Mortality and its predictors among hospitalized patients with infections due to extended spectrum beta-lactamase (ESBL) Enterobacteriaceae in Malaysia: a retrospective observational study

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Mortality and its predictors among hospitalized patients with infections due to extended spectrum beta-lactamase (ESBL) *Enterobacteriaceae* in Malaysia: a retrospective observational study

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Abstract

Background: Extended spectrum beta-lactamase (ESBL) pathogens are associated with morbidity and mortality. There is a paucity of data describing the treatments and outcomes of ESBL infections in Malaysia. This study evaluated the treatments, mortality and associated factors among patients hospitalized with infections due to ESBL positive *enterobacteriaceae*. This is a retrospective study conducted in a tertiary hospital from January 2018 to June 2020. Hospitalized patients with ESBL-positive *enterobacteriaceae* infections were included. A clinical pharmacist collected data by reviewing the patients' electronic medical records. The data were analysed using both descriptive and inferential analyses.

Results: This analysis included 110 patients with a mean age of 62.1 ± 14.4 years. *Klebsiella pneumoniae* (53.6%) and *Escherichia coli* (40.9%) were the most prevalent pathogens among the 110 infections. Bacteremia (42.7%) was the most frequent diagnosis. The isolates were resistant to majority of penicillins and cephalosporins. However, over a third (39.3%) were susceptible to piperacillin–tazobactam, while carbapenem susceptibility was extremely high (≥ 99%). The most frequently used empiric and definitive antibiotics was piperacillin–tazobactam and meropenem, respectively. Less than a third (28.2%) of patients received active empiric antibiotics, and the mean duration before active antibiotics was 3.9 ± 2.7. Overall, hospital mortality rate was 13.6%, and mortality was significantly associated with ICU admission (AOR 8.75; 95% CI 1.05–72.75; $P = 0.045$) and diabetes mellitus (AOR 9.85; 95% CI 1.04–93.09; $P = 0.046$).

Conclusions: Carbapenems are the major antibiotics used to treat ESBL-positive *enterobacteriaceae* infections. Hospital mortality rate is relatively high and is significantly associated with in patients admitted to ICU and those with diabetes mellitus. Antibiotic stewardship interventions are necessary to promote early administration of active antibiotics and to reduce overuse of carbapenem antibiotics.

Keywords: ESBL, *Enterobacteriaceae*, Mortality, Predictors, Treatment, Malaysia, Intensive care unit

Background

Gram negative pathogens that produce extended spectrum beta-lactamases (ESBLs) have emerged as a global public health problem. The organisms cause a variety of

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infections, including those acquired in the community, hospitals, and healthcare settings [1]. Infections caused by these organisms include pneumonia, bloodstream infection, urinary tract infection, peritonitis, biliary tract infection, central nervous system infection, skin and soft tissue infections, bone and joint infections [2]. Infections caused by ESBL producing pathogens are associated with higher mortality than corresponding infections due to non-ESBL pathogens [3]. The mortality rate for ESBL infections ranges between 3.7 and 22.1% [2, 4, 5] which may be explained by a delay in initiating active antibiotic therapy [1, 3]. Due to their higher susceptibility profile compared to other classes of antibiotics such as beta-lactam and beta-lactamase inhibitor combinations, cephalosporins, and fluoroquinolones, carbapenems are considered the drug of choice for both empiric and definitive therapy of infections caused by ESBL pathogens [1, 6]. The increased use of carbapenems, on the other hand, has resulted in the emergence and spread of carbapenem-resistant microorganisms [7].

Enterobacteriaceae is a family of Gram negative bacteria that includes Citrobacter, Klebsiella, Escherichia, and Proteus species. These organism cause a range of community and hospital-acquired infections. In Malaysia, approximately one-third of *Escherichia coli* and *Klebsiella pneumoniae* and two-third of *Acinetobacter baumanii* are resistant to third generation cephalosporin, respectively [8]. The National Antimicrobial Guideline recommends using carbapenems for empiric treatment of infections caused by ESBL producing gram-negative bacteria [9]. According to available data, the mortality rate associated with infection caused by an ESBL pathogen is quite high, ranging between 3.7 and 22.1% [2, 4, 5]. In addition, the mortality rate is higher in patients with severe infections, severe sepsis or shock, advanced age, hospital-acquired infections, and rapidly fatal underlying disease; in patients with *K. pneumoniae* infection; in patients who received inappropriate empirical therapy; and those admitted to the intensive care unit [2, 10–13]. There is a paucity of data in Malaysia on the rate and risk factors associated with mortality in patients infected with ESBL pathogens. Identification of risk factors for mortality is critical for designing effective interventions aimed at improving treatment outcomes and reducing antibiotic overuse and resistance. This study aims to determine the microbiological characteristics, treatment outcomes, and risk factors for mortality in patients with *enterobacteriaceae* infection caused by ESBL*s*.

