OPEN ACCESS

ORIGINAL ARTICLE

Epidemiology, Clinical Features, Outcomes, and Antimicrobial Resistance Patterns of Enterobacteriaceae Bacteremia in a Tertiary Care Hospital of Peshawar

Wajeeha Qayyum[1], Shahan Ahmad[2], Mamoona Zaman[3], Seema Ashraf[4]

[1-4]Rehman Medical Institute, Peshawar

ABSTRACT

Objective: To determine the frequency, antimicrobial resistance patterns, clinical outcomes, and predictors of in-hospital mortality with Enterobacteriaceae bacteraemia.

Methodology: This retrospective study was conducted at Rehman Medical Institute, Peshawar, over one year. Patients from all age groups with Enterobacteriaceae (excluding Salmonella spp.) bacteraemia presenting to hospital from March 2024 to March 2025 were included. Bacterial identification and antibiotic susceptibility testing followed CLSI guidelines. Clinical and demographic data were collected and analyzed by SPSS 27.

Results: Of 569 positive blood cultures, 154 (27.1%) yielded Enterobacteriaceae growth. Of 154 patients, 91 (59.1%) were male. The median (IQR) age of participants was 43 (55) years. The most common focus of infection was the respiratory tract (75, 48.7%). Around 57 (37.0%) cases required ICU admission, while 49 (31.8%) were mechanically ventilated and 55 (35.7%) received inotropic support. Meropenem was the most frequently prescribed empirical antibiotic (37.8%). Klebsiella pneumoniae (52.6%) was the commonest isolated pathogen. High resistance was observed for amoxicillin (97.8%), ceftriaxone (78.8%), and ciprofloxacin (76.9%). While 35.7% of pathogens were resistant to amikacin and 43.5% were resistant to meropenem. Mortality (26.90%) was significantly associated with age >60 years, malignancy, chronic kidney disease, altered consciousness, use of inotrope, and mechanical ventilation. Independent predictors of death included Age >60 years (OR 10.6), altered consciousness (OR 19.2), inotrope support (OR 35.7), mechanical ventilation (OR 142.9), extended-spectrum beta-lactamase (ESBL) strains (OR 8.3), and coagulation abnormality (OR 7.3).

Conclusion: Multidrug resistance among Enterobacteriaceae bacteremia isolates is alarmingly high. Advanced age, altered consciousness, haemodynamic instability, ventilator support, and ESBL strains were strongly associated with in-hospital mortality.

Keywords: Antibacterial Agents, Bacteremia, Drug Resistance, Enterobacteriaceae Infections, Hospital Mortality

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [3,4]Critical analysis and manuscript review; [4]Data analysis; Manuscript Editing.

Correspondence:
Shahan Ahmad
Email: shahan.ahmad@rmi.edu.pk

Article info:
Received: December 15, 2025
Accepted: March 03, 2026

Cite this article. Qayyum W, Ahmad S, Zaman M, Ashraf S. Epidemiology, Clinical Features, Outcomes, and Antimicrobial Resistance Patterns of Enterobacteriaceae Bacteremia in a Tertiary Care Hospital of Peshawar. J Islamabad Med Dental Coll. 2026; 15(2): *142-150.*
DOI: https://doi.org/10.35787/jimdc.v15i2.1515

Funding Source: Nil
Conflict of interest: Nil

Introduction

Bloodstream infections (BSIs) are among the most serious and potentially fatal infections encountered in clinical settings, particularly when caused by multidrug resistant organisms.[1] Enterobacteriaceae a diverse group of Gram-negative bacteria(GNB), with many species being significant pathogens, are responsible for a significant proportion of community- and hospital-acquired BSIs.[1] In the United States, approximately 12,700 infections and

more than 1,100 deaths occurred due to Carbapenem-resistant Enterobacteriaceae (CRE) in 2020.[2] The annual incidence of CRE rose 18% from 2019 to 2023.[3] The global burden of these infections is significant, with high mortality rates, especially in low- and middle-income countries where surveillance and antimicrobial stewardship may be limited.[4]

Antimicrobial resistance (AMR) in Enterobacteriaceae is an escalating threat to public health. The emergence of extended spectrum beta lactamases (ESBL) and carbapenem resistant Enterobacteriaceae (CRE) has significantly reduced the effectiveness of many antibiotics, hence increasing the cost of treatment and disease complications.[5] In a large study in Nepal on over 2000 cultures, about half of the isolated organisms were ESBL and around 90% isolates were multi-drug resistant.[6] Moreover, the resistance against colistin (last resort treatment against CRE strains) is also increasingly being documented especially in Africa.[7] The burden of antimicrobial resistance (AMR) is of great concern in developing countries owing to irrational use of antibiotics, limited diagnostic facilities, and inadequate infection control practices, all of these factors facilitate the spread of resistant organisms.[8]

Despite the growing threat of resistant Enterobacteriaceae, there is a paucity of local data regarding evolving resistance trends and clinical outcomes. Understanding these patterns is essential for formulating empirical therapy guidelines and infection control policies.

