Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Clinical characteristics, antibiotic-resistant patterns and prognostic factors in cancer patients with nosocomial infections caused by extended-spectrum beta-lactamase-producing Escherichia coli: a retrospective study from 2013 to 2019

Ai-min Jiang
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
https://orcid.org/0000-0002-4092-342X
Xin Shi
Xi'an Jiaotong University School of Medicine
Na Liu
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
Xuan Liang
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
Zhi-Ping Ruan
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
Xiao-Qiang Zheng
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
Xiao Fu
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
Tao Tian
Xi'an Jiaotong University Medical College First Affiliated Hospital Department of Medical Oncology
Yu Yao (✉ 13572101611@163.com)
https://orcid.org/0000-0003-3618-2363

Research

Keywords: Cancer patients, Nosocomial infection, Extended-spectrum β-lactamase, Escherichia coli, Prognosis

Posted Date: December 17th, 2019

DOI: https://doi.org/10.21203/rs.2.19049/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Abstract

Background: Nosocomial infections due to Extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-PE) is increasing worldwide. This study aimed to describe the clinical characteristics, antibiotic-resistant patterns, and prognostic factors associated with nosocomial infections caused by ESBL-PE in cancer patients.

Methods: This retrospectively analyzed patients with nosocomial infections caused by E. coli from August 2013 to May 2019 and was conducted to investigate the risk factors, clinical features, outcomes, and antibiotic-resistant patterns of these infections.

Results: Of the 1008 nosocomial infection episodes, 265 patients suffered from infections with E. coli, and 155 episodes were caused by ESBL-PE. A multivariate analysis showed that the length of antibiotics treatment more than 6.93 days was an independent risk factor for nosocomial infections in cancer patients caused by ESBL-PE. ECOG performance status score more than 2, presence of respiratory tract infection, septic shock, lymphocytopenia, and hypoproteinemia were independent risk factors for 30-day mortality in cancer patients caused by ESBL-PE. Antimicrobial susceptibility showed that the isolated ESBL-PE were highly resistant to aztreonam and third-generation cephalosporins.

Conclusions: The length of antibiotics treatment more than 6.93 days increased the risk ratio for ESBL-PE caused nosocomial infections. However, there was no significant difference in the prognoses of patients with ESBL-PE and non-ESBL-PE caused nosocomial infections. ECOG performance status score more than 2, presence of respiratory tract infection, septic shock, lymphocytopenia, and hypoproteinemia were independent risk factors for 30-day mortality in cancer patients with nosocomial infections caused by E. coli. The isolated ESBL-PE were highly resistant to aztreonam and third-generation cephalosporins.

Background

Recently, the incidence of nosocomial infections due to Extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-PE) is increasing worldwide. It was reported that ESBL-PE pathogens were causative of 20% of all Gram-negative nosocomial infections in patients with malignancy, and the isolation rate has been increasing over time [1]. Unfortunately, antibiotics administration for these infections are limited due to Extended-spectrum β-lactamases (ESBLs) mediates resistance to a wide variety of antibiotics [2].

Cancer patients are more susceptible to severe infection, including those caused by ESBL-PE as these patients can be immunocompromised due to malnutrition, invasive procedures, surgery, chemotherapy, radiation, and some new treatment modalities [3]. As a result, these infections became a significant therapeutic challenge for clinicians due to limited treatment strategy and are associated with delayed initiation of adequate treatment for malignancy, prolonged hospitalization, poor prognosis, increased health care costs, and high case-fatality rate [4, 5]. Therefore, rapid initiation of appropriate antibiotic therapy is pivotal for cancer patients with nosocomial infections caused by ESBL-PE, and since most

empirical regimens do not adequately cover these pathogens [6]. Besides, studies have also demonstrated that inappropriate empirical antibiotic treatment is associated with worse outcomes and survival [4].

To our knowledge, most of the previous studies have only focused on bloodstream infections (BSIs), although these infections in sites other than the bloodstream are not rare (such as the urinary tract, respiratory tract, and gastrointestinal tract). Few reports have compared the clinical, epidemiological, and microbiological characteristics of nosocomial infections caused by ESBL-PE in cancer patients. This study was therefore performed to describe the clinical characteristics, antibiotic-resistant patterns, and prognostic factors associated with nosocomial infections caused by ESBL-PE in cancer patients.

Methods

Study design

This retrospective observational single-center cohort study was conducted to evaluate clinical characteristics, antibiotic-resistant patterns, and prognostic factors associated with nosocomial infections caused by ESBL-PE in cancer patients. The electronic medical record database at the First Affiliated Hospital of Xi'an Jiaotong University, a 2560-bed medical center with a comprehensive cancer center in the northwest of China, was reviewed to identify cancer patients with nosocomial infections caused by ESBL-PE between August 2013 to May 2019. Patients with hematological malignancies were all excluded. Episodes of nosocomial infections were classified into two groups according to the status of ESBL, and the data for ESBL-producers was compared with that of non-ESBL-producers. In case of recurrence of infection after the initial hospital discharge, only the initial episode was analyzed.

Data collection

The following clinical data were collected from electronic medical records: age, gender, smoking history, Eastern Cooperative Oncology Group (ECOG) performance status, primary location of the disease, existence of distant metastasis, AJCC TNM categories, primary sites of infection, comorbidities and severity of underlying conditions according to the Charlson comorbidity index [7], existence of fever, types of cancer therapy within 30 days (surgery, chemotherapy, radiotherapy or concurrent chemoradiotherapy), corticosteroid treatment within previous 30 days, prior infection before hospital admission, Granulocyte colony-stimulating factor (G-CSF) use within 30 days, empirical antibiotics use within 30 days, the presence of indwelling catheters or other devices, invasive procedure within previous 30 days, length of antibiotics treatment, intensive care unit (ICU) admission during hospitalization, existence of septic shock, mechanical ventilation, outcome of the analyzed infection episode (death or discharged), the worst values of laboratory parameters before infection diagnosis including blood routine test, serum albumin, procalcitonin (PCT), antibiotic susceptibility tests of ESBL-negative E. coli and ESBL-positive E. coli.

Definitions

E. coli infection was defined as an infection manifested by the presence in at least one positive clinical sample for the same pathogen. Fever was defined as an axillary temperature of 38.3 °C on one occasion or a temperature of > 38.0 °C on two or more occasions during 12 h [8]. Nosocomial infection was defined as signs or symptoms of infection started > 48 h after hospital admission or < 48 h after hospital discharge. Otherwise, the case was considered community onset [9].

Study outcomes

We aimed to describe the clinical characteristics, antibiotic-resistant patterns, and prognostic factors associated with nosocomial infections caused by ESBL-PE in cancer patients and to present 30-day mortality and its associated risk factors during the seven-year study period.

Statistical Analysis

All statistical analyses were performed by the SPSS software version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). Means ± standard deviation was used for continuous quantitative variables, which were parametric (with normal distribution, checked by Shapiro test, boxplots, and histograms), while median and interquartile ranges were used for non-parametric continuous variables. The chi-square or Fisher's exact tests were used for categorical data analyses. Variables that were associated with ESBL in the univariate analysis ($P \leq 0.1$) were entered into a multivariate logistic regression analysis using stepwise selection. We used univariate and multivariate logistic regression analyses to identify the risk factors and independent risk factors for 30-day mortality of cancer patients with nosocomial infections caused by ESBL-PE as described above. All variables in the univariate analysis ($P \leq 0.1$) and variables with clinical significance were entered into a multivariable model.

