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Original Article

Risk factors and clinical characteristics of bloodstream infection caused by ESBL-producing *Klebsiella pneumoniae*

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Abstract

Introduction: The aim of this study was to analyze the clinical characteristics and risk factors of bloodstream infections (BSI) caused by extended-spectrum β-lactamase (ESBL)-producing *Klebsiella pneumoniae* (KP).

Methodology: A retrospective study was conducted by enrolling clinically confirmed KP-BSI cases (2019–2023). Clinical data were collected and analyzed through review of the electronic medical records. Patients with ESBL-positive KP-BSI were compared to those with ESBL-negative KP-BSI. Multivariate logistic regression analysis was used to identify risk factors associated with ESBL-producing KP-BSI.

Results: A total of 199 patients were included, among whom 47 (23.6%) had ESBL-producing KP-BSI. Univariate analysis revealed that the proportion of patients undergoing surgery within 48 hours before blood sampling was higher in the ESBL-positive group than in the ESBL-negative group (40.4% vs. 23.0%, $p < 0.05$). Regarding infection source, liver-origin infections were less frequent in the ESBL-positive group compared to the ESBL-negative group (6.4% vs. 24.3%, $p < 0.05$), while urinary tract-origin infections were significantly more frequent in the ESBL-positive group (38.3% vs. 18.4%, $p < 0.05$). Hospital-acquired infection was more common in the ESBL-positive group than in the ESBL-negative group (40.4% vs. 23.7%, $p < 0.05$). Multivariate analysis identified urinary tract origin (adjusted odds ratio [aOR], 2.162; 95% confidence interval [CI], 1.003–4.661) as an independent risk factor for ESBL-producing KP-BSI.

Conclusions: Primary urinary tract infections constitute an independent risk factor for ESBL-producing KP-BSI. Given the therapeutic complexity of ESBL-producing strains, KP-BSI of urinary tract origin warrant heightened clinical vigilance among clinicians.

Key words: ESBL; *Klebsiella pneumoniae*; bacteremia; phenotype; determinants.

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Introduction

Klebsiella pneumoniae (KP) is an opportunistic pathogen that is widely present in nature. According to the study for monitoring antimicrobial resistance trends (SMART) global surveillance program (2015–2019), the reported prevalence of extended-spectrum β-lactamase (ESBL)-producing KP is 23% in Asia (excluding China) and 21.8% in China [1]. The prevalence of ESBL-producing KP has been increasing globally [2,3], representing a serious public health concern. Clinically, KP strains are typically susceptible to extended-spectrum cephalosporins [4]. However, ESBL production reduces susceptibility to many β-lactam antibiotics, including broad-spectrum cephalosporins, potentially leading to increased mortality rates and more challenging treatment [5]. Consequently, ESBL-producing KP is listed by the World Health Organization as a priority antimicrobial resistance threat [6]. Studies indicate that hospital detection rates of ESBL-producing Enterobacteriaceae range from 10% to 30% [7], highlighting that infections caused by these organisms are a significant concern for hospitalized patients [8].

Among the causative agents of bloodstream infection (BSI), KP ranks second only to *Escherichia coli* [9]. Previous studies have indicated that BSI caused by ESBL-positive pathogens are associated with a higher mortality rate than those caused by ESBL-negative pathogens [10,11]. Therefore, whether the causative bacteria in patients with BSI produce ESBL is significantly associated with patient mortality.

However, significant knowledge gaps persist that hinder optimal clinical management of KP-BSI. Firstly, while several studies have investigated this topic, their

findings are inconsistent, potentially due to limited sample sizes, single-center designs, or being dated, which limits their generalizability to current clinical settings and antibiotic resistance patterns [12]. Secondly, many existing studies on risk factors for ESBL-producing Enterobacteriaceae BSIs have combined KP with *E. coli* or other species [5]. Given the distinct epidemiology and pathogenesis of these organisms, risk factors identified in combined analyses may not be directly applicable to KP-BSI alone. Thirdly, and most critically from a clinical perspective, there is a well-defined temporal gap between the initial report of a positive KP blood culture and the availability of formal antimicrobial susceptibility and β-lactamase identification results. This delay forces clinicians to make empirical therapy decisions without knowing the ESBL status of the infecting strain.

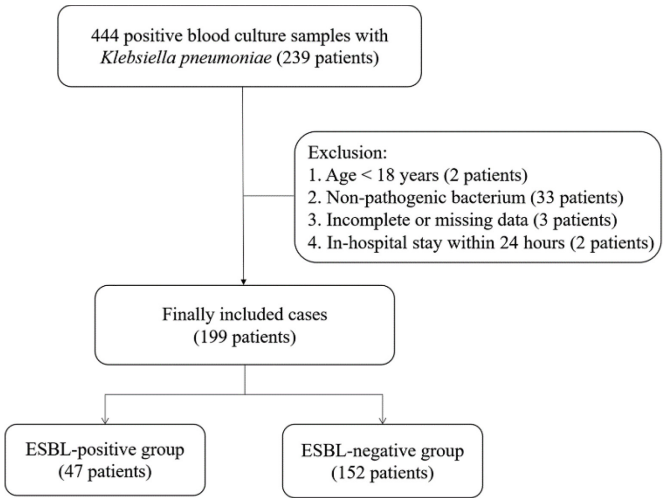
Thus, the aim of this study was to analyze cases of patients with KP-BSI to better understand the clinical features and risk factors associated with ESBL-producing KP infections, and to identify independent risk factors for ESBL production in these patients. These findings are intended to assist clinicians in assessing the likelihood of ESBL production in KP-BSI, thereby supporting more informed clinical decision-making and treatment approaches.