Our study aims to describe the frequency and spectrum of Enterobacteriaceae bacteremia among hospitalized patients, and to describe antimicrobial resistance patterns, clinical outcomes and predictors of hospital mortality. Generating such institution-specific evidence will provide evidence-based decisions to improve antibiotic stewardship, improve clinical outcomes and control the spread of resistant pathogens in the region.

Methodology

This retrospective study was conducted at Rehman Medical Institute, Peshawar, over a period of one year from March 2024- March 2025. All consecutive patients meeting the inclusion criteria during the study period were included and the final sample size was determined by the number of eligible cases presenting during the study period. Patient consent is routinely taken from all patients or their next of kin at the time of admission to retrieve and publish their clinical data for research purpose. All patients admitted with a provisional diagnosis of sepsis were initially recruited. Sepsis was defined as per 3rd international consensus definitions for sepsis and septic shock (sepsis3).[9]

Blood samples were collected aseptically from patients with clinical suspicion of sepsis and processed using an automated BacT/ALERT culture system. For identifying organisms, basic biochemical tests like oxidase, catalase, and motility tests were performed. Final identification was done on API 10 S, API 20 E, 20 NE and Vitek 2.0 compact system.

Antibiotic susceptibility testing for all Enterobacteriaceae was performed using Kirby Bauer disk diffusion method on Mueller-Hinton agar. Amikacin (30 µg), Amoxicillin (25 µg), Amoxicillin–Clavulanic acid (20/10 µg), Cefotaxime (30 µg), Ceftazidime (30 µg), Ceftriaxone (30 µg), Cefoperazone–Sulbactam (75/30 µg), Ciprofloxacin (5 µg), Doxycycline (30 µg), Co-trimoxazole (1.25/23.75 µg), Meropenem (10 µg), and Piperacillin–Tazobactam (100/10 µg) were checked for sensitivity. Colistin screen agar was used for colistin sensitivity as per CLSI guidelines 2023. The inoculated plates were incubated at 35 ± 2°C for 16–18 hours, and zone diameters were interpreted according to CLSI M100 Ed33. ESBL production was inferred from resistance to third-generation cephalosporins and confirmed by combined disc method with ceftazidime (30 µg) and cefotaxime (30 µg) with and without clavulanic acid, according to CLSI 2023 guidelines.

Demographic data such as age, gender, comorbidities, clinical features, severity of illness, focus of infection, and antibiotic therapy were retrieved from the record. Clinical outcomes were assessed in terms of length of hospital stay, ICU admission, and in-hospital mortality.

All patients of both genders with positive blood cultures for Enterobacteriaceae were included.

Blood cultures showing growth of Salmonella species were excluded due to their different clinical and biochemical profile that may have contributed to heterogeneity and confounded the study results. Blood cultures with concomitant growth of other organism with Enterobacteriaceae, patients who have received antibiotics prior to culture sampling, and those who expired within 24 hours of admission were excluded.

Data was entered and analyzed through Statistical Package for the Social Sciences (SPSS) version 27. Percentages were used to describe organism type, clinical features, and antimicrobial resistance patterns. Continuous variables were assessed for normality using the Shapiro–Wilk test. As most variables were not normally distributed, data was presented as median (interquartile range). To evaluate the factors associated with mortality, patients were divided into two groups according to the outcome at the time of discharge (Alive /Death). Patients who left against medical advice were excluded from outcome analysis. Continuous variables were expressed as median (IQR) and compared using Mann–Whitney U test. Categorical variables were expressed in percentages and compared using Chi-square test. P value < 0.05 was taken statistically significant. Furthermore, multivariate logistic regression was applied to predict the factors associated with in hospital death. Factors having P value < 0.05 on univariate analysis were included in multivariate regression analysis. Analysis was performed using available data in hospital information management system (HIMS), hence sample size (n) varies for few variable due to missing values in data.

Ethical approval was taken from the institutional review board committee of Rehman Medical Institute under reference number RMI/IRB-EC/Approval/260

Results

For one year of study period, 569 blood cultures came out to be positive, of which 154 (27.1%) yielded Enterobacteriaceae (excluding Salmonella species). Among these, Klebsiella pneumoniae was the most frequently isolated organism (81, 52.6%), followed by Escherichia coli (47, 30.5%) and Serratia marcescens (18, 11.7%). Proteus mirabilis (5, 3.2%) and Citrobacter braakii (3, 1.9%) were less commonly isolated.