Results

Essential characteristics of the study population

During the seven years, there were 14695 patients admitted to the oncology center of the First Affiliated Hospital of Xi'an Jiaotong University and received systemic treatment. In total, 1008 cancer patients developed nosocomial infection, and E. coli caused 265 episodes. These patients were classed into ESBL-PE infection group (n = 155, 58.5%) and non- ESBL-PE infection group (n = 110, 41.5%) (Fig. 1). It shows that the prevalence of ESBL-PE infection has been increased dramatically from 2013 to 2019, and the majority of patients had ESBL-PE caused nosocomial infections that were detected throughout the year with a peak in June and August (Fig. 2). The demographic and clinical characteristics of included patients are summarized in Table 1. There were no significant differences in age and gender between the two groups (59.74 ± 12.41 vs. 58.17 ± 11.20, P = 0.286; male, 33 vs. 46, P = 0.955). Diabetes mellitus, renal disease, and liver disease were found in 18 (6.8%), 16 (6.0%), and 13 (4.9%) patients, respectively. Of the primary infection sites of the 265 nosocomial infection episodes caused by E. coli, urinary tract infection was the major reason for nosocomial infections, accounting for 59.2% of the cases, followed by bloodstream infections (18.9%) and abdominal cavity infections (7.5%). The most frequent diagnoses

were gynecological cancer in 99 (37.4%), colon and rectal cancer in 39 (14.7%), and breast cancer in 26 (9.8%) patients.

Risk factors for nosocomial infections in cancer patients caused by ESBL-PE

A univariate analysis (Table 1) showed that risk factors for nosocomial infections in cancer patients caused by ESBL-PE included presence of urinary tract infection (P = 0.025), presence of abdominal cavity infection (P = 0.003), presence of indwelling urinary catheters (P = 0.011), presence of drains postoperation (P = 0.008), presence of nasogastric tube (P = 0.005), length of antibiotics treatment (P = 0.003), and intensive care unit admission (P = 0.014). The results of multivariate analysis showed that the length of antibiotics treatment more than 6.93 days (OR = 1.80, P = 0.049) was an independent risk factor for nosocomial infections in cancer patients caused by ESBL-PE.

Risk factors for 30-day mortality in cancer patients with nosocomial infections caused by E. coli

The cancer patients with nosocomial infections caused by E. coli were classified into survivor and non-survivor groups based on the outcome at 30 days. The overall case-fatality rate of the 265 patients was 10.2% (27/265), and the overall case-fatality caused by ESBL-PE was 6.8% (18/265). A survival curve analysis (Fig. 3) showed that the 30-day mortality among cancer patients with nosocomial infections caused by ESBL-PE group was higher than non-ESBL-PE group (11.6% vs. 8.2%, $\chi 2 = 0.381$, P = 0.537), and the difference was not statistically significant. Furthermore, the patients were divided into bloodstream infection group/non- bloodstream infection group and septic shock group/non-septic shock group according to primary infection sites and the presence of septic shock. There was no significant difference in the mortalities between these groups among patients with nosocomial infections, as detailed in Fig. S1 (Supplementary Material).

In this study, we used a stepwise logistics regression model to identify the prognostic significance of the clinical data for cancer patients with nosocomial infections caused by ESBL-PE and non-ESBL-PE. The results of the univariate analyses demonstrated that existence of distant metastasis, stage of cancer, primary sites of infection (respiratory tract infection, urinary tract infection, and bloodstream infection), presence of liver disease, received chemotherapy or concurrent chemoradiotherapy within 30 days, corticosteroid therapy within 30 days, prior G-CSF use within 30 days, presence of percutaneous pleural drainage tube, mechanical ventilation, septic shock, laboratory examination results including hemoglobin, lymphocytes count, and albumin were significantly variables (Table 2). Results of the multivariate stepwise logistic regression analyses identified ECOG performance status, presence of respiratory tract infection, septic shock, lymphocytes count, and albumin as independent factors for 30-day mortality in the study population (Table 2).

Antimicrobial susceptibility for cancer patients with nosocomial infections caused by E. coli

We then investigated the antimicrobial sensitivity of the isolated ESBL-PE and non-ESBL-PE to commonly used antibiotics. The results showed that both ESBL-PE and non-ESBL-PE were highly sensitive to meropenem (100.0% vs. 100.0%), imipenem (100.0% vs. 100.0%), amikacin (92.9% vs. 99.1%), tigecycline (89.3% vs. 100.0%), and piperacillin/tazobactam (88.3% vs. 99.1%). Compared with non-ESBL-PE, the isolated ESBL-PE were highly resistant to ceftriaxone (98.1% vs. 9.2%), ceftazidime (48.1% vs. 3.6%), cefepime (38.8% vs. 1.8%), aztreonam (77.3% vs. 6.4%), ciprofloxacin (76.5% vs. 54.5%), and levofloxacin (73.4% vs. 52.7%) (Fig. 4).

Discussion

Escherichia coli is one of the most common bacteria which producing extended-spectrum β-lactamase (ESBL) and is also one of the most common pathogens in clinical infections. In the past ten years, the prevalence of ESBL-PE colonization and infection has continued to increase dramatically worldwide [10], and these pathogens generally associated with delayed initiation of appropriate antimicrobial therapy and extra medical costs, hence leading to worse clinical outcomes [4]. Patients with malignancy are predisposed to developing infections caused by these resistant pathogens since cancer patients are easily immunocompromised due to frequently exposed to cytotoxic agents, surgery, radiation, malnutrition, and malignancy itself [3]. Therefore, timely and appropriate antibiotic therapy plays an essential role in cancer patients developed nosocomial infections caused by these pathogens. Thus, we conducted this seven years period retrospective study to investigate the clinical characteristics, antibiotic-resistant patterns, and prognostic factors associated with nosocomial infections caused by ESBL-PE in cancer patients.

In the present study, the prevalence of ESBL-PE infection is 15.4% (155/1008) among cancer patients. This finding was comparable with the studies conducted in Germany (17.5%) [11] and the Czech Republic (11.3%) [12] among patients with malignancy. Previous studies reported high colonization rates of ESBL-PE among cancer patients in Asia [13–15]. This could be explained by the fact that the prevalence of nosocomial infections among cancer patients varies widely from region to region. Our study demonstrated that ESBL-PE was primarily derived from urinary tract infections, followed by the bloodstream and abdominal cavity infections, which is consistent with the findings of many previous studies [16–19].

The results of this study suggested that the length of antibiotics treatment more than 6.93 days was independent risk factor for nosocomial infections in cancer patients caused by ESBL-PE. Biehl LM et al. [4] reported that nosocomial acquisition, recent antimicrobial use, ICU care, and prolonged hospitalizations were associated with increased ESBL-PE BSI risk in patients with malignancy. Besides, cancer patients constitute a population that is intrinsically vulnerable to developing FN since they frequently underwent radiation and chemotherapy. Therefore, beta-lactams with beta-lactamase

inhibitors and carbapenems are widely considered the first-choice treatment option for infections caused by ESBL-PE in our hospital, and generally, the length of antibiotics treatment at least more than one week.

