Systematic review on epidemiology of *Escherichia coli* in bloodstream infection of patients undergoing hematopoietic stem cell transplantation

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Abstract

Introduction **We aimed to conduct a systematic review of the epidemiology of *Escherichia coli* in bloodstream infections (BSI) of hematopoietic stem cell transplantation patients.**

Methods **For a comprehensive search of studies that reported the prevalence of *E. coli* and antibiotic resistance in bloodstream infections from 2000 to January 1, 2024, databases such as PubMed, EMBASE, Google Scholar, Scopus, and Web of Science were searched. The main keywords used were: *Escherichia coli*, epidemiology, bloodstream infection, microbial resistance, antibiotic resistance, hematopoietic malignancy, hematopoietic stem cell transplantation. After applying eligibility criteria, and quality assessment of studies, data analysis was done by comprehensive meta-analysis (CMA) software.**

Results **The prevalence of bacterial bloodstream infections amongst different studies varied between 8-51%. Also, bloodstream infections caused by *E. coli* varied between 2.5-57%. Prevalence of extended-spectrum β-lactamases (ESBLs) of *Escherichia coli* in bloodstream infections varied between 15-80%. As well, the mortality rate caused by *Escherichia coli* strains in bloodstream infection varied between 6.7-27.3%. Resistance to ciprofloxacin, cefepime, third- and fourth-generation cephalosporins, was reported to be the highest (prevalence of 100%), and the lowest was against amikacin, with a prevalence between 13-38%.**

Conclusions **The high prevalence of *Escherichia coli*-related BSI, and subsequent mortality, especially by multidrug resistance and ESBL strains, in patients undergoing hematopoietic stem cell transplantation, requires essential measures to prevent the spread of microbial resistance.**

Keywords ***Escherichia coli*, bloodstream infections, hematopoietic stem cell transplantation.**

Introduction

Hematological malignancies such as lymphatic and myeloid tumors are caused by disruption of normal hematopoietic function which include leukemia, non-Hodgkin lymphoma, multiple myeloma, and Hodgkin lymphoma.[1] Overall, the occurrence of hematologic malignancies has been growing since 1990, with prevalence of 1343.85 thousand in 2019.[2] The age-standardized death rate (ASDR) of 4.26, 1.42, 3.19, and 0.34 per 100,000 population in 2019, were respectively reported for leukemia, multiple myeloma, non-Hodgkin lymphoma, and Hodgkin lymphoma.[3]

Blood infection (BSI) is a common and serious complication with a prevalence of 12-46.2% in patients undergoing hematopoietic

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stem cell transplantation (HSCT).[4] This high rate of blood infection is associated with delay in chemotherapy, delay in patient discharge, increase in treatment, and antimicrobial costs.[5] In recent years, the use of targeted molecular therapeutic methods has reduced the risk of neutropenia in this group of patients.[6] Despite these measures, bacterial blood infections are still considered an important cause of death in stem cell transplant recipients.[7]

Both Gram-negative and Gram-positive microorganisms contribute to bloodstream infections of hematopoietic stem cell transplantation.[8] According to the geographical region, the type of microorganism and the pattern of microbial resistance is different. Today, due to the widespread use of broad-spectrum antibiotics, the rate of antibiotic resistance in strains of the Enterobacteriaceae family is increasing, of which a high quantity is attributed to *Escherichia coli*, whose prevalence in nosocomial infections is statistically significant.[9-11]

The increasing prevalence of multidrug-resistant (MDR) strains has become a widespread global concern today.[12] This is because the treatment of infections caused by these strains is very difficult, especially in HSCT patients who have a weak immune system, and has resulted in a high mortality rate. Therefore, it is very important to address this issue among the clinicians. Therefore, due to the lack of a comprehensive study, we tried to investigate the prevalence of *E. coli* and antibiotic resistance patterns in this systematic review.

Methods

Search strategy

We conducted a systematic review of epidemiology of *Escherichia coli* in bloodstream infections of hematopoietic stem cell transplantation patients. For a comprehensive search of studies that reported the prevalence of *E. coli* and antibiotic resistance in bloodstream infections of patients undergoing HSCT from 2000 to January 1, 2024, databases such as PubMed, EMBASE, Google Scholar, Scopus, and Web of Science were searched. The main keywords used were: *Escherichia coli*, *E. coli*, epidemiology, bloodstream infection, BSI, microbial resistance, antibiotic resistance, hematopoietic malignancy, hematopoietic stem cell transplantation, and HSCT. The review was performed by two reviewers independently. If there was a disagreement about inclusion of studies between the researchers, it was resolved through discussion, otherwise, a third researcher was asked for advice.

Eligibility criteria

Studies that correctly reported epidemiology (prevalence and microbial resistance) were included in this study. Review articles (narrative reviews, systematic reviews, and meta-analyses), case reports, meetings, and conferences were excluded.

