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Original Article

Factors affecting mortality in patients with healthcare-associated bloodstream infection due to *Klebsiella pneumoniae*

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Abstract

Introduction: *Klebsiella pneumoniae* is a common causative agent of hospital-acquired (HA) bloodstream infections (BSI) in intensive care units (ICU). This study aimed to investigate mortality rates and the factors affecting mortality in BSI due to *K. pneumoniae* acquired in the ICU.

Methodology: This retrospective study included adult patients hospitalized in the ICU between January 2021 and December 2022 who developed HA BSI due to *K. pneumoniae*. The association between clinical characteristics, invasive and medical treatment practices before bacteremia, and 15-day and 30-day mortality was investigated.

Results: A total of 232 patients (median age 68.0 years) were included. All-cause mortality rates on days 15 and 30 were 56.0% and 72.8%, respectively. The proportion of patients infected with carbapenem-resistant *K. pneumoniae* was 77.6%. Logistic regression analysis revealed significant associations between systemic corticosteroid use (OR: 2.38; $p = 0.014$), high qPitt score (OR: 1.32; $p = 0.046$), and presence of immunosuppression (OR: 2.70; $p = 0.020$); and 15-day mortality. Significant associations were found between systemic corticosteroid use (OR: 3.69; $p = 0.002$), high qPitt score (OR: 1.44; $p = 0.043$) and presence of immunosuppression (OR: 6.61; $p = 0.004$); and 30-day mortality.

Conclusions: Corticosteroid treatment before the development of bacteremia in ICU patients may contribute to mortality in BSI due to *K. pneumoniae*. Therefore, corticosteroids should be used with caution despite their benefit in the treatment of acute respiratory distress syndrome. High qPitt scores and the presence of immunosuppression may be used as predictors of mortality in HA BSI due to *K. pneumoniae*.

Key words: bloodstream infection; *Klebsiella*; mortality; corticosteroid; nosocomial.

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Introduction

Klebsiella pneumoniae causes complicated and difficult-to-treat nosocomial infections such as sepsis, urinary tract infections, catheter-related infections, pneumonia, and surgical site infections in the intensive care unit (ICU) [1]. Since *K. pneumoniae* shows multiple antibiotic resistance, treatment options are limited and lead to increased morbidity and mortality, especially in patients hospitalized in the ICU [2,3]. The mortality rate in bloodstream infections (BSI) due to *K. pneumoniae* has been reported to vary between 19.3% and 56% [3–12].

There is a strong association between the clinical status of patients and mortality in BSI due to *K. pneumoniae*. A systemic review and meta-analysis found that having carbapenem-resistant *K. pneumoniae* (CRKP) or BSI, ICU hospitalization, and solid organ transplantation were associated with mortality [5]. In another meta-analysis that included patients with bacteremia, hospitalization in the ICU and infection with extended-spectrum beta-lactamase (ESBL) or CRKP strains were found to be associated with higher mortality [3]. In previous studies, the main factors associated with 28-day or 30-day mortality with nosocomial hospital-acquired (HA) *K. pneumoniae* BSI were sepsis or septic shock [7–9,11,12], high Charlson comorbidity index (CCI) [6,12,13], high Pitt bacteremia score [10,13], invasive mechanical ventilation (MV) [6,12], and corticosteroid treatment before the development of infection [7,8].

This study was conducted during the coronavirus disease 2019 (COVID-19) pandemic at a hospital that was specially built in Türkiye for treating severe cases of COVID-19. The national COVID-19 treatment

guideline recommended systemic corticosteroid treatments in COVID-19 patients with severe respiratory failure [14]. As a result, systemic corticosteroid treatments have since been used more frequently in all patients with respiratory failure. On the other hand, some studies showed that prior systemic corticosteroid treatment increased mortality in patients with CRKP bacteremia in COVID-19 patients [6]. This study aimed to investigate the risk factors affecting mortality in patients with BSI due to HA *K. pneumoniae*, and hospitalized in the ICU. Additionally, the effect of systemic corticosteroids, which have recently been used intensively, on mortality was specifically explored.