Nosocomial infections in cancer patients have been associated with increased mortality in this patient population [4]. Several studies [14, 15, 20] reported that the overall case-fatality was significantly higher in the ESBL-positive group compared with ESBL-negative group. Conversely, there was no significant difference in the 30-day mortality between patients with nosocomial infections caused by ESBL-PE and those infected with non-ESBL-PE in this study, similar to the findings of some previous studies [19, 21, 22]. This may be attributed to the use of many broad-spectrum antibiotics in the clinic due to the current high prevalence of ESBL-PE. In multivariate analysis, we found that ECOG performance status score more than 2 is an independent risk factor for 30-day mortality in cancer patients with nosocomial infections caused by ESBL-PE, which is consistent with the previous study [19]. An interesting finding of our study is that the presence of respiratory tract infection is an independent risk factor for 30-day mortality in these patients as well despite its small proportion in our cohort. This may have been due to respiratory tract infection is a strong independent predictor of chemotherapy interruption, which in turn impacts disease control [23]. Our analysis demonstrated that septic shock is also an independent risk factor for 30-day mortality in patients with ESBL-PE caused nosocomial infections, which is also similar to previous studies [14–16]. We also found that low lymphocytes count and serum albumin are independent risk factors for 30-day mortality in cancer patients with nosocomial infections caused by ESBL-PE. Lymphocytes count level is a standard indicator for assessing a patient's immune status. Lymphocytopenia has been identified as a prognostic factor in several solid tumors since it was associated with a condition of cancer-induced immunodeficiency, which can limit tumor control following radiation and chemotherapy [24]. Several studies have shown that patients with hypoproteinemia were correlated with worse prognosis in hospitalized patients, and serum albumin level is generally used to evaluating patients' nutritional status, organ function, and comorbidity [19, 25].

In this retrospective study, we observed that E. coli was highly sensitive to carbapenems, beta-lactams with beta-lactamase inhibitors, amikacin, and tigecycline, regardless of ESBL status. Compared with non-ESBL-PE, the isolated ESBL-PE were highly resistant to aztreonam and third-generation cephalosporins. We also observed that both ESBL-PE and non-ESBL-PE were associated with slightly increased resistance to fluoroquinolones. These observations are consistent with previous studies [26]. Thus, piperacillin/tazobactam or carbapenem should be used for the initial empirical treatment of cancer patients with nosocomial infections caused by ESBL-PE [4]. To our knowledge, this is the first study evaluated clinical characteristics, antibiotic-resistant patterns, and prognostic factors associated with nosocomial infections caused by ESBL-PE among cancer patients in China. However, our study has several limitations. First, there might be hidden biases in the analyses of the relationship in this retrospective study. Besides, this study was conducted from data at a single center. Therefore, it needs to be further validated in a prospective multicenter study. Moreover, we should perform more precise drug resistance gene detection to better understand the drug resistance patterns and the appropriate treatment options.

Conclusions

In summary, the length of antibiotics treatment more than 6.93 days was independent risk factor for nosocomial infections in cancer patients caused by ESBL-PE. However, there was no significant difference in the prognoses of patients with ESBL-PE and non-ESBL-PE caused nosocomial infections. ECOG performance status score more than 2, presence of respiratory tract infection, septic shock, lymphocytopenia, and hypoproteinemia were independent risk factors for 30-day mortality in cancer patients with nosocomial infections caused by E. coli. The isolated E. coli were highly sensitive to carbapenems, beta-lactams with beta-lactamase inhibitors, amikacin, and tigecycline, regardless of ESBL status. Compared with non-ESBL-PE, the isolated ESBL-PE were highly resistant to aztreonam and third-generation cephalosporins.

Abbreviations

ESBL: extended-spectrum beta-lactamase; ESBL-PE: Extended-spectrum β-lactamase-producing Enterobacteriaceae; BSIs: bloodstream infections; ECOG: Eastern Cooperative Oncology Group; G-CSF: granulocyte colony-stimulating factor; PICC: peripherally inserted central catheter; CVC: central venous catheter; ICU: Intensive care unit; PCT: procalcitonin.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University. Waiving of informed consent was obtained due to the retrospective noninterventional study design.

Consent for publication

Not applicable.

Availability of data and material

Please contact author for data requests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions

YY and TT conceived the study. AMJ and XS were involved in data collecting, statistical analysis, and drafting the manuscript. NL carried out the data collection and analysis and provided the critical revision.

ZPR and XL participated in the study design and manuscript revision. XQZ and XF participated in the study design and helped with the data collection. All authors read and approved the final manuscript.

Acknowledgments

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Alevizakos M, Gaitanidis A, Andreatos N, Arunachalam K, Flokas ME, Mylonakis E (2017) Bloodstream infections due to extended-spectrum beta-lactamase-producing Enterobacteriaceae among patients with malignancy: a systematic review and meta-analysis. Int J Antimicrob Agents 50 (5):657-663. doi:10.1016/j.ijantimicag.2017.07.003
2. Paterson DL, Bonomo RA (2005) Extended-spectrum beta-lactamases: a clinical update. Clin Microbiol Rev 18 (4):657-686. doi:10.1128/CMR.18.4.657-686.2005
3. Gudiol C, Aguado JM, Carratala J (2016) Bloodstream infections in patients with solid tumors. Virulence 7 (3):298-308. doi:10.1080/21505594.2016.1141161
4. Biehl LM, Schmidt-Hieber M, Liss B, Cornely OA, Vehreschild MJ (2016) 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 42 (1):1-16. doi:10.3109/1040841X.2013.875515
5. Ndir A, Diop A, Ka R, Faye PM, Dia-Badiane NM, Ndoye B, Astagneau P (2016) 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 5:13. doi:10.1186/s13756-016-0114-7
6. Alevizakos M, Karanika S, Detsis M, Mylonakis E (2016) 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 48 (6):647-654. doi:10.1016/j.ijantimicag.2016.08.021
7. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of Chronic Diseases 40 (5):373-383. doi:https://doi.org/10.1016/0021-9681(87)90171-8
8. Chen CY, Tien FM, Sheng WH, Huang SY, Yao M, Tang JL, Tsay W, Tien HF, Hsueh PR (2017) Clinical and microbiological characteristics of bloodstream infections among patients with haematological malignancies with and without neutropenia at a medical centre in northern Taiwan, 2008-2013. Int J Antimicrob Agents 49 (3):272-281. doi:10.1016/j.ijantimicag.2016.11.009