Method

Study design and study setting

This is a retrospective observational cohort study involving patients who had ESBL positive *enterobacteriaceae* infections at a tertiary hospital located on the Eastern Coast of Malaysia. The hospital provides a range of services including medicine, surgery, orthopaedic, critical care, nursing, pharmacy, microbiological and laboratory services.

Study population

The study population includes all adults with ESBL positive *enterobacteriaceae* infections hospitalized at the hospital from January 2018 to June 2020. All infections including central nervous, respiratory tract, urinary tract, gastrointestinal tract, intra-abdominal and bloodstream infections, as well as both community and hospital-acquired infections were included. Those with mono- and polymicrobial infections were included. Those colonized (culture positive but without signs and symptoms of infection) with ESBL positive *enterobacteriaceae* and those with an infection without hospitalization were excluded.

Data collection

All adult patients hospitalized with an infection due to ESBL positive *enterobacteriaceae* infections from 01st January 2018 to 30th June 2020 in the selected hospital who fulfil the inclusion criteria were included in the study. A list of patients with infections due to ESBL positive *enterobacteriaceae* with their hospital numbers was obtained by the investigators from the medical microbiology unit of the hospital. The electronic medical records of the identified patients was reviewed by a clinical pharmacist, who has expertise in infectious diseases and antimicrobial stewardship, for data collection. The electronic medical record was accessed and reviewed after approval from the hospital management. Data was collected retrospectively through the review of patient's medical records and medication chart. The following information was collected: demographic information such as age, gender, race, ward location, date of admission and discharge; and clinical information such as (i) information related to diagnosis and type of infection (community- and hospital-acquired) [14], presentation with sepsis or shock [15], immune status (severe- versus non-severe immunosuppression), comorbidity, recent surgery (any surgical procedure within 3 months before diagnosis) and recent hospitalization (hospitalization within 3 months before diagnosis), (ii) information related to clinical monitoring: laboratory results, vital signs such as highest daily temperature, highest heart rate, highest respiratory rate and lowest daily blood pressure, and (iii) information regarding empiric and definitive antibiotics used for treatment. Other data collected include microbiological information such as date culture was taken, pathogen isolated and complete antibiotic susceptibility of the isolates, date of

subsequent culture(s), organism(s) and resistance profile. In-hospital mortality among the patients was also documented.

Definition of terms and outcomes

Community-acquired infections refer to any infection that starts outside hospital setting or manifests within 48 h after admission into the hospital [16]. Hospital-acquired infection is defined as an infection in which the signs and symptoms begin 48 h or more after hospital admission or infection present at the time of admission or manifests within 48 h after re-admission in patients who were recently discharged from the hospital [16]. Empirical therapy is defined as an antimicrobial therapy initiated before identification of the causative pathogen while definitive therapy is the treatment given after the isolate is known. Severe immunosuppression is defined as any of the following: neutropenia, (< 500/mL), leukaemia, lymphoma, HIV infection with < 200 CD4/mL, solid organ or hematopoietic stem cell transplantation, cytotoxic chemotherapy, steroids (> 15 mg of prednisone daily for > 2 weeks) [3]. Antimicrobial susceptibility was performed by automated system (Vitek 2) and interpreted using Clinical and Laboratory Standards Institute (CLSI) recommendations.

Data analysis

The data would be analysed using Statistical Package for the Social Sciences (SPSS) version 22. The data would be de-identified before analysis. Categorical data would be reported as frequency with percentage while continuous data would be presented as mean (with standard deviation) or median. Bivariate and multivariate regression analyses would be used to determine the risk factors associated with mortality. Only variables that demonstrated statistical significance ($P < 0.05$) in the bivariate analysis would be included in the multivariate model. P value less than 0.05 would be considered as statistical significance.

Results

Demographic and clinical characteristics of the patients

A total of 110 patients were included in this analysis with a mean age of 62.1 ± 14.4 years. There were more males (58.2%) and Malays (86.4%) included in the analysis. About 22% had intensive care unit admission while 48.5% had sepsis/septic shock. Bacteremia (42.7%) and urinary tract infection (34.5%) were the most common infections. Most of the infections (54.5%) were community-acquired infections. Table 1 summarises the characteristics of the patients included in the study.