Of 154 patients, 91 (59.1%) were male, rest were females. Mean age of patients was 40.09 ± 28.59 years. About 48 patients (31.2%) were older than 60 years. Fever was the most frequently presenting symptom (129, 83.8%), followed by tachypnea (91, 59.1%), and altered consciousness (81, 52.6%). The most common focus of infection was the respiratory tract (75, 48.7%), followed by urinary tract infections (38, 24.7%). Comorbid conditions were present in 67 (43.5%) patients, with more than one comorbidity seen in 57 (37.0%) patients. Hypertension (60, 39.0%) and diabetes mellitus (52, 33.8%) were the most prevalent. Around 57 (37.0%) cases got severe sepsis requiring ICU admission, while 49 (31.8%) required mechanical ventilation, and 55 (35.7%) received inotropic support for the management of hypotension. Detailed demographic, clinical, and laboratory features are presented in Table I. Due to the retrospective study design, laboratory investigations were not uniformly available for all patients in their medical records hence few of the laboratory data were missing. Analysis was performed using available data; hence the sample size (N) varies for few variables.

High levels of resistance (>70%) were observed with penicillin, cephalosporins and quinolones. Resistance to meropenem and amikacin was seen in

43.5% and 35.7% isolates, respectively. Colistin resistance remained low (0.6%).

Table I. Demographic, clinical and laboratory features of patients (n=154)	
Characteristic	**n (%) / Median (IQR)**
Gender	
Male	91 (59.1)
Female	63 (40.9)
Age (years)	43(55)
Age Groups	
<1 year	18 (11.7)
1–13 years	29 (18.8)
14–40 years	17 (11.0)
41–60 years	42 (27.3)
>60 years	48 (31.2)
Clinical Features	
Fever	129 (83.8)
SOB	73 (47.4)
Cough	47 (30.5)
Vomiting	82 (53.2)
Diarrhea	12 (7.8)
Altered consciousness	81 (52.6)
Tachypnea	91 (59.1)
Hypotension	56 (36.4)
Fits	15 (10.3)
Comorbid	67(43.5)
Diabetes mellitus	52 (33.8)
Hypertension	60 (39.0)
IHD	38 (24.7)
CKD	16 (10.4)
Cancer	10 (6.5)
Stroke	11 (7.1)
Trauma	9 (5.8)
Bedridden	3 (1.9)
Valvular heart disease	2 (1.3)
Preterm	27 (17.5)
Previous hospital admission in last 3 months	131 (85.1)
Recent invasive procedure in last 3 months	54 (35.1)
Urinary catheter	75 (48.7)
ICU admission	57 (37.0)
Mechanical ventilation	49 (31.8)
Length of hospital stay (days)	5.5(9)
Inotrope use	55 (35.7)
Focus of infection	
Chest	75 (48.7)
Urine	38 (24.7)
Abdomen	20 (13.0)
CNS	9 (5.8)
Undetermined	12 (7.8)
Laboratory Findings	
TLC (10^9/L)	13.16(9.92) (N=143)
Hemoglobin (g/dL)	11.8(18.9) (N=143)
Platelets (×10^9/L)	219(184.50) (N=141)
CRP (mg/L)	15.14(39.3) (N=128)
Serum creatinine (mg/dL)	1.12(1.85) (N=134)

