Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page:www.jamdsr.com doi:10.21276/jamdsr Index Copernicus value [ICV] =82.06

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

A Prospective Study on the Incidence and Clinical Outcome of Bloodstream Infections Caused by ESBL-Producing Enterobacteriaceae

Supriya Gambhir

Assistant Professor, Department of Microbiology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India

ABSTRACT:

Background: Bloodstream infections (BSIs) caused by extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* pose significant diagnostic and therapeutic challenges due to high resistance rates and associated morbidity. Identifying their incidence and clinical outcomes is essential to inform treatment and infection control strategies. **Aim:** To determine the incidence, antimicrobial susceptibility patterns, and clinical outcomes of bloodstream infections caused by ESBL-producing *Enterobacteriaceae* in hospitalized patients. **Materials and Methods:** This prospective observational study was conducted in the Department of Microbiology at a tertiary care teaching hospital. A total of 130 patients with blood culture-proven infections caused by *Enterobacteriaceae* were enrolled based on clinical suspicion of BSI. Blood cultures were processed using BacT/ALERT 3D system, and isolates were identified and screened for ESBL production using CLSI-recommended methods. Demographic, clinical, and outcome data were collected and statistically analyzed. **Results:** Among the 130 patients, the majority were aged 19–60 years (47.69%) and male (58.46%). ICU admission was required in 32.31% of cases. *Escherichia coli* (44.62%) and *Klebsiella pneumoniae* (32.31%) were the most common isolates. Overall, 59.23% of isolates were ESBL producers, with the highest prevalence in *K. pneumoniae* (66.67%) and *E. coli* (62.07%). ESBL strains showed 100% sensitivity to meropenem and 96–100% to colistin, while ciprofloxacin and third-generation cephalosporins had <30% sensitivity. Mortality was significantly higher among ESBL-positive patients (37.66%) compared to ESBL-negative cases (13.21%). The mean hospital stay was longer in the ESBL group (11.2 ± 4.1 days vs. 7.3 ± 2.5 days). **Conclusion:** There is a high incidence of ESBL-producing *Enterobacteriaceae* in BSIs, especially *E. coli* and *K. pneumoniae*, which are associated with increased mortality and prolonged hospitalization. Carbapenems remain the most effective agents. Regular ESBL screening and judicious antimicrobial use are critical to improve outcomes and contain resistance.

Keywords: Bloodstream infections, ESBL, *Enterobacteriaceae*, antimicrobial resistance, clinical outcome

Received: 19 February, 2019 Accepted: 24 March, 2019 Published: 10 April, 2019

Corresponding author: Supriya Gambhir, Assistant Professor, Department of Microbiology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India

This article may be cited as: Gambhir S. A Prospective Study on the Incidence and Clinical Outcome of Bloodstream Infections Caused by ESBL-Producing Enterobacteriaceae. J Adv Med Dent Scie Res 2019;7(4):192-198.

INTRODUCTION

Bloodstream infections (BSIs) are a critical cause of morbidity and mortality worldwide, particularly in hospitalized patients and immunocompromised individuals. Among the various causative agents of BSIs, gram-negative bacilli belonging to the family *Enterobacteriaceae* have emerged as significant pathogens due to their increasing resistance to multiple classes of antibiotics. Of particular concern is the rising incidence of extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*, which complicates the management of infections due to their resistance to penicillins, third-generation cephalosporins, and aztreonam, thus limiting effective treatment options[1].

ESBL enzymes, primarily produced by organisms such as *Escherichia coli* and *Klebsiella pneumoniae*, hydrolyze the beta-lactam ring of commonly used antibiotics, rendering them ineffective. These enzymes are encoded by plasmids, which can be easily transferred between bacteria, promoting the rapid dissemination of resistance genes[2]. The clinical implication of this mechanism is profound, as infections caused by ESBL producers are associated with delayed initiation of appropriate therapy, prolonged hospital stay, increased healthcare costs, and higher mortality rates[3].