Evaluation of the quality

The evaluation of the quality of the studies was done by the Critical Appraisal Skills Programme (CASP) checklist (www.casp-uk.net),[13] in which questions about the content of the studies, methodology, and how to present the results were raised. Finally, qualified studies were included and the remaining were excluded.

Extraction of data

Information such as first author, study type, geographical location, and year of publication, patients, bloodstream infection, and age were extracted and entered in designed forms.

Results

Study selection and characteristics

After searching, deleting duplicates, and applying all screening steps, finally, 30 studies were included in the present systematic review. Studies number from Turkey, Italy, Spain, Japan, Pakistan, Denmark, Thailand, Colombia, Germany, Brazil, China, Lebanon, Bulgaria, Belarus, Australia, USA, Egypt, South Korea, and other countries were respectively 2, 3, 2, 1, 1, 1, 1, 1, 1, 1, 3, 2, 1, 1, 1, 3, 1, 2, 1 (Table 1 and Figure 1).

Table 1. Features of articles included in the current review

First author	Study type	Geographical location	Year of publication	Patients (n)	Bloodstream infections
Denis Niyazi[25]	Retrospective	Bulgaria	2023	75	6/35 (17.1)
Qiang Zeng[15]	Retrospective	China	2022	741	65/741 (8.8)
Davide Mattei[2]	Retrospective	Italy	2022	111	149
Hyeah Choi[26]	Retrospective	South Korea	2022	334	380
Esma Eryilmaz-Eren[27]	Retrospective	Turkey	2022	553	68/553 (12.3)
Andrea J. Zimmer[28]	Cross-sectional observational	USA	2022	343	-
M. Weisser[29]	Prospective - cohort	Germany, Switzerland, Austria	2017	19 472	2388 (15.8)
Sara Haddad[3]	Retrospective	Lebanon	2021	165	226
Pedro Puerta-Alcalde[30]	Retrospective	Spain	2021	293	402
Elio Castagnola[8]	Retrospective	Multi-country	2021	1031	1291
Weijie Cao[7]	Retrospective	China	2021	397	52/397 (13.1)
Pedro Puerta-Alcalde[4]	Retrospective	Spain	2020	1164	1164
Sho Ogura[31]	Retrospective	Japan	2020	410	169/410 (41.2)
Paola Perez[32]	Retrospective cohort	Colombia	2019	111	46/111 (41.4)
Rima Moghnieh[22]	Retrospective	Lebanon	2018	190	24/190 (12.6)
A.M. Ferreira[33]	Retrospective	Brazil	2018	232	62/232 (26.7)
Michele Malagola[9]	Retrospective	Italy	2017	162	80/162 (49)
Gjærde[34]	Prospective - cohort	Denmark	2017	460	114/460 (24.7)
Worawut Choeyprasert[16]	Retrospective	Thailand	2017	215	33/215 (15.3)
Prakash Satwani[35]	Retrospective cohort	USA	2017	395	395
Sebastian Scheich[36]	Retrospective	Germany	2017	184	20/184 (10.9)
Igor Stoma[37]	Prospective observational	Belarus	2016	360	135/360 (27.5)
M.Yemişen[21]	Retrospective	Turkey	2016	312	142/312 (45.5)
L.Wang[23]	Retrospective	China	2015	273	85/273 (31.1)
N. Macesic[14]	Retrospective	Australia	2014	508	380/586 (51.2)
Hadir El-Mahallawy[38]	Retrospective	Egypt	2014	50	39/90 (43)
N. Ali[6]	Retrospective	Pakistan	2014	108	22
Michael J. Satlin[9]	Retrospective	USA	2014	-	306
Jae-Cheol Kwon[39]	Retrospective	South Korea	2013	159	159/851 (18.7)
M. Mikulska[40]	Retrospective	Italy	2011	382	149/382 (39)