Table II: Factors associated with in-hospital mortality (univariate analysis)				
Variable		**Non-Survivors (n=39)**	**Survivors (n=106)**	**p-value**
Age	<1	6.2% (1)	93.8% (15)	0.031
	1-13	22.2% (6)	77.8% (21)	
	Age 14–40	37.5% (6)	62.5% (10)	
	Age 41–60	17.9% (7)	82.1% (32)	
	>60 years	40.4% (19)	59.6% (28)	
Gender	Male	27.1% (23)	72.9% (62)	0.95
	Female	26.7% (16)	73.3% (44)	
Age (years) – median (IQR)		58(47)	42(53)	0.01
Comorbid	Single	50.0% (5)	50.0% (5)	0.08
	multiple	31.6% (18)	68.4% (39)	
	Nil	20.5% (16)	79.5% (62)	
Diabetes Mellitus		30.8% (16)	69.2% (36)	0.43
Hypertension		33.3% (20)	66.7% (40)	0.14
IHD		34.2% (13)	65.8% (25)	0.23
Stroke		54.5% (6)	45.5% (5)	0.03
Asthma		0.0% (0)	100.0% (7)	0.10
CKD		50.0% (8)	50.0% (8)	0.02
Cancer		55.6% (5)	44.4% (4)	0.04
Previous hospital admission n last 3 months		27.5% (36)	72.5% (95)	0.62
Recent invasive procedure in last 3c months		46.3% (25)	53.7% (29)	<0.001
Altered consciousness		44.4% (36)	55.6% (45)	<0.001
Hypotension		60.7% (34)	39.3% (22)	<0.001
ICU admission		57.9% (33)	42.1% (24)	<0.001
Mechanical ventilation		65.3% (32)	34.7% (17)	<0.001
Inotropes		63.6% (35)	36.4% (20)	<0.001
Lab values				
TLC (10^9/L) median (IQR)		14.48 (12.87)	11.23 (8.98)	0.112
Hemoglobin (g/dL) – median (IQR)		10.25 (3.92)	12.50 (4.57)	0.008
Platelets (×10^9/L) – median (IQR)		182.5 (171.0)	227.0 (187.5)	0.310
CRP (mg/L) – median (IQR)		15.93 (26.37)	12.98 (42.27)	0.275
Abnormal coagulation		33.3% (13)	8.5% (9)	<0.001
Serum creatinine (mg/dL) – median (IQR)		1.85(10.0)	1.07(1.51)	0.017
Focus of infection	Chest	29.7% (22)	70.3% (52)	0.13
	Urine	18.4% (7)	81.6% (31)	
	Abdomen	25.0% (5)	75.0% (15)	
	CNS	55.6% (5)	44.4% (4)	
	undetermined	0.0% (0)	100.0% (4)	
Response-based Antibiotic modification		14.0% (6)	86.0% (37)	0.04
Duration of stay (days) – median (IQR)		5(9)	6(10)	0.92
ESBL strains		37.7% (26)	62.3% (43)	0.005
CRE strains		37.7% (23)	62.3% (38)	0.012

ESBL production was detected in 75 of 154 isolates (48.7%), while CRE was observed in 67 (43.5%)

isolates. ESBL and CRE were most prevalent in Klebsiella pneumoniae (ESBL 68.3%, CRE 63.4%) and Serratia marcescens (ESBL 55.6%, CRE 44.4%). Statistical analysis showed a significant association between bacterial species and both ESBL production and carbapenem resistance ($p < 0.001$ for each). CRE was significantly associated with mortality in univariate analysis; however, it was not, in the multivariate model, due to collinearity with ESBL status.

Of total 154, 106 were discharged alive, 39 were dead at discharge and 9 patients left against medical advice. Outcome analysis was carried out after excluding patients who left against medical advice hence 145 patients were included in further analysis. At discharged mortality was 26.9% (39/145).

In this study, a total of 111 patients had a clear record to show antibiotic empirical and definitive therapy. Among them, Meropenem was the most frequently selected empirical antibiotic, used in 42 (37.8%) cases, followed by Cefoperazone–Sulbactam in 27 (24.3%), Cefoperazone in 24 (21.6%), and Ceftriaxone in 11 (9.9%) patients. Other empirical agents included Piperacillin–Tazobactam in 3 (2.7%), Moxifloxacin in 2 (1.8%), and Amoxicillin–Clavulanic acid and Colistin in 1 (0.9%) patient each.

Antibiotic modification based on clinical or microbiological response was carried out in 43 out of 111 patients. Of these, therapy was escalated to Piperacillin–Tazobactam in 4 patients, to Colistin in 2, while the remaining patients were switched to Meropenem.

Out of 154 patients, 9 patients took discharge against medical advice, so they were excluded from mortality analysis. Among the 145 patients, 39 (26.38%) did not survive. Mortality was significantly associated with age. Median (IQR) age was greater in non-survivors compared to survivors (58(47) Vs 42(53), $p = 0.01$). Patients aged >60 years had significantly higher mortality. (40.4%, $p = 0.031$),

Comorbidities such as stroke ($p = 0.03$), chronic kidney disease ($p = 0.02$), and malignancy ($p = 0.04$) were significantly associated with death. Altered consciousness, hypotension, use of inotropes, ICU admission, mechanical ventilation, were also significantly linked to high in-patient mortality ($p < 0.001$) each. Laboratory abnormalities such as deranged coagulation profile ($p < 0.001$) and elevated serum creatinine ($p = 0.03$) were associated with poor outcome in terms of mortality. Moreover, ESBL ($p = 0.005$) and CRE ($p = 0.012$) strains showed a significant association with in-hospital mortality. A comprehensive analysis of factors linked to in-hospital mortality is presented in Table III.