Methodology

Study population

This single-center retrospective cohort study was conducted from January 2019 to December 2023 at Taizhou Municipal Hospital (Taizhou University Affiliated Municipal Hospital), School of Medicine, Taizhou University, which is a 1200-bed teaching hospital in Taizhou, China. The institutional ethics committee approved this research (No. LWYJ2023021) and waived the requirement for patient consent due to its retrospective nature. Stringent confidentiality protocols were implemented for all records. No separate publication consent was required because no personally identifiable data were obtained.

Figure 1. Patient screening and enrollment flowchart for the retrospective cohort study of ESBL-producing KP-BSI.



ESBL: extended-spectrum β-lactamase; KP: *Klebsiella pneumoniae*; BSI: blood stream infection.

A total of 199 KP-BSI cases with β-lactamase identification results were included. The inclusion criteria were: identification of KP in at least one blood culture bottle with concurrent clinical diagnosis of BSI, availability of β-lactamase identification results, and selection of the first positive blood culture collection time for patients with multiple KP-positive blood cultures. The exclusion criteria were: age < 18 years, incomplete case data (e.g., missing components essential for analysis such as clinical scores), hospital stay < 24 hours, and non-pathogenic bacterium (Figure 1). A total of 40 patients who met the exclusion criteria were excluded from the analysis. The related definitions were as follows: septic shock was defined according to established guidelines [13]; multidrug resistance denoted resistance to 3 or more classes of antimicrobial agents [14]; and nosocomial infection (or hospital-acquired infection) was defined as an infection occurring > 48 hours after admission [15]. KP-BSI secondary to liver abscess was defined as a BSI of hepatic origin.

Data collection

Clinical indicators including age, gender, past medical history, and chronic comorbidities (e.g., hypertension, diabetes), relevant scoring systems such as the acute physiology and chronic health evaluation (APACHE) II and sequential organ failure assessment (SOFA) scores were analyzed. Additional parameters comprised intensive care unit (ICU) admission status, procedures within 48 hours pre-sampling (surgery, central venous catheterization), nosocomial infection status, and septic shock occurrence. Biological indicators included routine blood tests, liver and kidney function tests, procalcitonin (PCT), and highly sensitive C-reactive protein (CRP), etc. Intergroup comparisons included infection sites, antimicrobial susceptibility profiles, treatment regimens, and mortality rates.

Species identification and antibiotic sensitivity test

Blood cultures were processed using the BacT/ALERT 3D system (Becton-Dickinson, Sparks, MD, USA). Species identification was conducted with

Bruker Daltonics Data Analysis [16]. Antibiotic susceptibility testing was performed using the VITEK 2 system (bioMérieux, Hazelwood, MO, USA) with AST-GN334/AST-GP67 cards, following the guidelines published by the Clinical and Laboratory Standards Institute (CLSI; Wayne, PA, USA) [17]. The production of ESBL was identified and confirmed using the advanced expert system (AES) of the VITEK 2 system, which is the standard practice in the clinical microbiology laboratory.

Definitions

KP-BSI was defined as KP isolation from blood cultures in addition to ≥ 1 systemic symptom (fever, chills, or hypotension) with supporting clinical signs, excluding contamination [18]. Multidrug-resistant KP (MDR-KP) was defined as KP-BSI with resistance to ≥ 3 antimicrobial classes [14]. Septic shock necessitated vasopressor support post-fluid resuscitation to maintain mean arterial pressure > 65 mmHg alongside lactate > 2 mmol/L [19]. Definitive central venous catheter (CVC)-related BSI [20] was defined as the isolation of the same microorganism from at least one percutaneous blood culture and the catheter tip, or from two blood samples (one from the catheter hub and another from a peripheral vein) that meet quantitative blood culture or differential time to positivity criteria for catheter-related BSI. Cases without identifiable sources were designated unknown-origin KP-BSI, while hepatic-origin infections were classified as KP-BSI from liver abscess. Pre-culture antibiotic exposure encompassed any systemic antimicrobial administered within 2 weeks prior to sampling, categorized as: i) β-lactam/β-lactamase inhibitors (BL/BLI); ii) β-lactams (BL); or iii) other (fluoroquinolones/aminoglycosides), including monotherapy, combinations, or sequential regimens.