Table 1 Demographic and clinical characteristics of the patients

Variable	Frequency	Percentage
Mean age (SD) in years	62.1 ± 14.4	
Gender		
Male	64	58.2
Female	46	41.8
Race		
Malay	95	86.4
Chinese	4	3.6
Indian	8	7.3
Others	3	2.7
Intensive care unit admission	24	21.8
Recent surgery	56	50.9
Recent hospitalization	66	60.0
Immunocompromise	22	20.0
Presence of comorbidities	97	88.2
Type of comorbidity		
Hypertension	61	55.5
Diabetes	53	48.2
Chronic kidney disease	34	30.9
Malignancy	21	19.1
Dyslipidemia	17	15.5
Stroke	15	13.6
Ischemic heart disease	12	10.9
Benign prostate hyperplasia	11	10.0
Sepsis/septic shock	53	48.2
Diagnosis		
Bacteremia	47	42.7
Urinary tract infections	38	34.5
Surgical site infections	12	10.9
Pneumonia	7	6.4
Skin and soft tissue infections	5	4.5
Intra-abdominal infections	1	0.9
Type of infection		
Hospital-acquired	50	45.5
Community-acquired	60	54.5

SD, standard deviation

Patients' laboratory data on the first day of infection

Of the 110 patients, 37.3%, 68.2%, and 17.3% had fever, elevated total white blood cell count, and thrombocytopenia, respectively. About 50% had elevated serum creatinine and urea levels while 51.8% had hypoalbuminemia. Tachycardia and anemia was observed in 47.3% and 74.5% of the infections, respectively. Table 2

Table 2 Patients' laboratory data on the first day of infection

Variable	Frequency	Percentage (%)
Fever	41	37.3
Leucocytosis	75	68.2
Intubation	25	22.7
Hemodynamic support	6	5.5
Tachycardia	52	47.3
High serum creatinine	56	50.9
High serum urea	57	51.8
Anaemia	82	74.5
Thrombocytopenia	19	17.3
Hypoalbuminemia	57	51.8
Hyperbilirubinemia	17	15.5
Transaminitis	32	29.1

describes the laboratory parameters and the mortality rates among the patients.

Microbiology of extended spectrum beta-lactamase producing enterobacteriaceae

Of the 110 infections, *K. pneumonia* (53.6%) and *E. coli* (40.9%) were the most common pathogens. Other organisms include *Proteus mirabilis* and *Citrobacter* spp. About 18% of the infections were polymicrobial infections. Overall, there was high resistant rate to penicillins such as ampicillin and amoxicillin, and cephalosporins among the isolates. However, more than one-third (39.3%) were susceptible to piperacillin–tazobactam. Susceptibility to carbapenems including meropenem and imipenem was very high (≥ 99%). Table 3 shows the antibiotics susceptibilities of the ESBL *enterobacteriaceae* isolates.

Empiric and definitive antibiotic therapy for ESBL positive *enterobacteriaceae* infections

Several antibiotics were used for empiric antibiotics therapy among the patients including piperacillin–tazobactam (23.6%), ceftriaxone (12.2%), cefuroxime (10.6%) and meropenem (9.8%). Combination empiric antibiotics was administered in 13.6% of the infections. Less than one-third of the patients (28.2%) received an effective empiric antibiotics. Carbapenems including meropenem (80.4%) and imipenem (9.8%) were the most commonly used definitive antibiotics, followed by ciprofloxacin (4.3). The use of combination definitive antibiotics was lower (5.5%) compared to the empiric therapy. The mean duration before active antibiotic therapy was 3.9 days. Table 4 summarises the antibiotics used for empirical and definitive therapy among patients with carbapenem-resistant infections.

Table 3 Antibiotics susceptibilities of ESBL positive *enterobacteriaceae* isolates