Multivariate logistic regression identified several independent predictors of mortality. Altered consciousness increased the risk of death 19-fold. Dependence on inotropes was a strong predictor (OR 35.7, 95% CI 2.3–500, $p = 0.011$), while mechanical ventilation was linked with the highest mortality risk (OR 142.9, 95% CI 1.2–>800, $p = 0.041$). These results are described in Table III.

Table III: Predictors of in-hospital mortality after multivariate logistic regression

Predictor	Adjusted OR (risk of death)	95% CI	p-value
Abnormal coagulation	7.28	1.05 – 50.7	0.045
Impaired consciousness	19.2	2.3 – 166	0.006
Inotropes (vasopressor use)	35.7	2.3 – 500	0.011
ESBL positive	8.3	1.5 – 47.6	0.017
Age >60 years	10.6	1.42 – 79.9	0.022
Ventilator use	142.9	1.2 – >800	0.041

Discussion

In the present study, Enterobacteriaceae accounted for 27.1% of all positive blood cultures, a proportion comparable to reports from India (29%,146/505) by Neyazi et al.[10] but lower than reported from China (53.5%, 2569/4801)[11] and Spain (32.7%,

928/2840).[10] Variations in prevalence across studies may reflect differences in infection control practices, antimicrobial prescribing behaviors, and the demographic characteristics of hospitalized patients.

Klebsiella pneumoniae was the predominant in our cohort (52.6%), followed by Escherichia coli (30.5%). This distribution parallels reports from India, where Klebsiella species represented 65.6% and E. coli 21.9% of Enterobacteriaceae bacteremia.10 Comparable findings have been documented in multiple studies worldwide where Klebsiella and E. coli were mostly isolated pathogens.[13-15]

A rising level of antimicrobial resistance was observed across multiple drug classes, particularly to penicillin, cephalosporins, and quinolones, consistent with reports from other regions worldwide.[13,15,16] We have documented higher rates than observed in other studies. Lord J et al described that 67.6 % resistance was noted in Enterobacteriaceae against penicillin, 52.9% with cephalosporins and 30% with quinolones.13 A multicenter study by Roseau-Vincenti A et al, on Enterobacteriaceae described that 13.8% isolates were resistant to cephalosporins, 9.2% to piperacillin–tazobactam,12.9% to fluoroquinolones.17 Resistance to amikacin was 27.6% in Kenya13 and 1.2% in China.17 Colistin resistance remained minimal (0.6%), preserving its potential role as a last-line therapy. However, emerging global data indicate a concerning increase in colistin resistance—from 2.1% to as high as 17.8% in studies conducted between 2017 and 2020—emphasizing the need for vigilant antimicrobial surveillance.[7,18,19]

Nearly half (48.7%) of our isolates were ESBL producers, comparable to findings by Ara-Montojo et al (49.6%) and (63.4%) by Sahle et al.[12,14] Carbapenem resistance in our study (43.5%) was notably higher than rates reported from China (<5%), Malaysia (<1%), and Kenya (6.5%).11,13,16

We have reported alarmingly high frequency of carbapenem resistance as compared to rest of World. The growing trend of carbapenem resistance in our region is supported by a systematic review by Umair et al., evaluating 88 studies from Pakistan over a 30-year period. The review has reported a marked temporal rise in carbapenem resistance over the last few decades, which escalated from nearly 0% to 36% among Enterobacteriaceae. These findings are consistent with our study. [17] Klebsiella pneumoniae demonstrated higher rates of both ESBL production and carbapenem resistance compared to E. coli, consistent with previous reports from other studies. [10,11,12,15] Unjudicial use of antibiotic and their over-the-counter availability, lack of infection control and antimicrobial stewardship, limited access to diagnostic facilities and delayed diagnosis, may have contributed to the rapidly rising trend in antimicrobial resistance in our region.

Our study has highlighted multiple clinical factors associated with high hospital mortality. Elderly patients (>60 years) in our cohort exhibited significantly higher mortality ($p = 0.031$), a finding consistent with reports from a study from Malaysia (mean 62.1 ± 14.4 years) and China (mean 61.1 years), where older age was associated with adverse outcomes.[11,16] In another study, the mean age among non-survivors was significantly higher (67 vs 58 years, $p = 0.013$).18 This global age-related vulnerability reflects reduced physiological reserve and the higher burden of comorbidities among older adults.