Statistical analysis

Continuous variables were compared using Student's t test or the Mann–Whitney U test, and count variables were compared using Pearson's χ^2 test. Variables in the univariate analysis with $p < 0.05$ were considered candidates for building multivariate stepwise logistic regression models. Two-tailed $p < 0.05$ was considered statistically significant. Multicollinearity among the independent variables in the final multivariate model was assessed using the

Table 1. Baseline characteristics of patients with ESBL-producing KP-BSI.

Characteristics	Total (n = 199)	ESBL-positive group (n = 47)	ESBL-negative group (n = 152)	*p* value
Age, years, (mean ± SD)	67.56 ± 15.08	68.00 ± 17.54	67.43 ± 1 4.29	0.821
Male, n (%)	116 (58.3%)	26 (22.4%)	90 (77.6%)	0.761
Comorbidities, n (%)				
Hypertension	82 (41.2%)	23 (48.9%)	59 (38.8%)	0.288
Diabetes	65 (32.7%)	11 (23.7%)	54 (35.5%)	0.170
Hemiplegia	20 (10.1%)	4 (8.5%)	16 (10.5%)	0.901
Solid tumor	25 (12.6%)	8 (17.0%)	17 (11.2%)	0.422
Gastrointestinal bleeding	7 (3.5%)	3 (6.4%)	4 (2.6%)	0.443
Cerebrovascular accident	38 (19.1%)	10 (21.3%)	28 (18.4%)	0.824
Chronic kidney disease	14 (7.0%)	2 (4.3%)	12 (7.9%)	0.599
Chronic obstructive pulmonary disease or severe asthma	14 (7.0%)	5 (10.6%)	9 (5.9%)	0.436
Hematological malignancies	4 (2.0%)	6 (3.0%)	3 (2.0%)	> 0.999
APACHE II score, (IQR)	11 (8, 19)	11 (8, 18)	11 (8, 19)	0.716
SOFA score, (IQR)	4 (1, 7)	3 (1, 6)	4 (2, 8)	0.511
Charlson comorbidity index, (IQR)	3 (2, 4)	3 (2, 4)	3 (2, 4)	0.683
Pitt bacteremia score, (IQR)	1 (0,4)	1 (0,3)	1 (0,4)	0.717
Hospitalization ward, n (%)				
ICU	58 (29.1%)	11 (23.4%)	47 (30.9%)	0.419
Clinical operation before blood sampling within 48 hours, n (%)				
Surgery	54 (27.1%)	19 (40.4%)	35 (23.0%)	**0.019***
Indwelling central venous catheter	52 (26.1%)	12 (25.5%)	40 (26.3%)	> 0.999
Parenteral nutrition	29 (14.6%)	10 (21.3%)	19 (12.5%)	0.210
Enteral nutrition	64 (32.2%)	15 (31.9%)	49 (32.2%)	0.967
Indwelling urinary catheter	60 (30.2%)	18 (38.3%)	42 (27.6%)	0.164
Mechanical ventilation	33 (16.6%)	8 (17.0%)	25 (16.4%)	0.926
Blood transfusion	47 (23.6%)	13 (27.7%)	34 (22.4%)	0.455
Bronchoscopy therapy	16 (8.0%)	3 (6.4%)	13 (8.6%)	0.633
CRRT	15 (7.0%)	2 (4.3%)	12 (7.9%)	0.394
Nosocomial infection, n (%)	55 (27.6%)	19 (40.4%)	36 (23.7%)	**0.025***
Septic shock, (n%)	63 (36.7%)	15 (31.9%)	48 (31.6%)	> 0.999

IQR: interquartile range; SD: standard deviation; SOFA: sequential organ failure assessment; APACHE: acute physiology and chronic health evaluation; ICU: intensive care unit; CRRT: continuous renal replacement therapy; KP: *Klebsiella pneumoniae*; BSI: bloodstream infection; ESBL: extended-spectrum β-lactamase; *significant.

variance inflation factor (VIF), with a VIF value of 10 used as the threshold indicating severe multicollinearity; no variables in the final model exceeded this threshold. All data were statistically analyzed using SPSS 26.0 software (IBM Corp, Armonk, NY, USA).

Results

A total of 444 KP isolates were screened initially from pulmonary BSI obtained from 239 patients. The final cohort comprised 199 patients after excluding 40 patients (33 due to non-pathogenic bacteria, 2 for age < 18 years, 3 for missing or incomplete data, and 2 for hospital stay < 24 hours). These patients were stratified into ESBL-positive (n = 47) and ESBL-negative (n = 152) groups (Figure 1).