The global epidemiology of ESBL-producing pathogens has shown a disturbing trend. Over the past two decades, the prevalence of ESBL-producing *Enterobacteriaceae* has increased across both developed and developing nations. Surveillance data indicate that the incidence of ESBL-related BSIs varies geographically but is consistently higher in regions with widespread antibiotic misuse or limited infection control practices[4]. The threat posed by these pathogens is particularly severe in vulnerable populations, including patients with hematological malignancies, solid organ cancers, those undergoing chemotherapy, and critically ill patients admitted to intensive care units[5].

Risk factors for bloodstream infections caused by ESBL-producing organisms have been well documented. Prior hospitalization, exposure to broad-spectrum antibiotics, use of indwelling medical devices, recent surgery, and underlying immunosuppression are recognized predisposing conditions[6]. These risk factors not only increase susceptibility but also influence the clinical outcome and treatment response. Identifying these factors is essential for early diagnosis, appropriate empirical therapy, and implementation of preventive strategies.

Infections with ESBL-producing *Enterobacteriaceae* often present with nonspecific clinical features such as fever, chills, hypotension, and signs of sepsis, which are indistinguishable from infections caused by non-ESBL-producing organisms. Therefore, microbiological confirmation through blood cultures and antimicrobial susceptibility testing remains crucial in guiding appropriate therapy. However, empirical treatment is often initiated before results are available. In regions with a high prevalence of ESBL production, carbapenems are frequently used as first-line agents. Unfortunately, this practice has led to the emergence of carbapenem-resistant strains, creating a vicious cycle of resistance and therapeutic failure[7].

Clinical outcomes in patients with ESBL-BSIs are closely linked to the timing and appropriateness of antimicrobial therapy. Studies have shown that inappropriate empirical treatment is associated with significantly higher mortality rates. In contrast, timely initiation of active therapy, guided by local antibiograms and individual risk assessment, improves prognosis and reduces complications. Moreover, prompt source control—such as the removal of infected devices or drainage of abscesses—is essential for successful treatment[8].

In low-resource settings, the impact of ESBL-producing infections is even more pronounced due to the lack of diagnostic infrastructure, limited access to effective antimicrobials, and inadequate infection prevention measures. These challenges highlight the importance of regional epidemiological studies that provide insights into the local burden of disease, microbial trends, and patient outcomes. Such data are indispensable for formulating evidence-based policies, optimizing antimicrobial stewardship programs, and enhancing infection control practices.Despite the growing literature on ESBL-BSIs, there is a paucity of prospective data focusing on their incidence and clinical outcomes in the Indian subcontinent. Most existing studies are retrospective in nature or lack detailed patient follow-up. Furthermore, variations in study designs, diagnostic criteria, and definitions of clinical endpoints hinder meaningful comparisons. A prospective approach offers the advantage of standardized data collection, real-time assessment of risk factors, and accurate evaluation of outcomes.

MATERIAL AND METHODS

This prospective observational study was conducted in the Department of Microbiology at a tertiary care teaching hospital, following approval from the Institutional Ethics Committee.A total of 130 patients were enrolled in the study. These patients were admitted to various medical wards and intensive care units and were clinically suspected of having bloodstream infections (BSIs) based on symptoms such as fever (>38°C), chills, hypotension, or signs of sepsis. All participants were recruited consecutively based on the inclusion and exclusion criteria outlined below.

Inclusion Criteria

- Patients of all age groups and both sexes.
- Patients presenting with signs and symptoms suggestive of bloodstream infection.
- At least one positive blood culture yielding Enterobacteriaceae.
- Informed written consent obtained from patients or their legal guardians.

Exclusion Criteria

- Patients who had received systemic antibiotics for more than 48 hours before sample collection.
- Patients with polymicrobial infections not involving Enterobacteriaceae.
- Patients with contaminated blood culture specimens (e.g., coagulase-negative Staphylococci without clinical correlation).