Antibiotics	Frequency (%)		
	Sensitive	Intermediate	Resistant
Ampicillin ($n=108$)	0 (0.0)	0 (0.0)	108 (100.0)
Amoxicillin ($n=100$)	0 (0.0)	0 (0.0)	14 (100.0)
Piperacillin–tazobactam ($n=61$)	24 (39.3)	19 (31.1)	18 (29.5)
Amoxicillin-clavulanate ($n=79$)	1 (1.3)	19 (24.1)	59 (74.7)
Ampicillin-sulbactam ($n=21$)	0 (0.0)	2 (9.5)	19 (90.5)
Cefuroxime ($n=109$)	0 (0.0)	0 (0.0)	109 (100.0)
Ceftazidime ($n=89$)	0 (0.0)	3 (3.4)	86 (96.6)
Ceftriaxone ($n=56$)	0 (0.0)	0 (0.0)	56 (100.0)
Cefotaxime ($n=106$)	0 (0.0)	0 (0.0)	106 (100.0)
Cefepime ($n=90$)	0 (0.0)	4 (4.4)	86 (95.6)
Gentamicin ($n=69$)	18 (26.1)	2 (2.9)	49 (71.0)
Imipenem ($n=107$)	106 (99.1)	0 (0.0)	1 (0.9)
Meropenem ($n=107$)	106 (99.1)	1 (0.9)	0 (0.0)
Ertapenem ($n=104$)	103 (99.0)	0 (0.0)	1 (1.0)
Ciprofloxacin ($n=79$)	7 (8.9)	19 (24.1)	53 (67.1)
Cotrimoxazole ($n=90$)	14 (15.6)	0 (0.0)	76 (84.4)
Nitrofurantoin ($n=9$)	0 (0.0)	1 (11.1)	8 (88.9)

Treatment outcomes and univariate regression analysis for factors associated with in-hospital mortality

Overall, in-hospital rate among the patients was 13.6%. Secondary infections were reported in 12 (10.9%) patients including *candida* infection ($n=7$), *trichosporon asahii* ($n=2$) and carbapenem-resistant gram negative bacilli infection ($n=4$). Univariate logistic regression analysis showed that ICU admission (odds ratio [OR] 11.57; 95% confidence interval [CI] 3.43–38.96; $P<0.001$), sepsis/septic shock (OR 17.87; 95% CI 2.24–142.27; $P=0.006$), diabetes mellitus (OR 3.40; 95% CI 1.01–11.46; $P=0.048$), empiric piperacillin–tazobactam (OR 5.62; 95% CI 1.79–17.67; $P=0.003$) and elevated serum creatinine (OR 7.86; 95% CI 1.68–36.75; $P=0.009$). Other variables associated with mortality were thrombocytopenia (OR 4.20; 95% CI 1.28–13.78; $P=0.018$) and transaminitis (OR 4.69; 95% CI 1.51–14.60; $P=0.008$). Table 5 describes the univariate logistic regression analysis for factors associated with mortality.

Multivariate regression analysis for the predictors of mortality

Multivariate logistic regression analysis revealed ICU admission (AOR 8.75; 95% CI 1.05–72.75; $P=0.045$) and diabetes mellitus (AOR 9.85; 95% CI 1.04–93.09; $P=0.046$) were independently associated with in-hospital mortality among the patients. Table 6 summarises the

Table 4 Antibiotics used for empiric and definitive therapy among the patients

Variable	Frequency	Percentage (%)
Active empiric therapy	31	28.2
Empiric antibiotics used (n = 129)		
Piperacillin–tazobactam	29	23.6
Ceftriaxone	15	12.2
Cefuroxime	13	10.6
Meropenem	12	9.8
Ampicillin-sulbactam	12	9.8
Ciprofloxacin	8	6.5
Amoxicillin-clavulanate	6	4.9
Metronidazole	6	4.9
Ceftazidime	4	3.3
Vancomycin	4	3.3
Cefoperazone	4	3.3
Azithromycin	4	3.3
Imipenem	2	1.6
Trimethoprim/sulfamethoxazole	2	1.6
Clindamycin	1	0.8
Cefepime	1	0.8
Combination empiric therapy	15	13.6
Definitive antibiotics (n = 92)		
Meropenem	74	80.4
Imipenem	9	9.8
Ciproflocaxin	4	4.3
Piperacillin–tazobactam	3	3.3
Trimethoprim/sulfamethoxazole	1	1.1
Ertapenem	1	1.1
Combination definitive therapy	6	5.5
Mean duration before active antibiotics	3.9 ± 2.7	

multivariate logistic regression analysis for factors associated with in-hospital mortality.