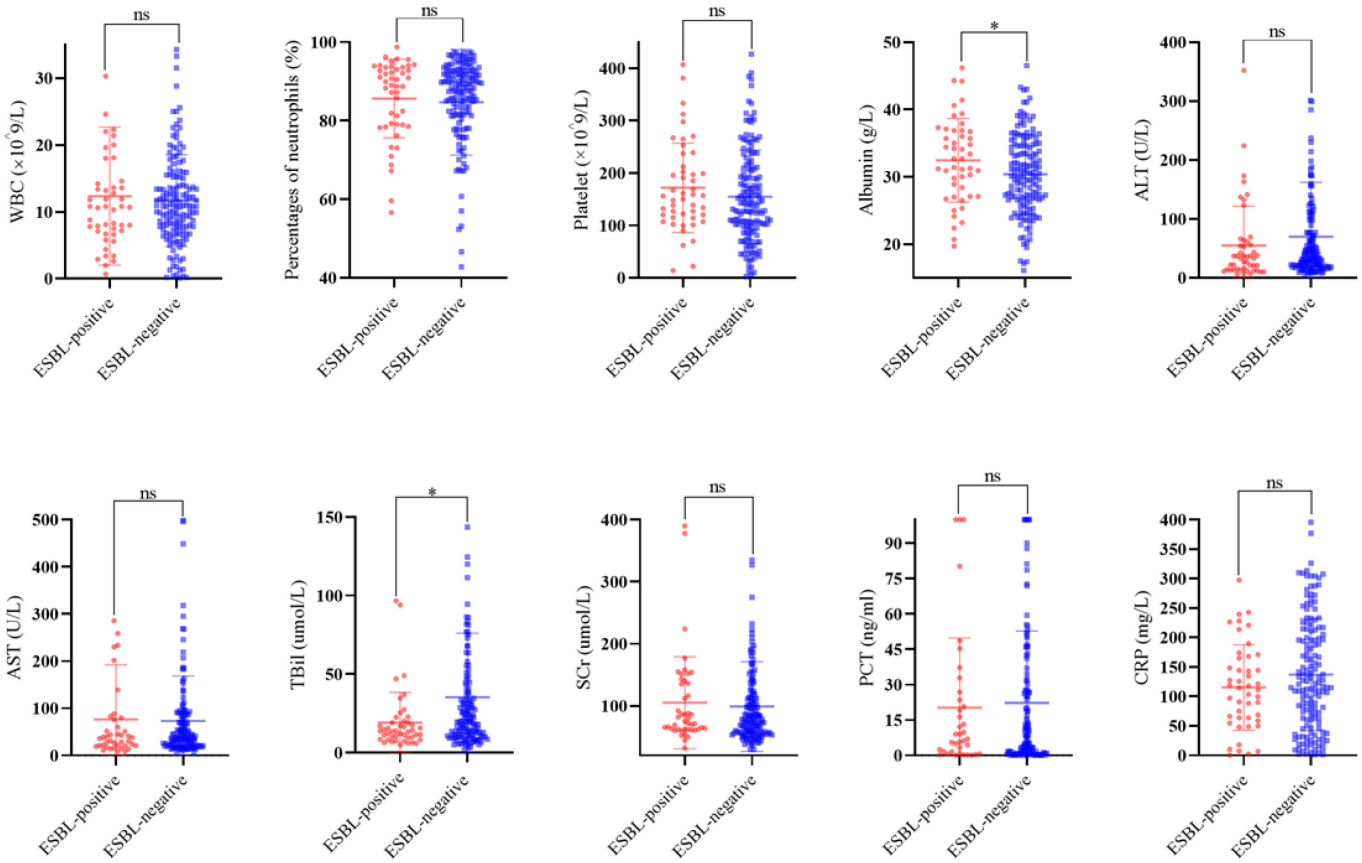
Demographic and clinical characteristics

Among the 199 patients analyzed for clinical characteristics, 116 (58.3%) were male and 83 (41.7%) were female, with a mean age of 67.56 years across both groups. Hypertension (41.2%) was the most common comorbidity, followed by diabetes (32.7%) and cerebrovascular accidents (19.1%). The ESBL-positive group demonstrated higher rates of surgery within 48 hours pre-blood sampling (40.4% vs. 23.0%, $p < 0.05$) and hospital-acquired infection (40.4% vs. 23.7%, $p < 0.05$) compared to the ESBL-negative group. No statistically significant differences were observed between the groups regarding gender, age, comorbidities, APACHE II score, SOFA score, Charlson comorbidity index, or Pitt bacteremia score (Table 1).

Biological indicators

Analysis of biological indicators showed statistically significant differences in liver and kidney function markers between the groups, specifically in total bilirubin and albumin levels. The ESBL-positive group exhibited higher albumin levels (32.5 ± 6.2 vs. 30.4 ± 5.9, $p < 0.05$) but lower total bilirubin levels [13.6 (9.4, 19.4) vs. 20.0 (10.8, 42.6), $p < 0.05$]

Figure 2. Comparative scatter plots of clinical indicators between ESBL-positive KP-BSI and ESBL-negative KP-BSI cohorts.



*Statistical significance: $p < 0.05$; ns: not significant; ALT: alanine aminotransferase; AST: aspartate transaminase; LDH: lactate dehydrogenase; TBil: total bilirubin; SCr: serum creatinine; CRP: C-reactive protein; PCT: procalcitonin; KP: *Klebsiella pneumoniae*; BSI: bloodstream infection; ESBL: extended-spectrum β-lactamase.

compared to the ESBL-negative group. No significant intergroup differences were observed in complete blood count parameters, procalcitonin (PCT), or high-sensitivity CRP levels (Figure 2).