Methodology

This study was conducted in the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital which has a capacity of 1800 beds; 120 of which are tertiary ICU beds. This is a health facility consisting of three separate hospitals in different neighborhoods where patients with different demographic characteristics and clinical conditions are treated. Approval for the study was obtained from the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Research Ethics Committee (Ethics committee approval date/no: 2022/150). The records of all patients hospitalized in the ICU between January 2021 and December 2022 were retrospectively reviewed, and the data of patients diagnosed with HA BSI due to *K. pneumoniae* were collected.

Patients who were older than 18 years of age, who tested positive for *K. pneumoniae* in one or more simultaneous blood cultures taken at least 48 hours after ICU admission, and who received antibiotic treatment for at least 48 hours were included in the study. Patients who had a positive blood culture for *K. pneumoniae* before the 48th hour after ICU admission were excluded because the study aimed to focus specifically on HA BSIs. Only the first episode of *K. pneumoniae* bacteremia per patient was included in the analysis.

Definitions

Blood culture was performed on samples collected from patients who had at least one of the following findings: body temperature < 36 °C or > 38 °C, respiratory rate > 20/min, heart rate > 90/min, and leukocyte count > 12,000/μL or < 4,000/μL. When any of the findings listed above were observed in the presence of *K. pneumoniae* in one or more blood cultures, it was defined as BSI due to *K. pneumoniae*. CRKP was defined as in vitro resistance to at least one of the antibiotics: meropenem, doripenem, imipenem or ertapenem [15]. Appropriate empirical antibiotic treatment was defined as the administration of at least one new systemic antimicrobial agent, to which the identified pathogen was susceptible, within the first 48 hours following blood culture collection [16]. Prior antibiotic use was defined as systemic antibiotic use in the last 30 days before the day of bacteremia. The diagnosis of COVID-19 was made with real-time polymerase chain reaction (RT-PCR) positivity in a nasopharyngeal swab sample, or a combination of thoracic computerized tomography and clinical findings [17]. Immunosuppression was defined as having any of the following factors: malignancy, autoimmune disease, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), organ transplantation, immunosuppressive therapy, and chemotherapy.

Data collection

Demographic characteristics, causes of hospitalization, COVID-19 diagnosis, comorbid diseases, body-mass index, immunosuppression, CCI score (based on myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer, mild liver disease, diabetes, hemiplegia, moderate or severe renal disease, diabetes with end organ damage, any tumor without metastasis, leukemia, lymphoma, moderate or severe liver disease, metastatic solid tumor, and AIDS) and acute physiology and chronic health assessment II (APACHE II) scores (based on rectal temperature; mean arterial pressure; heart and respiratory rate; oxygenation; arterial pH; serum sodium, potassium and creatinine; hematocrit; white blood count; and Glasgow Coma Score) on the day of ICU hospitalization were recorded [18,19]. Basic laboratory data, duration of hospitalization in the ICU, previous invasive and medical diagnosis/treatment procedures and their durations, and qPitt bacteremia scores at the time of blood culture were determined. qPitt bacteremia scores were calculated by assigning one point to each of the following variables: temperature < 36 °C, systolic blood pressure < 90 mmHg or vasopressor use, respiratory rate ≥ 25 breaths/min or need for mechanical ventilation, cardiac arrest, and altered mental status [20]. Mortality information of the patients on days 15 and 30 were noted.

Laboratory methods

The bacterial isolates were obtained from blood culture samples sent to the microbiological laboratory for diagnostic purposes. Blood culture bottles were incubated in the Bact/ALERT 3D system (bioMérieux, Marcy-l'Étoile, France). The identification of bacterial isolates and antimicrobial susceptibility testing were performed using the VITEK® 2 compact automated system (bioMérieux, Marcy-l'Étoile, France). Antibiogram evaluation was performed according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards [21].