Methodology

Two sets of peripheral venous blood samples (8–10 mL for adults and 1–3 mL for pediatric patients) were collected aseptically from each patient prior to the initiation of antibiotic therapy. Blood cultures were processed using the automated BacT/ALERT 3D system (bioMérieux) following standard protocol.Positive cultures were subcultured on blood agar and MacConkey agar. Identification of Enterobacteriaceae isolates was done using conventional biochemical tests and confirmed by automated systems such as VITEK 2 (bioMérieux).All Enterobacteriaceae isolates were initially screened for ESBL production using the ceftazidime (30 µg) and ceftriaxone (30 µg) disk diffusion method as per Clinical and Laboratory Standards Institute (CLSI)

guidelines. Confirmatory testing was done using the combined disk diffusion method with ceftazidime (30 µg) alone and in combination with clavulanic acid (30/10 µg). An increase in zone diameter of ≥5 mm in the presence of clavulanic acid indicated ESBL production.Demographic details, clinical features, underlying comorbidities, prior antibiotic use, ICU admission status, and outcome (recovery or death) were recorded using a pre-structured proforma. Treatment details and duration of hospital stay were also documented.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using SPSS version 21.0 (IBM Corp., Armonk, NY). Descriptive statistics were used for demographic and clinical variables. Categorical variables were compared using the Chi-square test, and continuous variables were analyzed using Student's t-test or Mann–Whitney U test as appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics (Table 1)

Out of the 130 patients with confirmed bloodstream infections (BSIs) due to *Enterobacteriaceae*, the majority belonged to the age group of 19–60 years (47.69%), followed by older adults above 60 years (26.15%), highlighting a higher risk in adults and elderly individuals. Pediatric patients, including infants (<1 year) and children up to 18 years, accounted for a smaller proportion, together forming 26.15% of the study population. Males constituted 58.46% of the participants, reflecting a mild male predominance. In terms of hospital distribution, 67.69% were admitted to general wards, whereas 32.31% required ICU care, indicating that nearly one-third of cases were severe or associated with complications. Regarding clinical features, fever was present in nearly all patients (93.85%), while chills and rigors were seen in 77.69%, both being classical signs of systemic infection. Hypotension, a marker of sepsis severity, was observed in 29.23%, particularly among ICU patients.

Microbiological Distribution of Isolates (Table 2)

Among the 130 blood culture-positive isolates, *Escherichia coli* was the most frequently identified organism, accounting for 44.62% of cases. This was followed by *Klebsiella pneumoniae* (32.31%), which, along with *E. coli*, constituted the majority of Enterobacteriaceae isolates. Other significant organisms included *Enterobacter cloacae* (9.23%), *Citrobacter freundii* (6.92%), *Proteus mirabilis* (4.62%), and *Serratia marcescens* (2.31%). The predominance of *E. coli* and *K. pneumoniae* aligns with their known pathogenic potential and their ability to acquire multidrug resistance, including extended-spectrum beta-lactamase (ESBL) production.

ESBL Production Among Enterobacteriaceae (Table 3)

Out of the 130 isolates, 77 (59.23%) were ESBL producers, reflecting a high prevalence of resistant strains. *K. pneumoniae* showed the highest ESBL positivity at 66.67%, followed closely by *E. coli* at 62.07%, highlighting their significant role in multidrug-resistant BSIs. *Enterobacter cloacae* and *Citrobacter freundii* also showed moderate rates of ESBL production at 50% and 44.44%, respectively. Less commonly isolated species like *Proteus mirabilis* and *Serratia marcescens* had lower ESBL rates (33.33% each), though their clinical implications remain serious due to intrinsic resistance traits. These findings underscore the growing threat of ESBL-producing pathogens in bloodstream infections, necessitating prompt identification and appropriate antimicrobial therapy.

Antibiotic Susceptibility Patterns (Table 4)

Antibiotic susceptibility testing revealed 100% sensitivity to meropenem across all six ESBL-producing species, reinforcing its status as the most reliable treatment option. Colistin also demonstrated excellent activity, with 96–100% sensitivity, although its use is typically reserved for critically ill patients due to toxicity. Among aminoglycosides, amikacin showed high sensitivity rates ranging from 85% to 100% across organisms, making it a potent option in combination therapies. Gentamicin was moderately effective, especially against *E. coli* (66.67%) and *K. pneumoniae* (64.29%).