9. Palacios-Baena ZR, Gutierrez-Gutierrez B, De Cueto M, Viale P, Venditti M, Hernandez-Torres A, Oliver A, Martinez-Martinez L, Calbo E, Pintado V, Gasch O, Almirante B, Antonio Lepe J, Pitout J, Akova M, Pena-Miralles C, Schwaber MJ, Tumbarello M, Tacconelli E, Origuen J, Prim N, Bou G, Giamarellou H, Bermejo J, Hamprecht A, Perez F, Almela M, Lowman W, Hsueh PR, Navarro-San Francisco C, Torre-Cisneros J, Carmeli Y, Bonomo RA, Paterson DL, Pascual A, Rodriguez-Bano J, Group REI (2017) Development and validation of the INCREMENT-ESBL predictive score for mortality in patients with bloodstream infections due to extended-spectrum-beta-lactamase-producing Enterobacteriaceae. J Antimicrob Chemother 72 (3):906-913. doi:10.1093/jac/dkw513
10. Pitout JDD, Laupland KB (2008) Extended-spectrum β-lactamase-producing Enterobacteriaceae: an emerging public-health concern. The Lancet Infectious Diseases 8 (3):159-166. doi:10.1016/s1473-3099(08)70041-0
11. Liss BJ, Vehreschild JJ, Cornely OA, Hallek M, Fatkenheuer G, Wisplinghoff H, Seifert H, Vehreschild MJ (2012) Intestinal colonisation and blood stream infections due to vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBLE) in patients with haematological and oncological malignancies. Infection 40 (6):613-619. doi:10.1007/s15010-012-0269-y
12. Kolar M, Htoutou Sedlakova M, Pudova V, Roderova M, Novosad J, Senkyrikova M, Szotkowska R, Indrak K (2015) Incidence of fecal Enterobacteriaceae producing broad-spectrum beta-lactamases in patients with hematological malignancies. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 159 (1):100-103. doi:10.5507/bp.2014.042
13. Kim Y-J, Jung SM, Kang J, Ryoo SM, Sohn CH, Seo D-W, Lim KS, Huh JW, Kim S-H, Kim WY (2019) Risk factors for extended-spectrum beta-lactamase-producing Enterobacteriaceae infection causing septic shock in cancer patients with chemotherapy-induced febrile neutropenia. Internal and Emergency Medicine 14 (3):433-440. doi:10.1007/s11739-018-02015-x
14. Zhang Q, Gao HY, Li D, Li Z, Qi SS, Zheng S, Bai CS, Zhang SH (2019) Clinical outcome of Escherichia coli bloodstream infection in cancer patients with/without biofilm formation: a single-center retrospective study. Infection and drug resistance 12:359-371. doi:10.2147/idr.s192072
15. Ha YE, Kang CI, Cha MK, Park SY, Wi YM, Chung DR, Peck KR, Lee NY, Song JH (2013) Epidemiology and clinical outcomes of bloodstream infections caused by extended-spectrum beta-lactamase-producing Escherichia coli in patients with cancer. Int J Antimicrob Agents 42 (5):403-409. doi:10.1016/j.ijantimicag.2013.07.018
16. Ortega M, Marco F, Soriano A, Almela M, Martinez JA, Munoz A, Mensa J (2009) Analysis of 4758 Escherichia coli bacteraemia episodes: predictive factors for isolation of an antibiotic-resistant strain and their impact on the outcome. J Antimicrob Chemother 63 (3):568-574. doi:10.1093/jac/dkn514
17. Hsieh C-J, Shen Y-H, Hwang K-P (2010) Clinical Implications, Risk Factors and Mortality Following Community-onset Bacteremia Caused by Extended-spectrum β-lactamase (ESBL) and non-ESBL Producing Escherichia coli. Journal of Microbiology, Immunology and Infection 43 (3):240-248. doi:https://doi.org/10.1016/S1684-1182(10)60038-2

18. Kerneis S, Valade S, Geri G, Compain F, Lavollay M, Rostane H, Carbonnelle E, Mainardi JL (2015) Cefoxitin as a carbapenem-sparing antibiotic for infections caused by extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae. Infectious diseases (London, England) 47 (11):789-795. doi:10.3109/23744235.2015.1062133
19. Xiao T, Yang K, Zhou Y, Zhang S, Ji J, Ying C, Shen P, Xiao Y (2019) Risk factors and outcomes in non-transplant patients with extended-spectrum beta-lactamase-producing Escherichia coli bacteremia: a retrospective study from 2013 to 2016. Antimicrob Resist Infect Control 8:144. doi:10.1186/s13756-019-0599-y
20. Chopra T, Marchaim D, Johnson PC, Chalana IK, Tamam Z, Mohammed M, Alkatib S, Tansek R, Chaudhry K, Zhao JJ, Pogue JM, Kaye KS (2015) Risk factors for bloodstream infection caused by extended-spectrum β-lactamase–producing Escherichia coli and Klebsiella pneumoniae: A focus on antimicrobials including cefepime. American Journal of Infection Control 43 (7):719-723. doi:https://doi.org/10.1016/j.ajic.2015.02.030
21. Denis B, Lafaurie M, Donay JL, Fontaine JP, Oksenhendler E, Raffoux E, Hennequin C, Allez M, Socie G, Maziers N, Porcher R, Molina JM (2015) Prevalence, risk factors, and impact on clinical outcome of extended-spectrum beta-lactamase-producing Escherichia coli bacteraemia: a five-year study. International Journal of Infectious Diseases 39:1-6. doi:https://doi.org/10.1016/j.ijid.2015.07.010
22. Harris PN (2015) Clinical management of infections caused by Enterobacteriaceae that express extended-spectrum beta-lactamase and AmpC enzymes. Seminars in respiratory and critical care medicine 36 (1):56-73. doi:10.1055/s-0034-1398387
23. Brand JS, Colzani E, Johansson ALV, Giesecke J, Clements M, Bergh J, Hall P, Czene K (2016) Infection-related hospitalizations in breast cancer patients: Risk and impact on prognosis. J Infect 72 (6):650-658. doi:10.1016/j.jinf.2016.04.003
24. Joseph N, Dovedi SJ, Thompson C, Lyons J, Kennedy J, Elliott T, West CM, Choudhury A (2016) Pre-treatment lymphocytopaenia is an adverse prognostic biomarker in muscle-invasive and advanced bladder cancer. Ann Oncol 27 (2):294-299. doi:10.1093/annonc/mdv546
25. Akirov A, Masri-Iraqi H, Atamna A, Shimon I (2017) Low Albumin Levels Are Associated with Mortality Risk in Hospitalized Patients. Am J Med 130 (12):1465.e1411-1465.e1419. doi:10.1016/j.amjmed.2017.07.020
26. Toner L, Papa N, Aliyu SH, Dev H, Lawrentschuk N, Al-Hayek S (2016) Extended-spectrum beta-lactamase-producing Enterobacteriaceae in hospital urinary tract infections: incidence and antibiotic susceptibility profile over 9 years. World J Urol 34 (7):1031-1037. doi:10.1007/s00345-015-1718-x

Tables

Table 1 Clinical and demographic characteristics of cancer patients with nosocomial infections caused by E. coli