Statistical analysis

Descriptive statistics of the measurements were calculated as mean, standard deviation (SD), median, 25th and 75th quartiles, and number and percentage frequencies. The conformity of the numerical characteristics obtained by measurement to the normal distribution was examined by the Shapiro-Wilks test and it was observed that all the variables deviated from the normal distribution. Differences in numerical characteristics between survivors and non-survivors at the end of 15 and 30 days were compared using the Mann-Whitney U test. Associations between categorical characteristics were analyzed using Pearson's Chi-square test. Additionally, the hypothesized risk factors (age, gender, presence of COVID-19, APACHE II, CCI, qPitt, CRKP, corticosteroid use, appropriate empirical antibiotic treatment, length of ICU stay, immunosuppression, concomitant bacteremia, and prior antibiotic use) were included in multiple binary logistic regression models to re-evaluate the 15-day and 30-day mortality risks and the adjusted effects were obtained. Statistical significance level $p < 0.05$ was accepted. IBM SPSS Statistics for Windows version 23 (IBM Corp, Armonk, NY, USA) was used for statistical analyses.

Results

Of the 7,923 patients hospitalized in the ICUs between January 2021 and December 2022, 232 who met the criteria were included in the study. The median age of the patients was 68.0 (range: 18–97) years and 50.4 % (n = 117) were female. The demographic and clinical characteristics on the day of ICU admission and the results of univariate analysis showing the association of these characteristics with 15-day and 30-day mortality are presented in Table 1. The all-cause 15-day mortality ratio was 56.0% (n = 130) and the 30-day mortality ratio was 72.8% (n = 169).

The rate of *K. pneumoniae* BSI secondary infections at other sites was 72% (n = 167). Secondary BSI sources were ventilator-associated pneumonia (33.6%; n = 78), central venous catheter-associated bacteremia (17.2%; n = 40), urinary tract infection (12.9%; n = 30), and skin and soft tissue infection (8.2%; n = 19). Sixty-five (28%) patients had primary bacteremia. *K. pneumoniae* was isolated with other agents (concomitant bacteremia) in blood culture in 27.2% (n = 63) of cases. *K. pneumoniae* was accompanied by *Acinetobacter baumannii* (n = 21), *Pseudomonas aeruginosa* (n = 20), *Candida* spp (n = 6), *Proteus mirabilis* (n = 6), *Escherichia coli* (n = 5), coagulase-negative staphylococci (n = 5), *Enterococcus* spp (n = 4), and *Stenotrophomonas maltophilia* (n = 3). Seven patients had positive blood cultures of more than one microorganism, other than *K. pneumoniae*. The clinical and laboratory variables at the time of blood culture, and the results of univariate analysis showing the relationship between these variables and 15-day and 30-day mortality are presented in Table 2. Appropriate empirical antibiotic treatment was initiated in 52.6% (n = 122) of the patients. The median length of ICU stay was 13.0 (range: 2–155) days when the causative agent was isolated. When post-ICU ward follow-up was included, the median total hospitalization period was 27.0 (range: 4–210) days.

Table 1. Baseline characteristics at the time of ICU admission and univariate analysis of their association with 15-day and 30-day mortality.

Variables	All patients (n = 232)	15-day mortality (56.0%)				30-day mortality (72.8%)			
	Median (min–max) or n (%)	Survivors (n = 102) Mean ± SD or n (%)	Non-survivors (n = 130) Mean ± SD or n (%)		*p*	Survivors (n = 63) Mean ± SD or n (%)	Non-survivors (n = 169) Mean ± SD or n (%)		*p*
Age	68.0 (18–97)	66.3 ± 17.5	65.0 ± 16.6	z = 0.90	0.369	61.3 ± 18.9	67.2 ± 16.0	z = – 1.86	0.063
Gender (female)	117 (50.4)	52 (44.4)	65 (55.6)	χ^2 = 0.02	0.882	31 (26.5)	86 (73.5)	χ^2 = 0.05	0.820
APACHE II score	19.0 (10–36)	19.4 ± 6.0	19.3 ± 6.1	z = 0.21	0.832	20.3 ± 6.6	19.0 ± 5.9	z = 1.22	0.221
CCI score	4.0 (0–17)	4.0 ± 2.6	4.0 ± 2.8	z = – 0.03	0.972	3.2 ± 2.2	4.3 ± 2.8	z = – 2.74	**0.006**
Body mass index	27.3 (16.3–57.7)	28.1 ± 5.1	29.3 ± 7.6	z = – 0.47	0.639	28.0 ± 4.9	29.0 ± 7.1	z = – 0.08	0.933
COVID-19	121 (52.2)	43 (35.5)	78 (64.5)	χ^2 = 6.92	**0.012**	31 (25.6)	90 (74.4)	χ^2 = 0.35	0.470
Immunosuppression	48 (20.7)	15 (31.3)	33 (68.8)	χ^2 = 3.97	**0.046**	7 (14.6)	41 (85.4)	χ^2 = 4.84	**0.028**