In contrast, fluoroquinolone resistance was alarmingly high, with ciprofloxacin sensitivity falling below 30% for *E. coli* and *K. pneumoniae*, and complete resistance noted in *Serratia marcescens*. Third-generation cephalosporins (cefotaxime and ceftazidime) showed 0% sensitivity across all ESBL-producing isolates, as expected due to their inactivation by ESBL enzymes. Piperacillin-tazobactam maintained good efficacy, with sensitivity ranging from 75% to 100%, though it is still inferior to carbapenems. Nitrofurantoin demonstrated high activity against *E. coli* (83.33%) and *C. freundii* (75%), but limited efficacy against *Proteus mirabilis*. Trimethoprim-sulfamethoxazole showed poor efficacy overall, with less than 40% sensitivity in *E. coli* and 50% in minor isolates. These results emphasize the need for tailored antibiotic policies and routine susceptibility testing to prevent treatment failure.

Clinical Outcome Based on ESBL Status (Table 5)

Clinical outcomes were significantly influenced by the ESBL status of the infecting organism. Among the 77 patients with ESBL-positive infections, 29 (37.66%) died, compared to only 7 (13.21%) deaths in the ESBL-negative group, indicating a markedly

higher mortality associated with resistant strains. Recovery was more common in the ESBL-negative group (86.79%) than in the ESBL-positive group (62.34%). Furthermore, ICU admissions were disproportionately higher in ESBL-positive patients (46.75%) than ESBL-negative ones (11.32%), reflecting greater disease severity. The average hospital stay for ESBL-positive patients was 11.2 ± 4.1 days, significantly longer than the 7.3 ± 2.5 days observed in ESBL-negative cases, contributing to increased healthcare costs and resource utilization. These findings clearly demonstrate that ESBL-producing pathogens not only complicate clinical management but also result in worse prognoses and prolonged hospitalization.

Table 1: Demographic and Clinical Characteristics of Patients with Bloodstream Infections (n = 130)

Parameter	Number of Patients (n)	Percentage (%)
Age Group (years)		
<1 year	10	7.69
1–18 years	24	18.46
19–60 years	62	47.69
>60 years	34	26.15
Gender		
Male	76	58.46
Female	54	41.54
Hospital Setting		
ICU	42	32.31
Ward	88	67.69
Clinical Features		
Fever	122	93.85
Hypotension	38	29.23
Chills and rigors	101	77.69

Table 2: Distribution of Enterobacteriaceae Isolates Identified from Blood Cultures (n = 130)

Organism Isolated	Number of Isolates (n)	Percentage (%)
Escherichia coli	58	44.62
Klebsiella pneumoniae	42	32.31
Enterobacter cloacae	12	9.23
Citrobacter freundii	9	6.92
Proteus mirabilis	6	4.62
Serratia marcescens	3	2.31

Table 3: ESBL Production Among Isolated Enterobacteriaceae (n = 130)

Organism	Total Isolates	ESBL Positive (n)	ESBL Positive (%)
E. coli	58	36	62.07
K. pneumoniae	42	28	66.67
Enterobacter cloacae	12	6	50.00
Citrobacter freundii	9	4	44.44
Proteus mirabilis	6	2	33.33
Serratia marcescens	3	1	33.33
Total	130	**77**	**59.23**

Table 4: Antibiotic Sensitivity and Resistance Profile of ESBL-Producing Enterobacteriaceae