	ESBL-negative (n =110)	ESBL-positive (n =155)	*P*-value	Multivariate analysis	
				OR (95% CI)	*P*-value
Demographic data					
Sex (male)	33(30.0)	46(29.7)	0.955		
Age (years)	59.74±12.41	58.17±11.20	0.286		
Smoking history			0.707		
Never smoker	91(82.7)	122(78.7)			
Former smoker	11(10.0)	20(12.9)			
Current smoker	8(7.3)	13(8.4)			
ECOG performance status			0.271		
0,1	88(80.0)	115(74.2)			
2,3,4	22(20.0)	40(25.8)			
Underlying cancer type					
Head and neck cancer	2(1.8)	2(1.3)	1.000		
Lung cancer	2(1.8)	8(5.2)	0.280		
Esophagus cancer	7(5.4)	13(8.4)	0.539		
Gastric cancer	7(5.4)	8(5.2)	0.676		
Gastroesophageal junction cancer	1(0.9)	4(2.6)	0.598		
Pancreatic cancer	5(4.5)	1(0.6)	0.092	0.12(0.01-1.13)	0.064
Hepatobiliary cancer	5(4.5)	6(3.9)	1.000		
Breast cancer	14(12.7)	12(7.7)	0.179		
Colon and rectal cancer	14(12.7)	25(16.1)	0.441		
Genitourinary cancer	5(4.5)	9(5.8)	0.651		
Gynecological cancer	44(40.0)	55(35.5)	0.454		
Lymphoma	1(0.9)	3(1.9)	0.870		
Metastatic disease	1(0.9)	1(0.6)	1.000		
Others[a]	2(1.8)	8(5.2)	0.280		
Existence of distant metastasis			0.284		
None	69(62.7)	107(69.0)			
Yes	41(37.3)	48(31.0)			
Stage of cancer			0.376		
Stage I	12(10.9)	25(16.1)			
Stage II	30(27.3)	44(28.4)			
Stage III	20(18.2)	33(21.3)			
Stage IV	48(43.6)	53(34.2)			
Primary sites of infection					
Respiratory tract	4(3.6)	12(92.3)	0.167		
Gastrointestinal	0(0.0)	1(0.6)	1.000		
Urinary tract	74(67.3)	83(53.5)	**0.025**	0.60(0.23-1.61)	0.312
Hepatobiliary	3(2.7)	0(0.0)	0.139		
Skin and soft tissue	4(3.6)	8(5.2)	0.773		
Thoracic cavity	0(0.0)	3(1.9)	0.380		
Abdominal cavity	2(1.8)	18(11.6)	**0.003**	3.15(0.54-18.40)	0.202
Catheter related	0(0.0)	1(0.6)	1.000		
Endogenous source	23(20.9)	27(17.4)	0.474	0.55(0.20-1.50)	0.242
Comorbidities					
Myocardial infarction	3(2.7)	0(0.0)	0.139		
Cerebrovascular disease	1(0.9)	3(1.9)	0.870		
Liver disease	4(3.6)	9(5.8)	0.420		
Diabetes	8(7.3)	10(6.5)	0.794		
Renal disease	6(5.5)	10(6.5)	0.737		
Charlson Co-morbidity Index score			0.397		
0	91(82.7)	122(78.7)			
1-2	15(13.6)	30(19.4)			
≥3	4(3.6)	3(1.9)			
Existence of fever	39(35.5)	60(38.7)	0.589		
Surgery (within 30 days)			0.061		0.57
None	91(82.7)	109(70.3)		REF (1.00)	
Curative surgery	16(14.5)	36(23.2)		0.82(0.31-2.18)	0.690

Palliative surgery	3(2.7)	10(6.5)		1.50(0.28-8.00)	0.632
Chemotherapy (within 30 days)			0.447		
None	54(49.1)	81(52.3)			
Neoadjuvant	1(0.9)	0(0.0)			
Adjuvant	17(15.5)	17(11.0)			
1st line	6(5.5)	4(2.6)			
2nd line	4(3.6)	5(3.2)			
≥3rd line	28(25.5)	48(31.0)			
Radiotherapy (within 30 days)	23(20.9)	23(14.8)	0.199		
Concurrent chemoradiotherapy (within 30 days)	29(26.4)	32(20.6)	0.276		
Corticosteroid therapy (within 30 days)	80(72.7)	96(61.9)	0.067	1.40(0.60-3.29)	0.441
Prior infection (within 30 days)	4(3.6)	8(5.2)	0.773	1.89(0.53-6.78)	0.328
Prior G-CSF use (within 30 days)	63(57.3)	70(45.2)	0.052	0.73(0.36-1.46)	0.374
Prior antibiotics (within 30 days)	6(5.5)	7(4.5)	0.727		
Presence of indwelling catheters or other devices					
Biliary stent	3(2.7)	1(0.6)	0.391		
Ureteral stent	5(4.5)	11(7.1)	0.390		
Indwelling urinary catheters	11(10.0)	34(21.9)	**0.011**	2.16(0.69-6.80)	0.187
PICC	9(8.2)	11(7.1)	0.742		
Venous port	3(2.7)	2(1.3)	0.697		
CVC	1(0.9)	7(4.5)	0.185		
Percutaneous pleural drainage tube	6(5.5)	12(7.7)	0.466		
Percutaneous abdomen drainage tube	2(1.8)	1(0.6)	0.764		
Drains postoperation	11(10.0)	35(22.6)	**0.008**	0.84(0.24-2.98)	0.783
Nasogastric tube	5(4.5)	24(15.5)	**0.005**	2.08(0.47-9.16)	0.332
Invasive procedure (within 30 days)	43(39.1)	78(50.3)	0.071	0.94(0.51-1.72)	0.829
Length of antibiotics treatment (days)			**0.003**		
<6.93	67(60.9)	66(42.6)		REF (1.00)	
≥6.93	43(39.1)	89(57.4)		1.80(1.00-3.24)	**0.049**
ICU admission	4(3.6)	19(12.3)	**0.014**	1.37(0.30-6.31)	0.687
Mechanical ventilation	4(3.6)	7(4.5)	0.967		
Septic shock			0.474		
None	87(79.1)	128(82.6)			
Yes	23(20.9)	27(17.4)			
Outcomes			0.363		
Death	9(8.2)	18(11.6)			
Discharge	101(91.8)	137(88.4)			
Laboratory examination results					
Hemoglobin(g/L)	104.80±19.42	102.16±19.25	0.274		
Platelet count($\times 10^9$/L)	194.46±99.46	211.70±121.48	0.222		
White-cell count($\times 10^9$/L)	6.62±3.84	7.49±5.26	0.142		
Neutrophils count ($\times 10^9$/L)	5.16±3.60	6.01±4.95	0.122		
Lymphocytes count ($\times 10^9$/L)	1.03±0.72	0.94±0.52	0.232		
PCT (ng/mL)	10.55±34.92	10.71±27.21	0.977		
Albumin(g/L)	36.84±6.54	35.38±5.91	0.058	0.98(0.93-1.02)	0.305

Abbreviations: ESBL, extended-spectrum beta-lactamase; ECOG, Eastern Cooperative Oncology Group; G-CSF, granulocyte colony-stimulating factor; PICC, peripherally inserted central catheter; CVC, central venous catheter; ICU, Intensive care unit; PCT, procalcitonin.

[a] Others: primitive neuroectodermal tumor (3 patients), thymic carcinoma and duodenal carcinoma two patients each, malignant teratoma, carcinoid cancer of appendix, and malignant pleural mesothelioma one patient each.

Bolded values indicate statistical significance.

Table 2 Analysis of risk factors for 30-day Mortality in cancer patients with nosocomial infections caused by E. coli