Discussion

The current study investigated the treatment of ESBL-positive *enterobacteriaceae* infections, as well as the factors associated with mortality, in hospitalised patients in a tertiary hospital in Malaysia. The most frequently used empiric antibiotics were piperacillin–tazobactam, third, and second generation cephalosporins. However, resistance to these antibiotics was greater than 95% among ESBL positive *enterobacteriaceae* isolates, with the exception of piperacillin–tazobactam. The current study found that less than a third of patients received active empiric antibiotics, implying a high rate of inactive empiric antibiotic use in *enterobacteriaceae* infections caused by ESBLs. It has been demonstrated that inactive empiric antibiotic therapy increases the risk of 30-day mortality in patients diagnosed with ESBL *enterobacteriaceae* bacteremia [2]. In addition, the duration before active antibiotic therapy was approximately 4 days, highlighting the length of time patients used inactive antibiotics. As a result, antimicrobial stewardship strategies that promote early and appropriate antibiotic administration to patients are recommended. Hospital pharmacists have an important role in promoting early and appropriate use of antibiotics for ESBL-positive *enterobacteriaceae* infections. Previous studies have demonstrated that hospital pharmacists contribute in promoting effective use of antibiotics and improving clinical outcomes [17, 18]. However, lack of training and support limit hospital pharmacists' participation in antimicrobial stewardship services [19]. Therefore, training of hospital pharmacists and their involvement in antimicrobial stewardship programme is recommended [20, 21].

Although, more than a third of the isolates had in-vitro susceptibility to piperacillin–tazobactam, carbapenems accounted for more than 90% of the definitive antibiotics used in patients. Evidence from observational studies and meta-analysis have demonstrated that combination of beta-lactam beta-lactamase inhibitor are not inferior to carbapenems for the treatment of ESBL positive infections [1, 2, 22]. The widespread use of carbapenem for definitive therapy in patients with urinary tract infection and community-acquired infections poses a threat to the emergence and spread of carbapenem resistant infections. Beta-lactam beta-lactamase inhibitor combinations have been shown to be effective as carbapenem alternatives, particularly in patients with community-acquired infections [1] or urinary tract infections [23]. This finding highlights the importance of antimicrobial stewardship interventions aimed at reducing patients' excessive carbapenem and preventing the emergence of carbapenem-resistant gram negative bacilli.

The study found a 13.6% in-hospital rate among patients hospitalised with infections caused by ESBL positive *enterobacteriaceae*. The mortality rate in this study is higher than that in a previous study conducted in the United States (US) [10], but lower than that in Singapore [22]. Admission to an intensive care unit was found to be significantly associated with an increased risk of mortality in patients, which was consistent with the findings of a previous study [10]. This is because patients admitted to the ICU typically have severe underlying infections often with septic shock and may be exposed to additional invasive procedures and devices. Previous research has established that advanced age, infections caused by *K. pneumoniae*, sepsis or septic shock, hospital-acquired infections, treatment with piperacillin–tazobactam and inactive empiric antibiotic therapy are all associated with increased mortality in patients diagnosed with ESBL producing *enterobacteriaceae* infections [2,

Table 5 Univariate logistic regression analysis for factors associated with in-hospital mortality

Variable	Odds ratio	95% Confidence Interval	*P* value
Age	1.02	0.97–1.06	0.382
Female gender	0.58	0.19–1.74	0.334
Race			
Malay	Reference	–	
Chinese	1.92	0.00–	0.581
Indian	1.82	0.00–	0.999
Others	1.46	0.00–	0.999
Intensive care unit admission	**11.57**	**3.43–38.96**	**< 0.001**
Active empiric antibiotics	1.11	0.39–3.18	0.838
Immunocompromised	1.55	0.44–5.45	0.490
Sepsis/septic shock	**17.87**	**2.24–142.27**	**0.006**
Type of infection	1.97	0.65–5.99	0.229
Pathogen			
K. pneumoniae	Reference	–	
E. coli	1.36	0.44–4.22	0.586
Others	1.48	0.15–14.63	0.734
Diabetes mellitus	**3.40**	**1.01–11.46**	**0.048**
Hypertension	1.68	0.53–5.31	0.372
Chronic kidney disease	2.17	0.71–6.57	0.170
Malignancy	1.64	0.46–5.80	0.437
Empiric piperacillin–tazobactam therapy	**5.62**	**1.79–17.67**	**0.003**
Empiric beta-lactam beta-lactamase inhibitor	2.35	0.77–7.15	0.132
Empiric meropenem	0.54	0.06–4.56	0.576
Empiric carbapenem	0.45	0.05–3.72	0.459
Days to active antibiotic therapy	1.00	0.99–1.00	0.308
Hemodynamic support	**28.00**	**2.17–361.21**	**0.011**
Fever	1.59	0.46–5.46	0.457
Leucocytosis	**6.65**	**0.83–53.08**	**0.074**
Tachycardia	0.91	0.29–2.82	0.882
Tachypnea	4.09	0.67–24.97	0.127
Elevated serum creatinine	**7.86**	**1.68–36.75**	**0.009**
Elevated serum urea	2.04	0.64–6.42	0.222
Anemia	2.44	0.51–11.60	0.259
Thrombocytopenia	**4.20**	**1.28–13.78**	**0.018**
Hypoalbuminemia	**4.44**	**1.17–16.76**	**0.028**
Hyperbilirubinemia	**5.09**	**1.51–17.05**	**0.008**
Polymicrobial infections	0.65	0.13–3.17	0.603
Lowest systolic blood pressure	0.98	0.95–1.01	0.432
Lowest diastolic blood pressure	0.99	0.95–1.04	0.840
Bacteremia	1.64	0.55–4.89	0.375
Pneumonia	**11.15**	**2.20–56.47**	**0.004**
Urinary tract infection	**0.11**	**0.01–0.88**	**0.038**
Skin and soft tissue infections	0.82	0.16–4.01	0.807
Transaminitis	**4.69**	**1.51–14.60**	**0.008**