Antibiotic	*E. coli* (n=36)	*K. pneumoniae* (n=28)	*E. cloacae* (n=6)	*C. freundii* (n=4)	*P. mirabilis* (n=2)	*S. marcescens* (n=1)
	S / R (n, %)	S / R (n, %)	S / R (n, %)	S / R (n, %)	S / R (n, %)	S / R (n, %)
Amikacin	32 / 4 (88.89% / 11.11%)	24 / 4 (85.71% / 14.29%)	6 / 0 (100.00% / 0.00%)	4 / 0 (100.00% / 0.00%)	2 / 0 (100.00% / 0.00%)	1 / 0 (100.00% / 0.00%)
Gentamicin	24 / 12 (66.67% / 33.33%)	18 / 10 (64.29% / 35.71%)	5 / 1 (83.33% / 16.67%)	3 / 1 (75.00% / 25.00%)	1 / 1 (50.00% / 50.00%)	1 / 0 (100.00% / 0.00%)
Ciprofloxacin	10 / 26	8 / 20 (28.57% /	3 / 3	1 / 3	1 / 1	0 / 1 (0.00% /

	(27.78% / 72.22%)	71.43%)	(50.00% / 50.00%)	(25.00% / 75.00%)	(50.00% / 50.00%)	100.00%)
Cefotaxime	0 / 36 (0.00% / 100.00%)	0 / 28 (0.00% / 100.00%)	0 / 6 (0.00% / 100.00%)	0 / 4 (0.00% / 100.00%)	0 / 2 (0.00% / 100.00%)	0 / 1 (0.00% / 100.00%)
Ceftazidime	0 / 36 (0.00% / 100.00%)	0 / 28 (0.00% / 100.00%)	0 / 6 (0.00% / 100.00%)	0 / 4 (0.00% / 100.00%)	0 / 2 (0.00% / 100.00%)	0 / 1 (0.00% / 100.00%)
Piperacillin-Tazobactam	28 / 8 (77.78% / 22.22%)	22 / 6 (78.57% / 21.43%)	5 / 1 (83.33% / 16.67%)	3 / 1 (75.00% / 25.00%)	2 / 0 (100.00% / 0.00%)	1 / 0 (100.00% / 0.00%)
Meropenem	36 / 0 (100.00% / 0.00%)	28 / 0 (100.00% / 0.00%)	6 / 0 (100.00% / 0.00%)	4 / 0 (100.00% / 0.00%)	2 / 0 (100.00% / 0.00%)	1 / 0 (100.00% / 0.00%)
Colistin	35 / 1 (97.22% / 2.78%)	27 / 1 (96.43% / 3.57%)	6 / 0 (100.00% / 0.00%)	4 / 0 (100.00% / 0.00%)	2 / 0 (100.00% / 0.00%)	1 / 0 (100.00% / 0.00%)
Nitrofurantoin	30 / 6 (83.33% / 16.67%)	20 / 8 (71.43% / 28.57%)	—	3 / 1 (75.00% / 25.00%)	1 / 1 (50.00% / 50.00%)	—
Trimethoprim-SMX	14 / 22 (38.89% / 61.11%)	—	—	2 / 2 (50.00% / 50.00%)	1 / 1 (50.00% / 50.00%)	—

Table 5: Association of ESBL Status with Clinical Outcomes (n = 130)

Outcome	ESBL Positive (n = 77)	ESBL Negative (n = 53)	Total (%)
Recovered	48	46	94 (72.31%)
Death	29	7	36 (27.69%)
ICU Admission	36	6	42 (32.31%)
Mean Hospital Stay	11.2 ± 4.1 days	7.3 ± 2.5 days	—

DISCUSSION

In the present study, the majority of bloodstream infection (BSI) cases were observed in the adult population aged 19–60 years (47.69%), with additional substantial representation from elderly individuals above 60 years (26.15%). This age-related distribution aligns with the findings of Sahu et al (2015), who also reported a higher prevalence of BSIs in adults, particularly those with comorbidities and hospital exposure. The male predominance (58.46%) in our study is comparable to previous reports, suggesting gender-based immune and exposure differences in hospital-acquired infections. Fever (93.85%) and chills (77.69%) were the most common clinical features, similar to the classical septic presentations noted in prior studies. Hypotension was present in nearly one-third of cases (29.23%), particularly in ICU patients, consistent with the patterns described in systemic infections by Sahu et al (2015)[9].