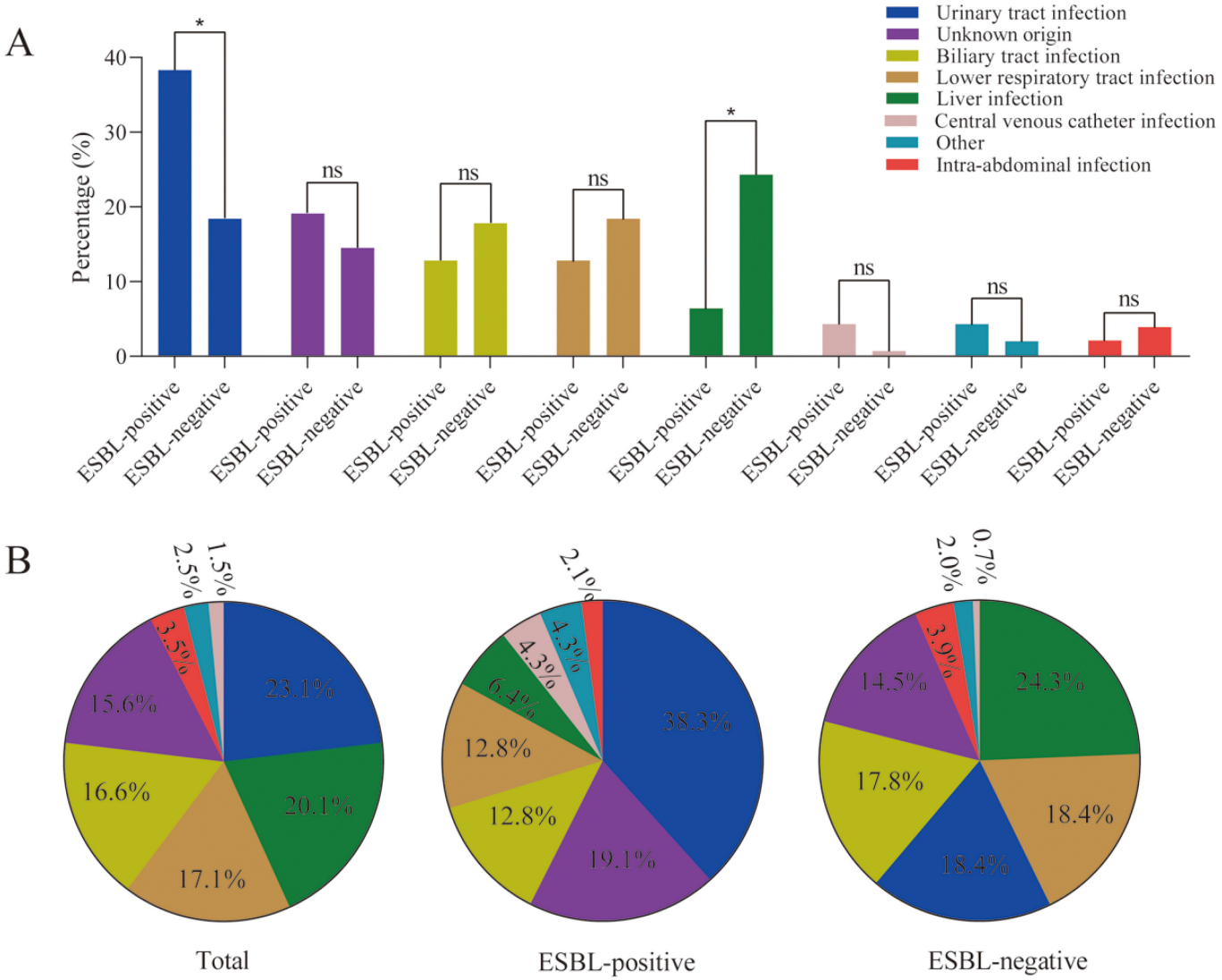
Source of KP-BSI

Urinary tract infections (UTIs; 23.1%) and liver infections (20.1%) were the predominant sources of KP-BSI in this cohort. The proportion of liver-origin infections was significantly lower in the ESBL-positive group than in the ESBL-negative group (6.4% vs. 24.3%, $p < 0.05$). Conversely, urinary tract-origin infections were significantly more frequent in ESBL-positive versus ESBL-negative cases (38.3% vs. 18.4%, $p < 0.05$) (Figure 3).

Prognosis and pre-BSI antimicrobial exposure of KP-BSI

As shown in Table 2, no statistically significant differences were observed in mortality at 7, 14, or 28 days between the two groups. Similarly, the utilization of β-lactam antibiotics (BL), β-lactam/β-lactamase inhibitors (BL/BLI), and other agents (fluoroquinolones and aminoglycosides) within 2 weeks prior to BSI onset demonstrated no significant intergroup variations ($p > 0.05$ for all comparisons).