	Survivor (n =238)	Non-survivor (n = 27)	*P*-value	Multivariate analysis	
				OR (95% CI)	*P*-value
Demographic data					
Sex (male)	68(28.6)	11(40.7)	0.190		
Age (years)	58.71±11.66	59.81±12.42	0.643		
Smoking history			0.180		
Never smoker	193(81.1)	20(74.1)			
Former smoker	25(10.5)	6(22.2)			
Current smoker	20(8.4)	1(3.7)			
ECOG performance status			0.077		
0,1	186(78.2)	17(63.0)		REF (1.00)	
2,3,4	52(21.8)	10(37.0)		2.85(1.80-4.52)	**<0.001**
Underlying cancer type					
Head and neck cancer	2(0.8)	2(7.4)	0.053	2.57(0.93-7.10)	0.068
Lung cancer	8(3.4)	2(7.4)	0.608		
Esophagus cancer	15(6.3)	5(18.5)	0.058	0.74(0.38-1.45)	0.381
Gastric cancer	14(5.9)	1(3.7)	0.980		
Gastroesophageal junction cancer	3(1.3)	2(7.4)	0.083	0.67(0.14-3.16)	0.615
Pancreatic cancer	4(1.7)	2(7.4)	0.116		
Hepatobiliary cancer	10(4.2)	1(3.7)	1.000		
Breast cancer	24(10.1)	2(7.4)	0.919		
Colon and rectal cancer	36(15.1)	3(11.1)	0.786		
Genitourinary cancer	14(5.9)	0(0.0)	0.400		
Gynecological cancer	93(39.1)	6(22.2)	0.086	0.50(0.20-1.21)	0.122
Lymphoma	4(1.7)	0(0.0)	1.000		
Others[a]	9(3.8)	1(3.7)	1.000		
Existence of distant metastasis			**0.011**		
None	164(68.9)	12(44.4)		REF (1.00)	
Yes	74(31.1)	15(55.6)		2.36(0.92-6.05)	0.074
Stage of cancer			**0.017**		0.968
Stage I	36(15.1)	1(3.7)		REF (1.00)	
Stage II	71(29.8)	3(11.1)		1.00(0.44-2.28)	0.998
Stage III	47(19.7)	6(22.2)		1.07(0.48-2.39)	0.867
Stage IV	84(35.3)	17(63.0)		1.28(0.44-3.73)	0.650
Primary sites of infection					
Respiratory tract	9(3.8)	7(25.9)	**<0.001**	2.90(1.50-5.60)	**0.001**
Urinary tract	150(63.0)	7(25.9)	**<0.001**	1.50(0.64-3.53)	0.353
Hepatobiliary	2(0.8)	1(3.7)	0.277		
Skin and soft tissue	11(4.6)	1(3.7)	1.000		
Abdominal cavity	19(8.0)	1(3.7)	0.679		
Endogenous source	40(16.8)	10(37.0)	**0.011**	1.09(0.41-2.94)	0.858
Comorbidities					
Liver disease	9(3.8)	4(14.8)	**0.041**	1.97(0.92-4.23)	0.082
Diabetes	16(6.7)	2(7.4)	1.000		
Renal disease	13(5.5)	3(11.1)	0.458		
Charlson Co-morbidity Index score			0.140		
0	194(81.5)	19(70.4)			
1-2	39(16.4)	6(22.2)			

≥3	5(2.1)	2(7.4)			
Existence of fever	85(35.7)	14(51.9)	0.100		
Surgery (within 30 days)			0.213		
None	176(73.9)	24(88.9)			
Curative surgery	50(21.0)	2(7.4)			
Palliative surgery	12(5.0)	1(3.7)			
Chemotherapy (within 30 days)			**0.006**		0.165
None	115(48.3)	20(74.1)		REF (1.00)	
Neoadjuvant	1(0.4)	0(0.0)		1.86(0.20-17.30)	0.584
Adjuvant	73(30.7)	3(11.1)		1.27(0.53-3.07)	0.590
1st line	34(14.3)	0(0.0)		0.33(0.13-0.87)	0.025
2nd line	8(3.4)	2(7.4)		1.13(0.39-3.28)	0.828
≥3rd line	7(2.9)	2(7.4)		1.97(0.92-4.23)	0.082
Radiotherapy (within 30 days)	43(18.1)	3(11.1)	0.525		
Concurrent chemoradiotherapy (within 30 days)	59(24.8)	2(7.4)	**0.042**	1.87(0.71-4.94)	0.204
Corticosteroid therapy (within 30 days)	164(68.9)	12(44.4)	**0.011**	0.72(0.33-1.57)	0.405
Prior infection (within 30 days)	11(4.6)	1(3.7)	1.000		
Prior G-CSF use (within 30 days)	127(53.4)	6(22.2)	**0.002**	0.82(0.39-1.72)	0.614
Prior antibiotics (within 30 days)	13(5.5)	0(0.0)	0.438		
Presence of indwelling catheters or other devices					
Biliary stent	2(0.8)	2(7.4)	0.053	0.74(0.17-3.27)	0.689
Ureteral stent	16(6.7)	0(0.0)	0.335		
Indwelling urinary catheters	42(17.6)	3(11.1)	0.557		
PICC	18(7.6)	2(7.4)	1.000		
Venous port	5(2.1)	0(0.0)	1.000		
CVC	7(2.9)	1(3.7)	0.582		
Percutaneous pleural drainage tube	12(5.0)	6(22.2)	**0.003**	0.55(0.28-1.07)	0.080
Drains postoperation	43(18.1)	3(11.1)	0.525		
Nasogastric tube	25(10.5)	4(14.8)	0.723		
Invasive procedure (within 30 days)	107(45.0)	14(51.9)	0.496		
Length of antibiotics treatment (days)			0.320		
<6.93	117(49.2)	16(59.3)			
≥6.93	121(50.8)	11(40.7)			
ICU admission	20(8.4)	3(11.1)	0.910		
Mechanical ventilation	7(2.9)	4(14.8)	**0.015**	2.02(0.95-4.31)	0.067
Septic shock			**<0.001**		
None	200(84.0)	15(55.6)		REF (1.00)	
Yes	38(16.0)	12(44.4)		4.73(2.17-10.28)	**<0.001**
ESBL status			0.363		
Negative	101(42.4)	9(33.3)			
Positive	137(57.6)	18(66.7)			
Laboratory examination results					
Hemoglobin(g/L)	104.76±18.90	90.04±18.28	**<0.001**	1.00(0.99-1.01)	0.891
Platelet count($\times 10^9$/L)	207.71±109.77	176.70±137.42	0.177		
White-cell count($\times 10^9$/L)	7.14±4.71	7.09±5.01	0.957		
Neutrophils count ($\times 10^9$/L)	5.62±4.44	5.96±4.69	0.714		
Lymphocytes count ($\times 10^9$/L)	1.00±0.62	0.70±0.48	**0.015**	0.92(0.88-0.97)	**0.001**
PCT (ng/mL)	7.18±22.79	26.87±52.01	0.121		
Albumin(g/L)	36.62±5.93	30.42±5.96	**<0.001**	0.92(0.88-1.0)	**0.001**

Abbreviations: ECOG, Eastern Cooperative Oncology Group; G-CSF, granulocyte colony-stimulating factor;

PICC, peripherally inserted central catheter; CVC, central venous catheter; ESBL, extended-spectrum beta-lactamase; ICU, Intensive care unit; PCT, procalcitonin.
[a] Others: primitive neuroectodermal tumor (3 patients), thymic carcinoma and duodenal carcinoma, two patients each, malignant teratoma, carcinoid cancer of appendix, and malignant pleural mesothelioma one patient each.
Bolded values indicate statistical significance.