The microbiological profile revealed *E. coli* (44.62%) and *K. pneumoniae* (32.31%) as the predominant organisms, reflecting their strong association with nosocomial and community-acquired BSIs. These results are in close agreement with the study by Ranjan et al (2010), who found *E. coli* and *Klebsiella spp.* to be the most frequently isolated Gram-negative organisms in bloodstream infections across tertiary hospitals in India. Lesser proportions of *Enterobacter cloacae* (9.23%), *C. freundii* (6.92%), *P. mirabilis* (4.62%), and *S. marcescens* (2.31%) indicate the growing role of non-fermenters and opportunistic pathogens in hospitalized patients[10].

A significant finding in our study was the high overall prevalence of ESBL-producing isolates (59.23%). Among them, *K. pneumoniae* (66.67%) and *E. coli* (62.07%) were the leading contributors. These rates are notably higher than those reported by Rodrigues et al (2004), who observed ESBL production in 40% of *K. pneumoniae* and 32% of *E. coli* isolates in a Mumbai hospital setting. This increase over time may be attributed to widespread and often unregulated use of broad-spectrum antibiotics, particularly third-generation cephalosporins. Moderate ESBL rates in *Enterobacter cloacae* (50%) and *C. freundii* (44.44%) were consistent with their intrinsic resistance potential. Though lower in *P. mirabilis* and *S. marcescens* (33.33% each), their clinical importance remains high due to the limited treatment options available once ESBL production is confirmed, reinforcing concerns raised by Rodrigues et al (2004)[11].

Our antibiotic susceptibility results showed 100% sensitivity to meropenem across all ESBL producers, reaffirming its efficacy as a first-line therapy in severe infections. Colistin also demonstrated excellent activity (96–100%), though its nephrotoxicity restricts use. High sensitivity to amikacin (85–100%) across

all species is encouraging, while gentamicin showed moderate sensitivity (50–83%). These findings mirror the study by Mathai et al (2008), which reported similar susceptibility patterns in Indian ICUs, with meropenem and amikacin being the most reliable agents. Alarmingly, ciprofloxacin showed resistance exceeding 70% in *E. coli* and *K. pneumoniae*, and complete resistance in *S. marcescens*, comparable to fluoroquinolone failure rates reported by Mathai et al (2008). Resistance to third-generation cephalosporins was universal (0% sensitivity), as expected in ESBL producers. Piperacillin-tazobactam maintained moderate efficacy (75–83%), suggesting its possible role in mild to moderate infections where carbapenem-sparing strategies are appropriate[12].

The clinical outcome data highlighted that ESBL-positive infections were associated with worse prognosis. Mortality among ESBL-positive cases was significantly higher (37.66%) than in ESBL-negative patients (13.21%), echoing findings by Babini et al (2000), who reported elevated mortality rates in patients with ESBL-producing Gram-negative bacteremia due to delays in initiating effective therapy. Our study also demonstrated longer hospital stays in ESBL-positive patients (11.2 ± 4.1 days vs. 7.3 ± 2.5 days), consistent with increased healthcare burdens described in earlier reports. ICU admission rates were also higher in the ESBL-positive group (46.75%), reflecting disease severity and therapeutic complexity. The difference in recovery outcomes (62.34% vs. 86.79%) further underscores the negative clinical impact of ESBL pathogens, validating the prognostic concerns raised by Babini et al (2000)[13].

The overall burden of resistance and unfavorable outcomes in our cohort stresses the urgent need for strengthened antimicrobial stewardship. Similar concerns were raised in the study by Tankhiwale et al (2004), who emphasized the role of local antibiogram surveillance and infection control policies to curb the spread of resistant organisms in Indian hospitals. Our findings support this recommendation, particularly as the high prevalence of ESBLs continues to challenge empirical treatment protocols. A tailored approach involving early identification, prompt susceptibility testing, and rational antimicrobial use is critical to improving patient outcomes, reducing mortality, and minimizing hospital stays, especially in resource-limited settings[14].