APACHE II: acute physiology and chronic health assessment II; CCI: Charlson comorbidity ındex; COVID-19: coronavirus disease 2019; ICU: intensive care unit; SD: standard deviation. Significant *p* values are shown in bold.

Table 2. Univariate analysis of the relationship between the patients' clinical and laboratory variables on the day of blood culture collection, and 15-day and 30-day mortality.

Variables	All patients (n = 232)	15-day mortality (56.0%)				30-day mortality (72.8%)			
		Survivors (n = 102)	Non-survivors (n = 130)		*p*	Survivors (n = 63)	Non-survivors (n = 169)		*p*
	Median (min–max) or n (%)	Mean ± SD or n (%)	Mean ± SD or n (%)			Mean ± SD or n (%)	Mean ± SD or n (%)		
qPitt bacteremia score	3.0 (0–5)	2.4 ± 1.2	2.8 ± 1.1	z = – 2.21	**0.027**	2.3 ± 1.1	2.8 ± 1.2	z = – 2.67	**0.007**
Mechanical ventilation	199 (85.8)	79 (39.7)	120 (60.3)	$\chi^2 = 7.60$	**0.005**	47 (23.6)	152 (76.4)	$\chi^2 = 9.08$	**0.002**
Inotrope support	158 (68.1)	55 (34.8)	103 (60.3)	$\chi^2 = 15.53$	**0.001**	30 (19.0)	128 (81.0)	$\chi^2 = 15.84$	**0.001**
Central venous catheter	187 (80.6)	81 (43.3)	106 (56.7)	$\chi^2 = 0.04$	0.845	51 (27.3)	136 (72.7)	$\chi^2 = 0.01$	0.977
Urinary catheter	210 (90.5)	94 (44.8)	116 (55.2)	$\chi^2 = 1.23$	0.267	58 (27.6)	152 (72.4)		0.537
ECMO	9 (3.9)	3 (33.3)	6 (66.7)		0.531	3 (33.3)	6 (66.7)		0.660
TPN	33 (14.2)	18 (54.5)	15 (45.5)	$\chi^2 = 1.94$	0.163	11 (33.3)	22 (66.7)	$\chi^2 = 0.85$	0.356
Steroid use	148 (63.8)	51 (34.5)	97 (65.5)	$\chi^2 = 15.00$	**0.001**	28 (18.9)	120 (81.1)	$\chi^2 = 14.02$	**0.001**
Pulse steroid use	73 (31.5)	23 (31.5)	50 (68.5)	$\chi^2 = 6.71$	**0.010**	13 (17.8)	60 (82.2)	$\chi^2 = 4.71$	**0.030**
WBC (10^3/uL)	12.2 (1.1–76.6)	12.6 ± 8.6	14.3 ± 9.0	*z* = – 1.54	0.123	11.7 ± 5.6	14.2 ± 9.7	z = – 1.52	0.128
Lymphocyte (10^3/uL)	0.84 (0.06–10.1)	1.3 ± 1.4	1.1 ± 1.2	*z* = 2.26	**0.024**	1.4 ± 1.5	1.1 ± 1.2	z = 2.84	**0.005**
Platelet (10^3/uL)	202 (5–867)	274 ± 154	184 ± 125	*z* = 4.66	**0.001**	291 ± 148	198 ± 136	z = 4.42	**0.001**
CRP (mg/L)	190 (6–458)	178 ± 98	203 ± 102	*z* = – 1.39	0.164	177 ± 100	197 ± 101	z = – 0.93	0.351
Procalcitonin (µg/L)	1.57 (0.1–100)	9.29 ± 20.76	11.35 ± 22.39	*z* = – 3.28	**0.001**	10.37 ± 22.63	10.46 ± 21.35	z = – 2.33	**0.020**
Creatinine (mg/dL)	1.01 (0.16–6.07)	1.20 ± 1.06	1.48 ± 1.04	*z* = – 3.09	**0.002**	1.09 ± 1.04	1.46 ± 1.05	z = – 3.56	**0.001**
Albumin (g/L)	23.1 (1.7–39.1)	23.6 ± 5.8	22.1 ± 4.8	*z* = 2.95	**0.003**	24.4 ± 6.1	22.2 ± 4.9	z = 3.01	**0.003**
D-dimer (mg/L)	3.79 (0.3–35)	4.49 ± 4.38	6.74 ± 7.29	*z* = – 2.45	**0.014**	4.68 ± 5.04	6.13 ± 6.62	z = – 1.42	0.155
Ferritin (µg/L)	917 (14–17330)	1361 ± 2083	2108 ± 2793	*z* = – 2.83	**0.005**	895 ± 984	2102 ± 2828	z = – 4.20	**0.001**
LDH (U/L)	389 (125–11820)	368 ± 295	654 ± 1123	*z* = – 6.25	**0.001**	339 ± 133	600 ± 1013	z = – 4.88	**0.001**
ICU length of stay	13.0 (2–155)	20.3 ± 22.2	16.9 ± 16.4	*z* = 1.16	0.247	20.7 ± 24.2	17.6 ± 17.0	z = 0.75	0.452
Appropriate empirical antibiotic treatment	122 (52.6)	66 (54.1)	56 (45.9)	$\chi^2 = 10.72$	**0.001**	39 (32.0)	83 (68.0)	$\chi^2 = 3.01$	0.083
CRKP	180 (77.6)	76 (42.2)	104 (57.8)	$\chi^2 = 1.36$	0.590	44 (24.4)	136 (75.6)	$\chi^2 = 3.89$	0.360
Concomitant bacteremia	63 (27.2)	31 (49.2)	32 (50.8)	$\chi^2 = 0.96$	0.326	21 (33.3)	42 (66.7)	$\chi^2 = 1.67$	0.196
Prior antibiotic use	201 (86.6)	88 (43.8)	113 (56.2)	$\chi^2 = 0.02$	0.885	54 (26.9)	147 (73.1)	$\chi^2 = 0.06$	0.801