Figure 3. Comparative distribution of infection sources in ESBL-positive versus ESBL-negative KP-BSI cohorts. **A:** Bar graph depicting proportional differences (%) in infection sources. *Statistical significance: $p < 0.05$; ns: not significant. **B:** Tripartite pie charts quantifying percentage composition of infection sources across: (i) aggregate cohort (Total, n = 199), (ii) ESBL-positive group (n = 47), and (iii) ESBL-negative KP-BSI group (n = 152). Other sources: skin/soft tissue, bone/joint infections.



ESBL: extended-spectrum β-lactamase; KP: *Klebsiella pneumoniae*; BSI: bloodstream infection.

Table 2. Comparison of prognosis and pre-BSI antimicrobial exposure between EBSL-positive and EBSL-negative groups.

	Total (n = 199)	ESBL-positive group (n = 47)	ESBL-negative group (n = 152)	*p* value
Antibiotic exposure within 2 weeks before KP-BSI onset				
BL/BLI	75 (37.7%)	20 (42.6%)	55 (36.2%)	0.431
BL	100 (50.3%)	21 (44.7%)	79 (52.0%)	0.382
other[a]	24 (12.1%)	6 (12.8%)	18 (11.8%)	0.865
Prognosis				
Death within 7 days	26 (13.1%)	5 (10.6%)	21 (13.8%)	0.572
Death within 14 days	32 (16.1%)	5 (10.6%)	27 (17.8%)	0.245
Death within 28 days	36 (18.1%)	6 (12.8%)	30 (19.7%)	0.278

[a]Fluoroquinolones and aminoglycosides. BL/BLI: β-lactam/β-lactamase inhibitors; BL: β-lactam antibiotics; KP: *Klebsiella pneumoniae*; BSI: bloodstream infection; ESBL: extended-spectrum β-lactamase; * significant.

Antibiotic resistance rate

Antimicrobial susceptibility testing revealed significantly higher resistance rates among ESBL-positive KP compared to ESBL-negative KP for specific cephalosporins. Resistance to the second-generation cephalosporins cefotaxime (93.6% vs. 14.3%) and ceftriaxone (89.4% vs. 16.1%), and the third-generation cephalosporin ceftazidime (46.8% vs. 12.9%) was significantly higher in the ESBL-positive group (all $p < 0.05$). Similarly, resistance to the fourth-generation cephalosporin cefepime was notably higher in the ESBL-positive group (54.5% vs. 12.0%, $p < 0.05$). In contrast, resistance to the second-generation cephalosporin cefuroxime showed no significant difference between groups. The ESBL-positive group also exhibited significantly higher resistance to trimethoprim-sulfamethoxazole (co-trimoxazole) (46.7% vs. 12.7%) and levofloxacin (34.8% vs. 13.4%) compared to the ESBL-negative group (both $p < 0.05$). However, resistance to carbapenems, penicillin and cephalosporin/inhibitor combinations did not differ significantly between the groups (Table 3).

Independent risk factors for mortality in patients with ESBL-producing KP-BSI

Multivariate logistic regression analysis identified that BSI originating from the urinary tract (adjusted odds ratio [aOR], 2.162; 95% confidence interval [CI], 1.003–4.661) were an independent risk factor for ESBL-producing KP-BSI (Figure 4).

Discussion

In line with the observational nature of this study, the analysis revealed the following associations: (1) a significantly higher proportion of patients in the ESBL-positive group underwent surgery within 48 hours prior to blood sampling compared to the ESBL-negative group, and this group also had a higher rate of hospital-acquired infections; (2) ESBL-positive KP strains demonstrated higher resistance rates to most broad-spectrum cephalosporins (cefotaxime, ceftriaxone, ceftazidime, and cefepime), as well as to co-trimoxazole and levofloxacin; (3) KP-BSI originating from the urinary tract was independently associated with ESBL-producing KP-BSI.

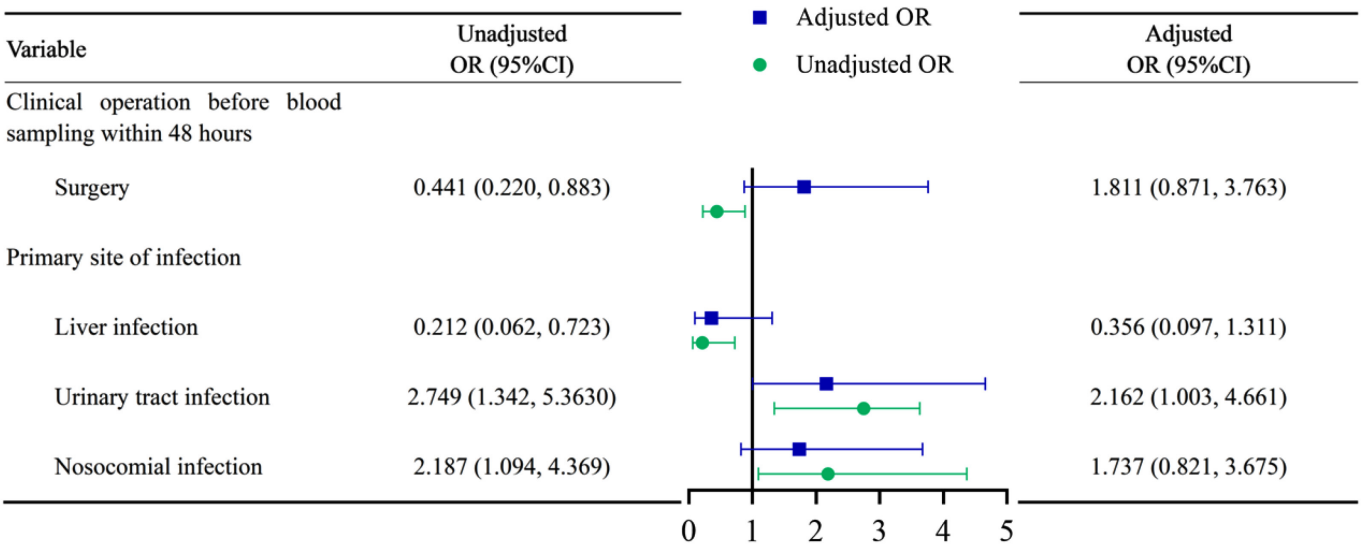
In this study, the urinary tract was identified as the predominant primary infection source for ESBL-producing KP-BSI, and this was independently associated with ESBL production by the strains. KP is

