 4; HR=1.22, p=0.493). Another study reported that the type of bacteria is one of the most important determinants of the risk of death from bloodstream infection.[22] The host and disease severity can significantly affect the outcome of patients with bacteremic pneumonia. Baseline data indicated that patients with KP-BP had a more severe underlying condition. The high rate of carbapenem resistance increased the 30-day mortality risk, which provided a reasonable explanation for this trend. Nevertheless, due to the small sample size of our study, PSM analysis was not carried out, and only crude mortality rates were analyzed in the 2 groups. Therefore, further analysis is required to validate our findings.

The 30-day mortality rate of the KP-BP group in this study was 43.75%, which was lower than previously reported in another study (55.1%) but higher than another study (36.5%).[7,23] The high mortality rate suggests that KP-BP is a serious threat to human health and should be prioritized clinically. With the widespread use of antibiotics, carbapenem-resistant *Enterobacteriaceae* (CRE) is increasingly prevalent. Its multi-drug resistance, rapid spread of resistance, high morbidity and mortality rates, and the limited clinical availability of antimicrobial drugs pose a serious challenge to clinical management. *Klebsiella pneumoniae* is the main causative agent of CRE bloodstream infections (85.6%, n=178/208).[24] Moreover, the present study unveiled a significantly elevated prevalence of carbapenem resistance, amounting to 36.25% of patients. These results were consistent with a prior inquiry in Taiwan, which documented an even more pronounced rate of carbapenem resistance (58.2%).[7] Current evidence suggests that tigecycline is effective in treating CRE, but it is limited by its low blood drug

concentration.[25] Polymyxin is another effective treatment for CRE but is limited by heterogeneous drug resistance, complex dose calculations, and nephrotoxicity.[26,27] Ceftazidime/avibactam (CAZ/AVI) is a combination of a third-generation cephalosporin and the novel non-β-lactam β-lactamase inhibitor, avibactam. The combination reported excellent antibacterial activity against multi-drug resistant bacteria and has become an option for the treatment of CRE infections in recent years, which has led to an increasing rate of drug resistance.[28,29] Consequently, CRE treatment should account for the patient's medication history, underlying disease, drug resistance, organ function, and other conditions. Sensitive drugs should be selected to deliver accurate and targeted treatment. More importantly, existing antibacterial drugs should be used rationally to minimize the emergence of drug-resistant bacteria. In line with other research, the current study found that inappropriate empirical treatment increased the risk of death (HR=2.35, p=0.014).[30] Hence, appropriate antibiotics should be administered in conjunction with the patient's drug-sensitivity results to minimize the risk of death. However, the statistical analysis did not reveal a significant difference in the time interval between the administration of inappropriate empirical antibiotics and appropriate definitive antibiotics among *K. pneumoniae* and *E. coli* groups (p>0.05). This lack of significance might be attributed to the limited sample size of the present study, necessitating further validation through larger datasets and multicenter studies. In addition, ICU admission and higher SOFA scores are predictors of increased 30-day mortality risk, which were confirmed by numerous studies.[31,32] Although carbapenem-resistant strains were highly correlated with the 30-day mortality rate, the genotypes and phenotypes of resistant strains were not determined in this study, thereby requiring further research.

In another study, patients with *E. coli*-BP exhibited a 30-day mortality rate of 21.95%.[10] In the present study, more than 30% of the *E. coli* samples were resistant to quinolones, and many previous studies have reported increasing resistance to quinolone antibiotics.[33] Nevertheless, our study displayed that *E. coli* isolates were highly susceptible to amikacin and piperacillin, which could be used as first-line empirical therapy. Notably, a high proportion of ESBL-producing *E. coli* was observed in nosocomial infections (50.88%). This could be attributed to the patients having more severe conditions, comorbid cardiovascular and cerebrovascular diseases, ICU admission, or undergoing invasive operations. These are risk factors for multidrug-resistant *Enterobacteriaceae* bacterial infection.[6,34] Moreover, effective medications are challenged by the notable prevalence of ESBL-producing *E. coli*. Although the proportion of *E. coli* exhibiting resistance to carbapenem antibiotics was found to be low in this investigation, it should be noted that 28.5% of patients were administered carbapenem antibiotics before obtaining drug sensitivity results, thereby facilitating the development of carbapenem-resistant strains. Consequently, using such antibiotics should be approached cautiously following the recommended indications for carbapenem antibiotics. The Pitt bacteremia scores serve as a biomarker for evaluating the gravity of illness and the likelihood of mortality in individuals afflicted with bloodstream infections caused by both Gram-negative and Gram-positive bacteria. Typically, elevated scores indicate a critical state and an unfavorable prognosis for the patient.[35,36] In this study, higher Pitt bacteremia scores were significantly associated with an increased risk of 30-day mortality in cases of *E. coli*-BP, thereby establishing Pitt bacteremia scores as an independent risk factor. Although Pitt bacteremia and SOFA scores were relatively similar, the present study found no difference in SOFA scores in *E. coli*-BP, which could be related to the single-center, small sample size of the present study. Therefore, further validation is required in a large-scale prospective clinical trial.

Study limitations. Despite the prospective findings in this study, there were several inherent limitations. First, this research was carried out at a single center with a small number of cases, thereby limiting its reliability and validity to the study hospital, albeit still offering some degree of reference value. Second, the retrospective nature of this analysis rendered it susceptible to selection bias. Furthermore, it is imperative to note that patients who tested negative from blood cultures were not included within the scope of this research. Next, it is imperative to note that the aforementioned strains primarily originated from HAP cases, thereby necessitating further exploration in subsequent research endeavors. Additionally, a comprehensive assessment of sample size was not carried out. Finally, the study did not analyze the prevalence of drug-resistant strains within the hospital and evaluate the genotypes associated with these strains. These limitations should be addressed in subsequent investigations.

In conclusion, KP-BP and *E. coli*-BP groups exhibited notable differences, but the prognosis (30-day mortality) of patients with KP-BP was similar to that of patients with *E. coli*-BP. The prevalence of drug-resistant strains posed a significant challenge in this study, thereby highlighting the importance of prioritizing appropriate antibiotic therapy.

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