CRKP: carbapenem-resistant *Klebsiella pneumoniae*; CRP: C-reactive protein; ECMO: **e**xtracorporeal membrane oxygenation; ICU: intensive care unit; LDH: lactate dehydrogenase; SD: standard deviation; TPN: total parenteral nutrition; WBC: white blood cells. Significant *p* values are shown in **bold**.

The most common causes of ICU admission were respiratory failure (67.7%; n = 157) and altered mental status (21.6%; n = 50). The median CCI score on the days of ICU hospitalization was 4.0 (range: 0–17). The most common comorbidity was hypertension (47.4%; n = 110). The distribution of comorbidities at ICU admission and the results of univariate analysis associated with 15-day and 30-day mortality are presented in Table 3.

Logistic regression analysis was performed to investigate the relationship between systemic corticosteroid use and mortality; including age, gender, appropriate empirical antibiotic treatment, critical patient scoring systems (CCI, APACHE II, qPitt), infection with CRKP, presence of COVID-19, length of ICU stay, immunosuppression, concomitant bacteremia, and prior antibiotic use as confounding factors. The analysis revealed significant associations between systemic corticosteroid use (OR: 2.38; $p = 0.014$), high qPitt score (OR: 1.32; $p = 0.046$), presence

Table 3. Univariate analysis results showing the relationship between patients' comorbidity distributions, and 15-day and 30-day mortality.