Table 3. Comparison of the microbiological characteristics of the ESBL-positive and ESBL-negative groups.

Antibiotic resistance[a]	Total (n = 199)	ESBL-positive group (n = 47)	ESBL-negative group (n = 152)	*p* value
Cefoperazone/sulbactam (47 vs. 152)[b]	3 (1.5%)	2 (4.3%)	1 (0.7%)	0.278
Ceftazidime (47 vs. 147)[b]	41 (21.1%)	22 (46.8%)	19 (12.9%)	**< 0.001***
Cefoxitin (46 vs. 149)[b]	27 (13.8%)	6 (13.0%)	21 (14.1%)	0.857
Imipenem (47 vs. 150)[b]	18 (9.1%)	1 (2.1%)	17 (11.3%)	0.105
Ceftriaxone (47 vs. 147)[b]	65 (33.5%)	44 (93.6%)	21 (14.3%)	**< 0.001***
Cefepime (44 vs. 150)[b]	42 (21.6%)	24 (54.5%)	18 (12.0%)	**< 0.001***
Tigecycline (46 vs. 150)[b]	17 (8.7%)	7 (15.2%)	10 (6.7%)	0.071
Cotrimoxazole (45 vs. 142)[b]	39 (20.9%)	21 (46.7%)	18 (12.7%)	**< 0.001***
Amikacin (47 vs. 145)[b]	5 (2.6%)	1 (2.1%)	4 (2.8%)	> 0.999
Amoxicillin (45 vs. 144)[b]	28 (14.8%)	11 (24.4%)	17 (11.8%)	**0.037***
Piperacillin/Tazobactam (39 vs. 151)[b]	27 (14.2%)	9 (23.1%)	18 (11.9%)	0.075
Levofloxacin (46 vs. 149)[b]	36 (18.5%)	16 (34.8%)	20 (13.4%)	**0.001***
Ertapenem (45 vs. 143)[b]	16 (8.5%)	1 (2.2%)	15 (10.5%)	0.083
Cefuroxime (47 vs. 149)[b]	66 (33.7%)	42 (89.4%)	24 (16.1%)	< **0.001***
CRE	18 (9.0%)	1 (2.2%)	17 (11.2%)	0.109

[a] Not all listed drugs have been tested in all isolates. [b] The numbers in parentheses indicate the total number of *Klebsiella pneumoniae* isolates tested for drug sensitivity. CRE: carbapenem-resistant; ESBL: extended-spectrum β-lactamase; *significant.

Figure 4. Multivariable logistic regression analysis identifying independent risk factors for ESBL-producing KP-BSI.



CI: confidence interval; OR: odds ratio; ESBL: extended-spectrum β-lactamase; KP: *Klebsiella pneumoniae*; BSI: bloodstream infection.

a common pathogen in UTIs, accounting for approximately 23.5% of UTI causative agents [21]. Moreover, ESBL-positive Enterobacteriaceae are frequently implicated in UTIs [22], constituting up to 59.7% of UTI pathogens [23]. As a common gut commensal, KP exhibits a non-negligible proportion of ESBL-producing strains. Studies report notably high fecal carriage rates (41.8% to 82.6%) of ESBL-producing Enterobacteriaceae among healthy individuals in China [24]. ESBL-producing UTI may often result from cross-transmission of fecal ESBL strains [25]; or, alternatively, endogenous infection linked to early lower urinary tract colonization in hospital settings [26]. Bacterial polysaccharide and iron uptake systems facilitate uroepithelial cell invasion and the formation of intracellular bacterial communities, contributing to urinary tract diseases [27]. These mechanisms enable bacterial adherence, colonization, and potential breach of the uroepithelial barrier, fostering UTI development. Consequently, clinicians treating KP-BSI, particularly those of urinary tract origin, should consider implementing regimens specifically targeted to cover ESBL-producing bacteria.