Figures

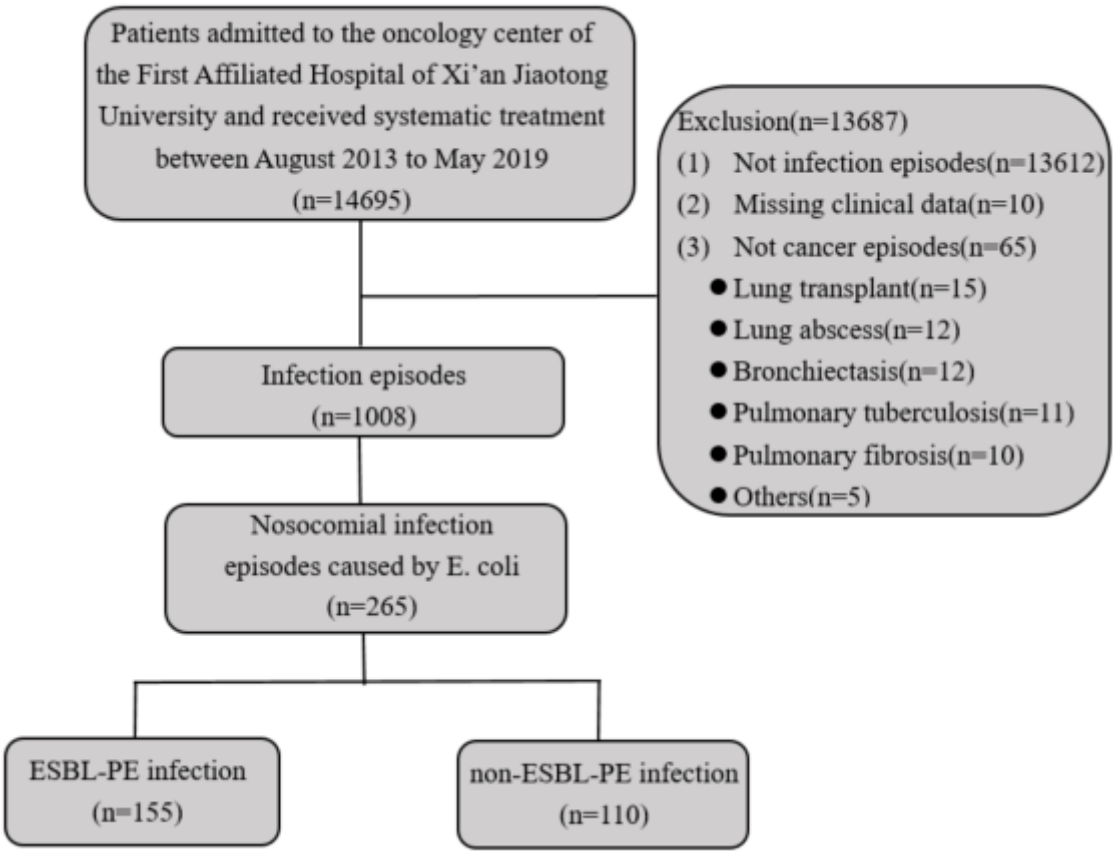

Figure 1

Flow chart of clinical characteristics, antibiotic resistant patterns and prognostic factors associated with nosocomial infections caused by ESBL-PE in cancer patients treated at the First Affiliated Hospital of Xi'an Jiaotong University between August 2013 to May 2019.

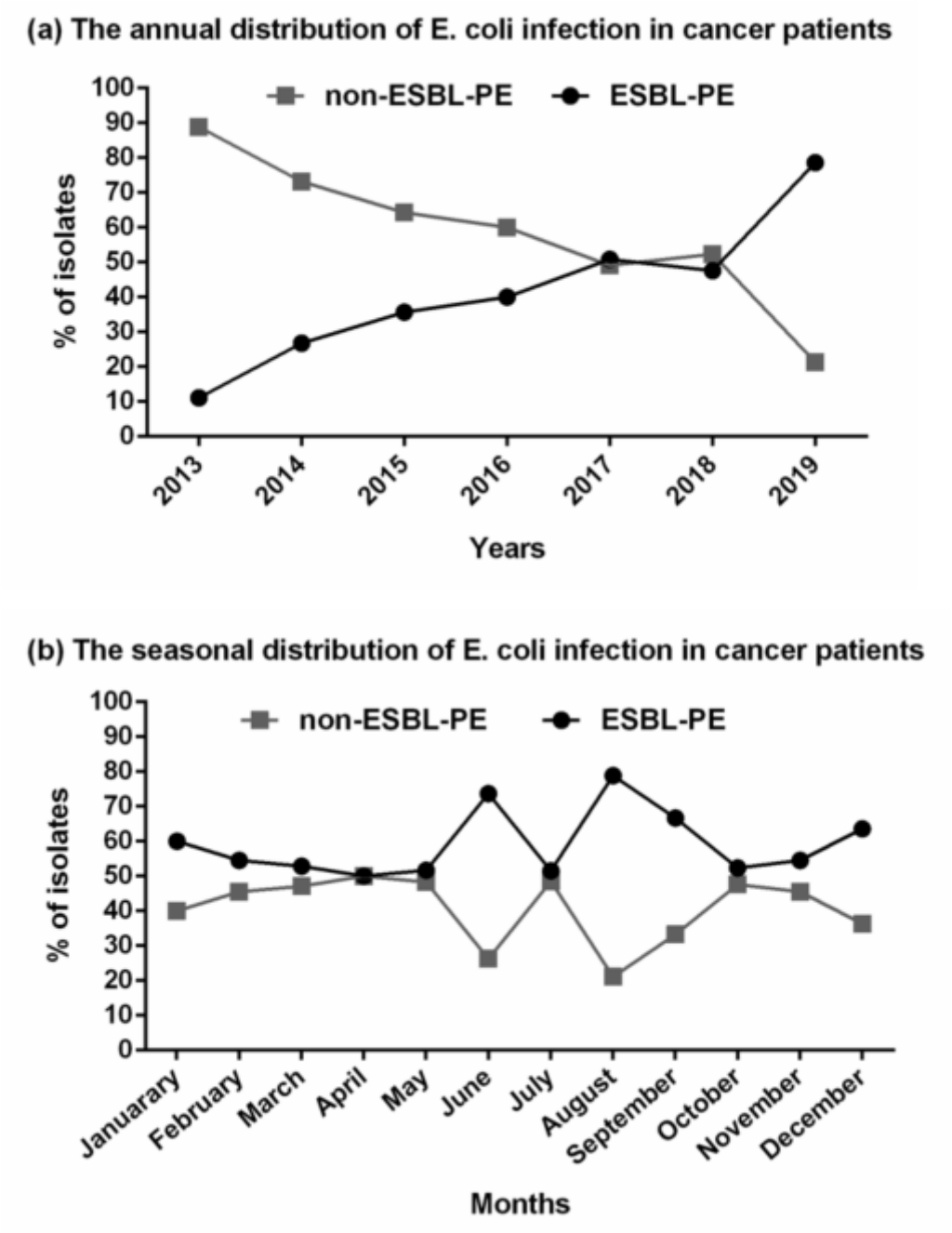

Figure 2

Trend in etiology of nosocomial infections in cancer patients caused by E. coli treated at the First Affiliated Hospital of Xi'an Jiaotong University between August 2013 to May 2019. (a) The annual distribution of E. coli infection in cancer patients. (b) The seasonal distribution of E. coli infection in cancer patients.