Bold font in the tables denotes statistical significance

10]. However, these factors were not associated with mortality in the currents study, although, some factors, such as sepsis or septic shock and empiric therapy with piperacillin–tazobactam were associated with mortality in the univariate regression analysis. This could be explained by the small sample size. Therefore, a large

Table 6 Multivariate logistic regression analysis for factors associated with in-hospital mortality

Variable	Adjusted odds ratio	95% Confidence Interval	*P* value
Intensive care unit admission	**8.75**	**1.05–72.75**	**0.045**
Sepsis/septic shock	13.80	0.78–243.21	0.073
Hyperbilirubinemia	2.27	0.14–35.30	0.556
Pneumonia	17.53	0.97–315.04	0.052
Urinary tract infection	0.15	0.00–3.48	0.240
Diabetes mellitus	**9.85**	**1.04–93.09**	**0.046**
Empiric piperacillin–tazobactam	2.87	0.27–29.76	0.376
Elevated total white blood cell count	3.00	0.18–48.99	0.440
Elevated serum creatinine	1.60	0.19–13.21	0.660
Thrombocytopenia	6.58	0.57–75.53	0.130
Hypoalbuminemia	2.35	0.13–40.02	0.554
Transaminitis	2.43	0.29–20.38	0.413

Bold font in the tables denotes statistical significance

multicentre study is being planned to examine the association between these factors and mortality in patients diagnosed with ESBL positive *enterobacteriaceae* infections. The current study revealed that presence of diabetes mellitus among patients diagnosed with ESBL positive *enterobacteriaceae* infections was independently associated with mortality. This may be due to immune impairment in patients with diabetes mellitus as a result of the hyperglycemic environment [24]. Therefore, adequate glycemic control is important to improve treatment outcomes among diabetes mellitus patients infected with ESBL-positive infection.

Due to some limitations, the findings should be interpreted with caution. This is a retrospective single-centre study with a relatively small sample size, which may affect the validity and generalizability of the results. However, the study sheds light on the treatments, mortality rate, and risk factors associated with mortality among patients diagnosed with ESBL-positive *enterobacteriaceae* infections in Malaysia. A large multicentre study is recommended to investigate treatment approaches used and to identify potential antimicrobial stewardship service opportunities.

Conclusions

There is a high rate of inactive empiric antibiotic use and excessive use of carbapenems for definitive therapy in ESBL-positive *enterobacteriaceae* infections including those with urinary tract infections and community-acquired infections. The mortality rate is relatively high among patients diagnosed with ESBL-positive *enterobacteriaceae* infections and is associated with intensive care unit admission and diabetes mellitus. Antibiotic stewardship is recommended to promote early active empiric antibiotic administration and to decrease carbapenem use in patients with ESBL positive *enterobacteriaceae* infections.

Abbreviations

CLSI: Clinical and Laboratory Standards Institute.; SPSS: Statistical Package for the Social Sciences.; ESBL: Extended Spectrum Beta-Lactamase.; ICU: Intensive care unit; OR: Odds ratio; AOR: Adjusted odds ratio; CI: Confidence interval.

Authors' contributions

AU and BT conceived the idea and designed the study. AU collected the data. AU and BT analyzed and interpreted the data. AU and FUK drafted the manuscript. BT, MHE, and SASS reviewed the manuscript draft. The author read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the IIUM Research Ethics Committee with the following reference number: IIUM/504/14/11/2/IREC 2020-092. Consent was waived due to the retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

The author declare that there is no competing interests.

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