This study identified an association between hospital-acquired infections and BSI caused by ESBL-producing KP. Hospitalization exposure is a known risk factor for ESBL-producing bacterial UTIs [28]. KP accounts for a significant proportion of hospital-acquired infections, with incidence rates ranging from 5% to 7% [29]. Furthermore, over 19% of hospital infections are caused by ESBL-producing bacteria [30], and the intra-hospital spread of ESBL-positive KP is frequently observed [5]. Given that KP is currently one of the most common ESBL-producing pathogens in hospitals [31], with 14% to 40% of hospital-isolated KP strains producing ESBL enzymes [29], KP colonization on healthcare workers' hands, medical equipment, or the skin of long-term hospitalized patients is a plausible scenario. This colonization suggests KP's potential role as a vector for spreading ESBL-producing bacteria within healthcare facilities, which could help explain the acquisition of these strains in hospital settings. In this study, surgical procedures prior to blood sampling were associated with ESBL-producing KP-BSI. Inadequate hand hygiene during invasive surgery could potentially allow ESBL-producing strains to enter the bloodstream. These findings highlight the importance of healthcare providers maintaining rigorous adherence to aseptic techniques during invasive procedures.

Despite the significantly high mortality rate (20–40%) [32] associated with KP-BSI, which typically corresponds to disease severity scores (e.g., APACHE, SOFA), this analysis found no direct association between ESBL production in KP-BSI strains and mortality, consistent with previous research [33]. This lack of an observed association is supported by the lack of statistically significant differences in APACHE and SOFA scores between the two groups in this study. The extensive use of extended-spectrum cephalosporins has been linked to an increase in drug-resistant Gram-negative bacilli [4]. Consistent with this trend, patients with ESBL-positive KP-BSI in this study exhibited resistance to most cephalosporins. Indeed, extended-spectrum cephalosporin use is a well-established driver

of ESBL emergence [34], and Enterobacteriaceae have developed resistance mechanisms against diverse antibiotics [35]. Prior research [33] has reported that ESBL-positive Enterobacteriaceae exhibit higher antibiotic resistance rates than ESBL-negative strains, aligning with the findings of this study. Furthermore, this study observed increased resistance to co-trimoxazole and levofloxacin in the ESBL-positive group, consistent with a previous 5-year retrospective case study [36]. These findings collectively support the view that the multidrug resistance in KP strains is associated with ESBL positivity, a widely recognized correlation [37]. Resistance genes in ESBL-producing bacteria are often linked to genes conferring resistance to other antibiotic classes, enabling resistance beyond β-lactams. Additionally, antimicrobial susceptibility testing in this study revealed general KP susceptibility to amikacin, aligning with prior research [38]. Earlier studies suggest that this susceptibility may arise from amikacin's ability to restrict ESBL production in Enterobacteriaceae by enhancing the activity of related antimicrobials, offering an alternative clinical treatment strategy [39].

There are some limitations of this study. First, routine tests for co-existing resistance mechanisms, such as AmpC β-lactamases or carbapenemases, in the ESBL-producing KP isolates were not performed. This limitation means that the potential impact of these co-existing enzymes on the resistance profile and clinical outcomes could not be assessed. Second, the identification of ESBL production relied solely on the VITEK 2 system, without additional phenotypic confirmation tests (e.g., double-disk synergy test). Therefore, the reported ESBL prevalence should be interpreted within the context of the automated diagnostic methods used. Third, regarding the statistical analysis, the use of a stepwise selection method for multivariate modeling, while objective and standard for exploratory risk factor studies, may have limitations compared to clinician-driven purposeful selection. However, this risk was mitigated by employing an initial univariate screen ($p < 0.05$) to select candidate variables for the multivariate model. Fourth, the single-center nature of this study conducted at a Chinese tertiary hospital may limit the generalizability of the findings to other geographic regions or healthcare settings with different epidemiological patterns. Fifth, the retrospective design restricted data collection to electronic medical records, which may have resulted in unavailable critical information. Finally, uncontrolled variables, such as antibiotic regimens and treatment duration, may have confounded the results. Despite these limitations, this study provides valuable insights into the risk factors and antimicrobial resistance patterns of ESBL-producing KP-BSI in a Chinese tertiary hospital.

Conclusions

ESBL-producing KP-BSI is not uncommon among all KP-BSI. Surgery within 48 hours before blood sampling, hospital-acquired infections, and urinary tract infection sources were associated with ESBL-producing KP-BSI, with primary UTIs constituting an independent risk factor. Given the therapeutic complexity of ESBL-producing strains, KP-BSI of urinary tract origin warrant heightened clinical vigilance.

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Authors' contributions

PX: research concept and design, data collection, manuscript draft; QS: data collection, manuscript draft; XZ: data collection, manuscript draft; CZ: research concept and design, supervision, statistical analysis, manuscript revision. All authors were responsible for acquiring, analyzing or interpreting data, and critical revision of the manuscript for important intellectual content. Panpan Xu, Yifeng Mao, and Qingqing Chen contributed equally to this work.

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Conflict of interest

No conflict of interest is declared.

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