Variables	All patients	15-day mortality				30-day mortality			
		Survivors (n = 102)	Non-survivors (n = 130)		*p*	Survivors (n = 63)	Non-survivors (n = 169)		*p*
	n (%)	n (%)	n (%)			n (%)	n (%)		
Arterial hypertension	110 (47.4)	49 (44.5)	61 (55.5)	$\chi^2 = 0.03$	0.866	28 (25.5)	82 (74.5)	$\chi^2 = 0.31$	0.580
DM	80 (34.5)	30 (37.5)	50 (62.5)	$\chi^2 = 2.07$	0.150	16 (20.0)	64 (80.0)	$\chi^2 = 3.16$	0.075
CAD	58 (25.0)	23 (39.7)	35 (60.3)	$\chi^2 = 0.58$	0.445	16 (27.6)	42 (72.4)	$\chi^2 = 0.01$	0.932
COPD	38 (16.4)	12 (31.6)	26 (68.4)	$\chi^2 = 2.83$	0.093	7 (18.4)	31 (81.6)	$\chi^2 = 1.75$	0.186
Malignancy	35 (15.1)	11 (31.4)	24 (68.6)	$\chi^2 = 2.63$	0.105	3 (8.6)	32 (91.4)		**0.007**
Cerebrovascular disease	27 (11.6)	16 (59.3)	11 (40.7)	$\chi^2 = 2.90$	0.089	10 (37.0)	17 (63.0)	$\chi^2 = 1.51$	0.219
Chronic renal failure	21 (9.1)	6 (28.6)	15 (71.4)		0.136	3 (14.3)	18 (85.7)		0.164
Surgical intervention	8 (3.4)	4 (50)	4 (50)		0.726	3 (37.5)	5 (62.5)		0.503
Collagen tissue disease	8 (3.4)	0 (0)	7 (100)		**0.017**	0 (0)	7 (100)		0.101
Pregnancy	4 (1.7)	2 (50)	2 (50)		0.806	2 (50)	2 (50)		0.180
Liver failure	2 (0.9)	1 (50)	1 (50)		0.863	2 (100)	0 (0)		0.386
Transplantation	2 (0.9)	2 (100)	0 (0)		0.109	1 (50)	1 (50)		0.466

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus. Significant *p* values are shows in **bold**.

of immunosuppression (OR: 2.70; $p = 0.020$); and 15-day mortality. Regression analysis of the relationship between the same variables and 30-day mortality showed significant associations between systemic corticosteroid use (OR: 3.69; $p = 0.002$), high qPitt score (OR: 1.44; $p = 0.043$), presence of immunosuppression (OR: 6.61; $p = 0.004$); and 30-day mortality (Table 4). All patients treated with corticosteroids were given methylprednisolone.

Discussion

This retrospective study investigated mortality rates and factors affecting mortality in critically ill patients with HA BSI due to *K. pneumoniae* hospitalized in the ICU. All-cause 15-day and 30-day mortality rates were 56.0 % and 72.8 %, respectively. Logistic regression analysis revealed associations between systemic corticosteroid use prior to the development of bacteremia, high qPitt score on the day of bacteremia, immunosuppression; and both 15-day and 30-day mortality.

The mortality rates in this study were higher than the results of previously published studies [3–12]. The reasons for this may be that this study was conducted during the intensive period of the COVID-19 pandemic and the hospital is a tertiary-care center where critically ill patients are referred. Another reason might be that the inclusion criteria such as hospitalization in the ICU, HA infection, and BSI may have resulted in a severe and specific patient group. A meta-analysis reported 14 and 30-day pooled mortality to be 24% and 29%, respectively. In that study, hospitalization in ICU, HA infection, and infection with CRKP or ESBL were found to be associated with higher mortality in *K. pneumoniae* bacteremia [3]. All the patients included in the current study had BSI acquired in the ICU. In addition to this, 77.6% (n = 180) of patients were infected with CRKP strains. In an 8-year retrospective study investigating mortality markers, 28-day pooled mortality was found to be 26.9% in all patients and 42.5% in CRKP-infected patients. In that study, only 42.5% of the patients acquired the infection while hospitalized in the ICU [7]. Compared with that study, age, comorbidity rates, APACHE II scores, CCI scores, need for inotropic support, and infection rate with CRKP of the patients included in the present study were higher.