Finally, the evolving trends in ESBL epidemiology and antimicrobial resistance among Enterobacteriaceae, as demonstrated in our study, are in agreement with the observations by Pitout et al (2005), who documented the global dissemination of ESBL-producing *E. coli* and *K. pneumoniae* as a serious public health threat. The comparison underscores the universal challenge posed by multidrug-resistant Enterobacteriaceae, reinforcing the necessity for global and local responses to monitor, prevent, and manage their spread[15].

CONCLUSION

This prospective study highlights a high prevalence (59.23%) of ESBL-producing *Enterobacteriaceae* in bloodstream infections, with *E. coli* and *K. pneumoniae* being the predominant pathogens. ESBL-positive cases were associated with significantly higher mortality, prolonged hospital stays, and increased ICU admissions. While carbapenems and colistin remained highly effective, alarming resistance to third-generation cephalosporins and fluoroquinolones was observed. These findings underscore the urgent need for routine ESBL detection, rational antibiotic use, and robust infection control practices.

REFERENCES

1. Paterson DL, Bonomo RA. Extended-spectrum beta-lactamases: a clinical update. Clin Microbiol Rev. 2005;18(4):657–86.
2. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.
3. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603–5.
4. Biehl LM, Schmidt-Hieber M, Liss B, Cornely OA, Vehreschild MJ. Colonization and infection with extended spectrum beta-lactamase producing Enterobacteriaceae in high-risk patients—review of the literature from a clinical perspective. Crit Rev Microbiol. 2016;42(1):1–16.
5. Gudiol C, Aguado JM, Carratala J. Bloodstream infections in patients with solid tumors. Virulence. 2016;7(3):298–308.
6. Ndir A, Diop A, Ka R, Faye PM, Dia-Badiane NM, Ndoye B, et al. Infections caused by extended-spectrum beta-lactamases producing Enterobacteriaceae: clinical and economic impact in patients hospitalized in 2 teaching hospitals in Dakar. Senegal. Antimicrob Resist Infect Control. 2016;5:13.
7. Alevizakos M, Karanika S, Detsis M, Mylonakis E. Colonisation with extended-spectrum beta-lactamase-producing Enterobacteriaceae and risk for infection among patients with solid or haematological malignancy: a systematic review and meta-analysis. Int J Antimicrob Agents. 2016;48(6):647–54.
8. Alevizakos M, Gaitanidis A, Andreatos N, Arunachalam K, Flokas ME, Mylonakis E. Bloodstream infections due to extended-spectrum beta-lactamase-producing Enterobacteriaceae among patients with malignancy: a systematic review and meta-analysis. Int J Antimicrob Agents. 2017;50(5):657–63.
9. Sahu MC, Padhy RN. Prevalence of bloodstream infection in pediatric patients and the antibiotic susceptibility pattern of the pathogens. Asian Pac J Trop Dis. 2015;5(6):497–504.
10. Ranjan KP, Ranjan N, Bansal SK, Arora DR. Prevalence of bloodstream infections and antibiotic resistance pattern in a tertiary care hospital. J Acad Med Sci. 2010;1(2):52–5.

11. Rodrigues C, Joshi P, Jani SH, Alphonse M, Radhakrishnan R, Mehta A. Detection of beta-lactamases in nosocomial gram-negative clinical isolates. Indian J Med Microbiol. 2004;22(4):247–50.
12. Mathai AS, Oberoi A, Cottom R. Antimicrobial resistance surveillance in ICU settings in India. Indian J Med Res. 2008;128(5):588–92.
13. Babini GS, Livermore DM. Antimicrobial resistance amongst Klebsiella spp. collected from intensive care units in Southern and Western Europe in 1997–1998. J AntimicrobChemother. 2000;45(2):183–9.
14. Tankhiwale SS, Jalgaonkar SV, Ahamad S, Hassani U. Evaluation of extended-spectrum beta-lactamase in urinary isolates. Indian J Med Res. 2004;120(6):553–6.
15. Pitout JD, Laupland KB. Extended-spectrum beta-lactamase-producing Enterobacteriaceae: An emerging public-health concern. Lancet Infect Dis. 2008;8(3):159–66.