Comorbidities such as stroke, chronic kidney disease (CKD), and malignancy were significantly associated with mortality in our study, it is parallel to the findings from two studies which also linked CKD and neoplastic disease to poor outcomes in Enterobacteriaceae bacteremia.[13,16In] another study, dialysis dependent CKD (RR 26.9), Organ transplantation (RR 20.3), and malignancy (RR 14.9) was predictors of poor outcome in Enterobacteriaceae infection.20In contrast, diabetes and hypertension, though common in our cohort, were not independently associated with

mortality, differing from reports from Malaysia and Korea, where these comorbidities were predictors of unfavorable outcomes, particularly in carbapenem-resistant Enterobacteriaceae (CRE) infections.[16,21] This discrepancy may stem from differences in study populations, since the referenced studies exclusively included patients infected with CRE strains.

A recent invasive procedure was another significant factor associated with mortality in our study, consistent with a regional study, which demonstrated a strong association between invasive procedures, resistant strains, and mortality.[22] Bonten M, et al also described a 3–10-fold increase in E. coli bacteremia after recent procedures.[20]

Laboratory parameters such as elevated serum creatinine and abnormal coagulation profiles were significantly associated with mortality. Notably, coagulation abnormalities carried an adjusted odds ratio (OR) of 7.28, underscoring the contribution of sepsis-induced coagulopathy to unfavorable prognosis. These results align with the studies reporting the association of renal impairment and coagulopathy with increased mortality in bloodstream infections.[12,21,22]

Indicators of severe infection—such as altered consciousness, septic shock, inotropic support, ICU admission, and mechanical ventilation, —were all significantly linked to in-hospital mortality ($p < 0.001$). These findings are in line with published literature narrating critical illness parameters and ICU admission as major predictors of death among patients with Enterobacteriaceae bloodstream infections.[11,12,23,24]

The infections associated with ESBL and CRE significantly increased the mortality ($p = 0.005$ and $p = 0.012$, respectively). After multivariate adjustment, ESBL positivity remained an independent predictor of death (OR 8.3, 95% CI 1.5–47.6, $p = 0.017$). Similar findings have been reported in literature, where ESBL and CRE infections are associated with prolonged hospitalization, limited therapeutic options, and higher fatality rates.[19,25] These results underscore the clinical and public health burden of multidrug-resistant Enterobacteriaceae in hospital settings.

In our findings, Although CRE was significantly associated with mortality on univariate analysis ($p = 0.012$), it did not remain an independent predictor in the multivariate model. This may be due to collinearity with ESBL status, as well as overlap with markers of severe illness such as inotropic support and mechanical ventilation. Furthermore, the limited sample size and number of mortality events may have reduced the statistical power to detect an independent association.

In a multicenter study by Roseau-Vincenti et al., conducted on patients with Enterobacteriaceae bloodstream infections, reported that empirical therapy with β-lactam/β-lactamase inhibitor combinations and cephalosporins were the most frequently used agents, while carbapenems were used in only 4.06% patients. After susceptibility results, therapy was narrowed in 52 (61%) cases.[18] In another study by AbuBakar et al, similar empirical antibiotic choices were reported. In that cohort, cephalosporins (22.8%) and piperacillin–tazobactam (23.6%) were used empirical agents, Meropenem was used in 9.8% patients as an empirical antibiotic.16 In contrast, meropenem was the most frequently used empirical antibiotic in our study. This indicates a predominant reliance on broad-spectrum antibiotics for initial management. Moreover, the majority of the patients who didn't receive meropenem as empirical therapy were escalated to meropenem. This consistent preference for carbapenems may have contributed to growing AMR. Similar findings have been reported in other studies.[11,21,26] These observations emphasize the urgent need for antimicrobial stewardship interventions, optimized empirical antibiotic selection, and de-escalation based on culture results to mitigate further resistance development.

This study provides valuable insight of Enterobacteriaceae bacteremia within a tertiary care setting, representing one of the few comprehensive analyses from our region. The

inclusion of detailed microbiological and clinical data allowed for robust identification of mortality predictors. However, there are few limitations of this study. A single-center, retrospective design may have limited the generalizability of results. Secondly, molecular characterization of resistance gene (e.g., carbapenemase genes) was not performed. This approach may have overestimated true CRE prevalence, as reduced susceptibility to carbapenems can also result from mechanisms such as extended-spectrum beta-lactamase (ESBL) production combined with porin loss or efflux pump activity, rather than true carbapenemase production. Finally, being a single centered study from a tertiary care hospital, significant numbers of complicated patients referred from peripheral hospitals may have translated into referral bias toward more severe and resistant cases.