There is a strong association between the clinical status of patients and mortality in BSI due to *K. pneumoniae* [5]. Based on univariate analysis, both 15 and 30 mortality rates were significantly higher in patients receiving MV and vasopressor support. In

Table 4. Logistic regression analysis of factors affecting 15-day and 30-day mortality.

Vsriable	15-day mortality			30-day mortality		
	OR	95% CI	*p*	OR	95% CI	*p*
Gender						
Male	ref	–		ref	–	
Female	1.20	0.65–2.22	0.567	1.43	0.68–2.98	0.344
Age	1.00	0.98–1.02	0.848	1.02	0.99–1.05	0.201
Appropriate empirical antibiotic treatment						
Yes	ref	–		ref	–	
No	1.70	0.92–3.12	0.089	1.14	0.54–2.40	0.736
CCI score	1.01	0.87–1.17	0.910	1.13	0.92–1.39	0.234
qPitt score	1.32	1.01–1.74	**0.046**	1.44	1.01–2.05	**0.043**
APACHE II score	1.00	0.95–1.06	0.951	0.95	0.90–1.01	0.090
COVID-19						
Negative	ref	–		ref	–	
Positive	1.80	0.92–3.53	0.088	0.97	0.42–2.24	0.943
Corticosteroid use						
No	ref	–		ref	–	
Yes	2.38	1.19–4.74	**0.014**	3.69	1.61–8.49	**0.002**
CRKP						
No	ref	–		ref	–	
Yes	0.98	0.44–2.15	0.951	1.57	0.62–4.01	0.343
Length of ICU stay	0.99	0.97–1.01	0.259	0.99	0.98–1.01	0.455
Immunosuppression						
No	ref	–		ref	–	
Yes	2.70	1.17–6.23	**0.020**	6.61	1.84–23.81	**0.004**
Concomitant bacteremia						
No	ref	–		ref	–	
Yes	0.75	0.37–1.50	0.408	0.64	0.29–1.44	0.280
Prior antibiotic use						
No	ref	–		ref	–	
Yes	0.80	0.31–2.05	0.637	0.85	0.28–2.60	0.771

APACHE II: acute physiology and chronic health assessment II; CCI: Charlson comorbidity index; CI: confidence interval; COVID-19: CRKP: carbapenem-resistant *Klebsiella pneumoniae*; OR: odds ratio. Significant *p* values are shown in **bold**.

addition, it was observed that mortality rates were higher in patients with higher procalcitonin, D-dimer, ferritin, lactate dehydrogenase (LDH), and creatinine values on the day of blood culture. These laboratory values are expected to increase in severe sepsis or septic shock and are known to be indicators of a more severe clinical condition [22]. The results of the present study also revealed a higher mortality rate in patients with lower counts of lymphocytes and platelets and lower albumin values. These clinical factors may also be related to the dysfunction of organs such as bone marrow and liver, and therefore be observed in patients who are clinically more severe [23,24].

In the present study, a significant relationship was found between higher qPitt scores, and 15-day and 30-day mortality rates in logistic regression analyses. This finding is generally in line with the previous literature. In a prospective, multicenter cohort study investigating patients infected with CRKP, the Pitt bacteremia score was found to be effective in determining mortality [10]. Battle *et al.* derived a shorter version of the Pitt bacteremia score, the qPitt score, which was effective in predicting mortality in Gram-negative BSI. The same study also found the qPitt score to be more effective in predicting mortality than the quick sepsis-related organ failure assessment (qSOFA) and systemic inflammatory response syndrome (SIRS) [20].