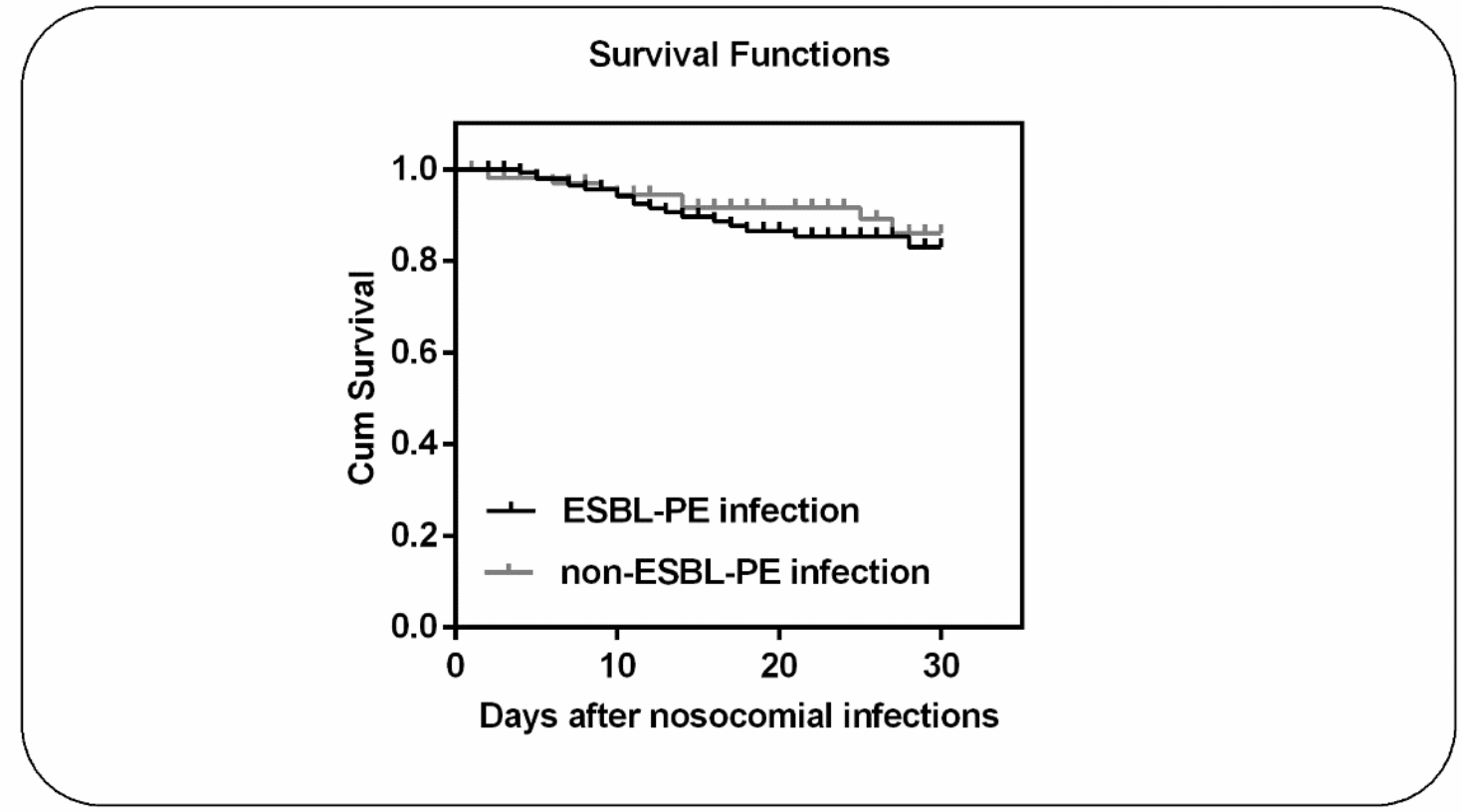

Figure 3

Kaplan-Meier 30-day survival estimates among cancer patients with nosocomial infections caused by ESBL-PE and non-ESBL-PE.

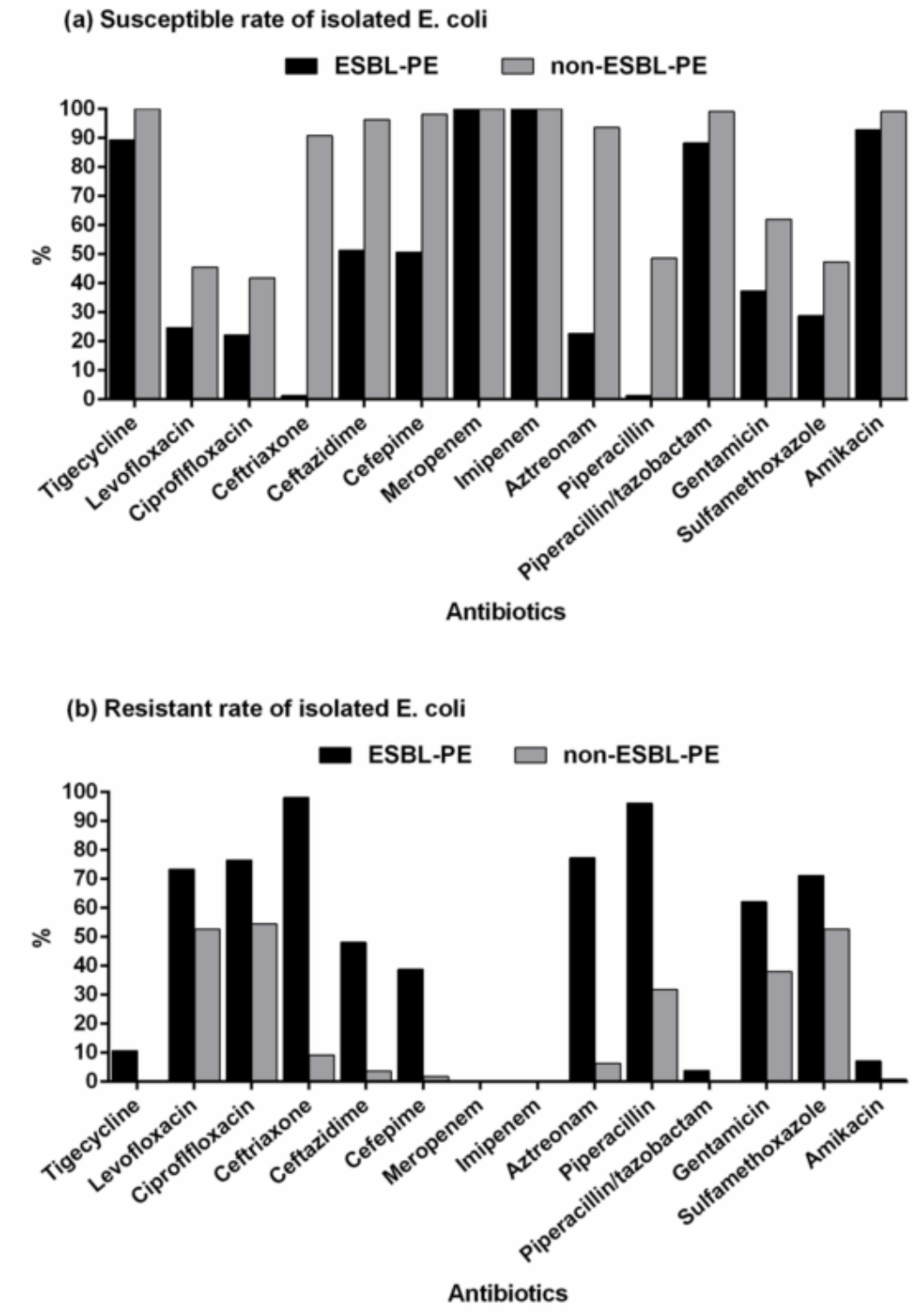

Figure 4

Antimicrobial susceptibility comparison among cancer patients with nosocomial infections caused by ESBL-PE and non-ESBL-PE. (a) Susceptible rate of isolated E. coli. (b) Resistant rate of isolated E. coli.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionnalfile1.docx