Despite these limitations, the study highlights the burden of multidrug-resistant Enterobacteriaceae, risk factors, mortality, and use of broad-spectrum antibiotics in BSI. The study fills the critical gaps in antimicrobial stewardship and offers evidence-based guidance for improving management of Enterobacteriaceae infections. Prospective multicenter studies are required to validate these findings and determine targeted interventions' impact on mortality outcomes.

Conclusion

Enterobacteriaceae accounted for over one-fourth of all positive blood cultures, with Klebsiella pneumoniae and Escherichia coli predominating. Nearly half of the isolates produced ESBL, and over 40% showed carbapenem resistance. Advanced age, altered mental status, abnormal coagulation, hemodynamic instability, requirement for ICU, ventilator support, and ESBL-producing strains were predictors of in-hospital mortality.

Acknowledgements: We are deeply obliged to Department of microbiology Rehman Medical Institute, Peshawar for providing Laboratory data for this study.

References

1. Holmes CL, Anderson MT, Mobley HLT, Bachman MA. Pathogenesis of Gram-Negative Bacteremia. Clin Microbiol Rev. 2021;34(2):e00234-20. https://doi.org/10.1128/cmr.00234-20
2. Centers for Disease Control and Prevention (CDC). COVID-19: U.S. impact on antimicrobial resistance, 2022 special report. Atlanta (GA): U.S. Department of Health and Human Services; 2022. Available from: https://www.cdc.gov/antimicrobial-resistance/data-research/threats/covid-19.html
3. Rankin DA, Stahl A, Sabour S, Khan MA, Armstrong T, Huang JY, et al. Changes in carbapenemase-producing carbapenem-resistant Enterobacterales, 2019 to 2023. Ann Intern Med. 2025 [Epub ahead of print]. https://doi.org/10.7326/ANNALS-25-02404
4. Gumus DD, Demir OO, Aykac K, Hazirolan G, Avci H, Ceyhan M, et al. Gram-negative bacteremia, the risk factors, and outcome in children. Diagn Microbiol Infect Dis. 2024;109(3):116324. https://doi.org/10.1016/j.diagmicrobio.2024.116324
5. Tilahun M, Kassa Y, Gedefie A, Ashagire M. Emerging carbapenem-resistant Enterobacteriaceae infection, its epidemiology and novel treatment options: a review. Infect Drug Resist. 2021;14:4363–4374. https://doi.org/10.2147/idr.s337611
6. Manandhar S, Zellweger RM, Maharjan N, Dongol S, Prajapati KG, Thwaites G, et al. A high prevalence of multi-drug resistant Gram-negative bacilli in a Nepali tertiary care hospital and associated widespread distribution of Extended-Spectrum Beta-Lactamase (ESBL) and carbapenemase-encoding genes. Ann Clin Microbiol Antimicrob. 2020;19(1):48. https://doi.org/10.1186/s12941-020-00390-y
7. Gashaw Y, Asmare Z, Tigabie M, Sisay A, Getatachew E, Tadesse S, et al. Prevalence of colistin-resistant Enterobacteriaceae isolated from clinical samples in Africa: a systematic review and meta-analysis. BMC Infect Dis. 2025;25(1):437. https://doi.org/10.1186/s12879-025-10826-5.
8. Endale H, Mathewos M, Abdeta D. Potential Causes of Spread of Antimicrobial Resistance and Preventive Measures in One Health Perspective-A Review. Infect Drug Resist. 2023;16:7515-7545. https://doi.org/10.2147/IDR.S428837.
9. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-10. https://doi.org/10.1001/jama.2016.0287.