In the present study, initiation of appropriate empirical antibiotic treatment was found to be significant in 15-day mortality in the univariate analysis, but not in 30-day mortality. The same analysis revealed that a high CCI score was not associated with 15-day mortality, but with 30-day mortality. This may indicate that despite the positive effect of early microbiologic cure on survival, later mortality is associated with comorbidities. Zarkotou *et al.* found that appropriate antibiotic use was the only intervenable factor that reduced mortality in BSI due to CRKP [25]. The results of the present study highlight the importance of early initiation of appropriate empirical antibiotic treatment.

In the current study, a significant independent association was found between the presence of immunosuppression, which was included in the logistic regression analysis as a confounding factor, and 15- and 30-day mortality. In a study of patients with HA BSI due to carbapenemase-producing *K. pneumoniae*, corticosteroid use and immunosuppressive therapy in the last 30 days before bacteremia were found to be independent predictors of 30-day mortality [26]. In another study, immunocompromised states (e.g., leukemia/lymphoma, metastatic cancer, chemotherapy, high dose steroids) were associated with 7, 15, and 30-day mortality in HA infections caused by extremely drug-resistant Gram-negative bacilli in the ICU [27]. Unlike these studies, the current investigation analyzed corticosteroid use as a separate factor from other immunosuppressive factors.

Identifying the relationship between corticosteroid use before bacteremia, and mortality was one of the goals of this study. Of all patients included in this study, 67.7% were hospitalized in the ICU due to respiratory failure, 52.2% were diagnosed with COVID-19, and 63.8% received methylprednisolone treatment before the development of bacteremia. The use of corticosteroids in acute respiratory distress syndrome (ARDS) has been shown to provide an advantage in survival by reducing inflammation [28]. In addition, its use in patients with severe pneumonia and ARDS was recommended in the COVID-19 guidelines of Turkey [14]. Casale *et al.* found an association between prior corticosteroid use and mortality in patients hospitalized due to COVID-19 and CRKP bacteremia [6]. A case-control study published before the COVID-19 pandemic also found an association between mortality in CRKP bacteremia and prior corticosteroid use [8]. The regression analysis in the present study found that the use of methylprednisolone before the development of bacteremia was associated with 15-day and 30-day mortality. These results are consistent with similar studies and suggest that corticosteroid use may increase mortality in nosocomial BSI due to *K. pneumoniae*.

The strengths of this study were that it was conducted in a large-scale healthcare institution with a substantial sample size and it focused on a specific patient group. The results of the study should be considered in light of several limitations. The study was planned in a tertiary-care center, causing the sample to consist mostly of older patients with comorbidities. This limits the generalizability of the findings to other patient groups. The retrospective design of the study and collection of data using hospital records limited the variety of the variables included in the analyses. Laboratory methods required for the detection of carbapenemases were not available. This situation caused a limitation in choosing the appropriate antibiotherapy in cases of some carbapenemase-producing *K. pneumoniae* strains, while aiming to arrange antibiotic treatments in accordance with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines [29].

Conclusions

A high qPitt score was identified as a predictor for

15-day and 30-day mortality in patients with nosocomial BSI due to *K. pneumoniae* hospitalized in the ICU. This quick scoring system may be a practical tool to predict mortality in daily clinical practice in this patient group. The results also show that mortality risk increases if the patient is receiving immunosuppressive treatments or has concomitant immunosuppressive diseases. Moreover, corticosteroid use before the development of bacteremia contributes to both 15-day and 30-day mortality, even when controlled for other immunosuppressive factors. Unlike other immunosuppressive factors which cannot be altered, corticosteroid use may be modified by the clinician to some extent. The results suggest that corticosteroids should be used with caution, especially in patients admitted to ICUs where BSI due to *K. pneumoniae* are commonly present.

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Authors' contributions
All authors contributed to the study's conception and design. EA, ÖÇ, AŞÇ, EA, and AAB, data collection; HA, data analysis; EA, literature search, manuscript first draft; DÖE and FYK, manuscript review and editing. All authors were involved in the critical revision of the manuscript. All authors read and approved the final version of the manuscript.

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Conflict of interest
No conflict of interest is declared.

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