10. Neyazi N, Khan F, Sultan A, Akhtar A. Prevalence of Enterobacteriaceae in Blood Stream Infections and their Resistance Profile: A Brief Study at a Tertiary Care Hospital. Int J Hum Health Sci. 2023;7(i700):S138-S148. https://doi.org/10.31344/ijhhs.v7i700.551.
11. Zheng B, Xu H, Guo L, Yu X, Ji J, Ying C, et al. Genomic and phenotypic diversity of carbapenemase-producing Enterobacteriaceae isolates from bacteremia in China: a multicenter epidemiological, microbiological, and genetic study. Engineering. 2022;12:90–100. https://doi.org/10.1016/j.eng.2020.10.015.
12. Ara-Montojo MF, Escosa-García L, Alguacil-Guillén M, Seara N, Zozaya C, Plaza D, et al. Predictors of mortality and clinical characteristics among carbapenem-resistant or carbapenemase-producing Enterobacteriaceae bloodstream infections in Spanish children. J Antimicrob Chemother. 2020;75(7):2014–2021. https://doi.org/10.1093/jac/dkaa111.
13. Lord J, Gikonyo A, Miwa A, Odoi A. Antimicrobial resistance among Enterobacteriaceae, Staphylococcus aureus, and Pseudomonas spp. isolates from clinical specimens from a hospital in Nairobi, Kenya. Front Microbiol. 2021;12:631608. https://doi.org/10.3389/fmicb.2021.631608.
14. Sahle Z, Engidaye G, Shenkute D, Metaferia Y. High prevalence of multi-drug resistance and extended-spectrum beta-lactamase-producing Enterobacteriaceae among hospitalized patients presumptive for bacterial infection at Debre Berhan Comprehensive Specialized Hospital, Ethiopia. Infect Drug Resist. 2022;15:2365–2376. https://doi.org/10.2147/IDR.S364822.
15. Arafah AA. Antibiotic resistance trends among Enterobacteriaceae in Saudi Arabia: a systematic review. Cureus. 2023;15(6):e40137. https://doi.org/10.7759/cureus.40137.
16. Abubakar U, Ahmad A, Azmi S. Mortality and its predictors among hospitalized patients with infections due to extended-spectrum beta-lactamase (ESBL) Enterobacteriaceae in Malaysia: a retrospective observational study. BMC Infect Dis. 2020;20(1):897.
17. https://doi.org/10.1186/s12879-020-05666-2.
18. Muhammad Umair, Timothy R. Walsh, Mashkoor Mohsin. A systematic review and meta-analysis of carbapenem resistance and its possible treatment options with focus on clinical Enterobacteriaceae: Thirty years of development in Pakistan. Heliyon. 2024;10(7):e28052. https://doi.org/10.1016/j.heliyon.2024.e28052.
19. Roseau-Vincenti A, Forestier E, Lanoix JP, Ricard C, Carret MC, Caraux-Paz P, Paccalin M, Gavazzi G, Roubaud-Baudron C; GInGer group (SPILF-SFGG). Empirical antibiotic therapy modalities for Enterobacteriaceae bloodstream infections in older patients and their impact on mortality: a multicentre retrospective study. Infection. 2024;52:155–163. https://doi.org/10.1007/s15010-023-02073-0.
20. Obaid NA, Abuhussain SA, Mulibari KK, Alotaibi N, Mostafa AM, Hagag A, et al. Antimicrobial-resistant pathogens related to catheter-associated urinary tract infections in intensive care units: a multicenter retrospective study in the Western region of Saudi Arabia. Clin Epidemiol Glob Health. 2023;21:101291. https://doi.org/10.1016/j.cegh.2023.101291
21. Bonten M, Johnson JR, van den Biggelaar AHJ, Georgalis L, Geurtsen J, Ibarra de Palacios P, et al. Epidemiology of Escherichia coli bacteremia: a systematic literature review. Clin Infect Dis. 2021;72(7):1211–1219. https://doi.org/10.1093/cid/ciaa179.
22. Lee SH, Kim CH, Lee HY, Park KH, Han SH. Epidemiology of carbapenem-resistant Enterobacteriaceae bacteremia in Gyeonggi Province, Republic of Korea, between 2018 and 2021. Antibiotics (Basel). 2023;12:1286. https://doi.org/10.3390/antibiotics1208128
23. Li X, Ye H. Clinical and mortality risk factors in bloodstream infections with carbapenem-resistant Enterobacteriaceae. Can J Infect Dis Med Microbiol. 2017;2017:6212910. https://doi.org/10.1155/2017/6212910.
24. So-ngern A, Osaithai N, Meesing A, Chumpangern W. Mortality rate and factors associated with mortality of carbapenem-resistant Enterobacteriaceae infection. Drug Target Insights. 2023;17:120–125. https://doi.org/10.33393/dti.2023.2622.
25. Liu YC, Lu CY, Yen TY, Chang LY, Chen JM, Ping-Ing L. Clinical characteristics and outcomes of carbapenem-resistant Enterobacterales bacteremia in pediatric patients. J Microbiol Immunol Infect. 2023;56(1):84–92.
26. Taha R, Mowallad A, Mufti A, Althaqafi A, Jiman-Fatani AA, El-Hossary D, et al. Prevalence of Carbapenem-Resistant Enterobacteriaceae in Western Saudi Arabia and Increasing Trends in the Antimicrobial Resistance of Enterobacteriaceae. Cureus. 2023;15(2):e35050. https://doi.org/10.7759/cureus.35050.
27. Deng S, Chen J, Zhou P, Hu Q. Mortality-related risk factors of carbapenem-resistant Enterobacteriaceae infection with focus on antimicrobial regimens optimization: a real-world retrospective study in China. BMC Infect Dis. 2025;25:110. https://doi.org/10.1186/s12879-025-10454.