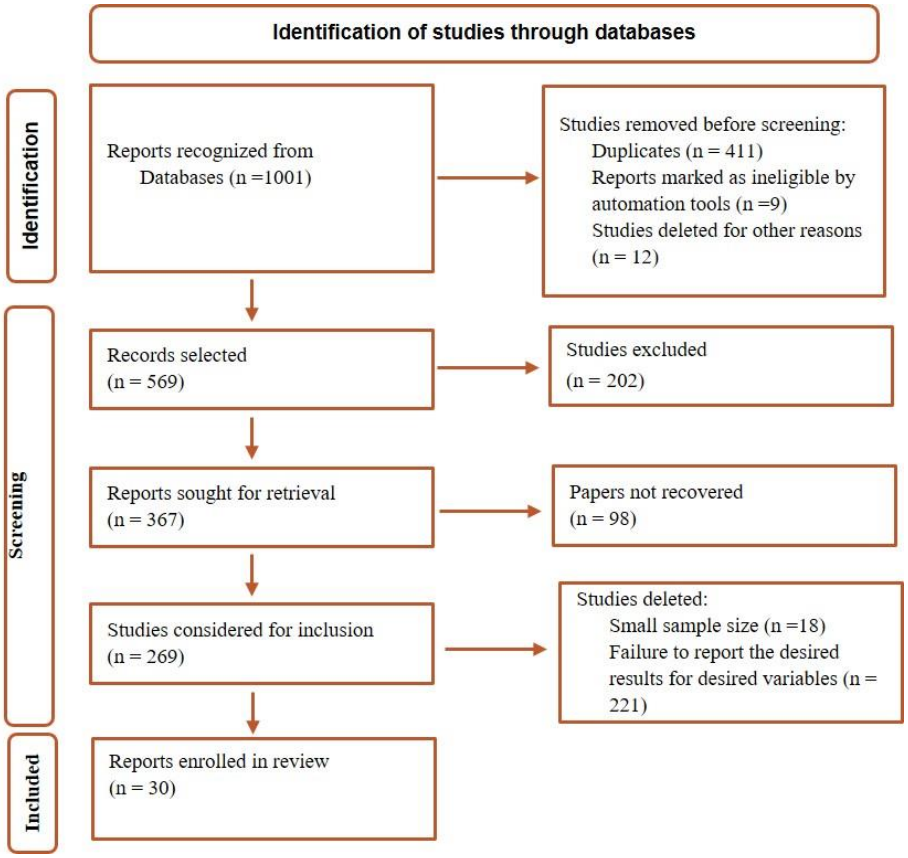

Figure 1. PRISMA diagram for studies screening

Prevalence of ESBL strains and mortality caused by *E. coli* strains

Prevalence of ESBLs strains of *E. coli* in bloodstream infections varied between 15-80%, whereas the mortality rate caused by *E. coli* strains in bloodstream infection varied between 6.7-27.3% (Table 2).

Antibiotic susceptibility in *E. coli* strains

As shown in Supplementary Table 1, resistance to ciprofloxacin, cefepime, third- and fourth-generation cephalosporins was reported to be the highest (prevalence of 100%), and the lowest was against amikacin with a prevalence of 13-38%. Also, resistance against fluoroquinolones was between 53-92%.

Discussion

As stated earlier, a large share of problems and deaths following bacterial blood infection in people undergoing stem cell transplantation is caused by Gram-negative bacteria, among which a significant part is represented by *E. coli*. For that, in our review, the prevalence of bacterial bloodstream infection amongst different studies varied between 8-41%. Also, BSI caused by *E. coli* varied between 2.5-57%. In some studies, a high BSI rate has been reported, for example, 51% by Macesic et al.,[14] while others have reported a moderate rate, and in some other studies, a low prevalence between 8% and 15% has been reported.[15,16]

Table 2. Features of articles listed in this review

First author	Location	*E. coli* ESBL strains	Bloodstream infections N (%)	Bloodstream infections by *E. coli* n (%)	Bloodstream infections-related death by *E. coli* n (%)
A.M. Ferreira	Brazil	-	62	8/67 (11.9)	-
Qiang Zeng	China	-	65/741 (8.8)	4/25	-
Moghniyee	Lebanon	-	24/190 (12.6)	7/24	-
Prakash Satwani	USA	-	395	50/848 (5.9)	-
Sara Haddad	Lebanon	82/103 (80)	226	103/226 (45.6)	-
Pedro Puerta-Alcalde	Spain	17/54 (31.5)	402	54/397 (13.4)	-
Sho Ogura	Japan	10/21 (47.6)	169/410 (41.2)	21/169 (12.4)	-
Denis Niyazi	Bulgaria	-	6	3/6	-
Igor Stoma	Belarus	-	135/360 (37.5)	25/135 (18.5)	-
L. Wang	China	-	85/273 (31.1)	36/85	3/11 (27.3)
N. Macesic	Australia	-	380/586 (51.2)	43/380 (11)	2/27 (7)
M. Yemişen	Turkey	3/13 (23)	142/312 (45.5)	13/142 (9.1)	-
M. Mikulska	Italy	-	149/382 (39)	25/149 (16.8)	10/149 (6.7)
Hadir El-Mahallawy	Egypt	-	39/90 (43)	1/39 (2.5)	
Gjærde	Denmark	-	114/460 (24.7)	7/147 (4.8)	
Jae-Cheol Kwon	South Korea	23/72 (32)	159/851 (18.7)	72/220 (32.7)	-
Davide Mattei	Italy	-	-	30/149 (20.1)	-
Pedro Puerta-Alcalde	Spain	21/140 (15)	1164	140/1164 (12)	-
N. Ali	Pakistan	-	22/108	10/25 (41)	8/108 (7.4)
Elio Castagnola	Multi-country	20.5%	1291	264/1289 (20.5)	-
Weijie Cao	China	7/15 (46.7)	52/397 (13.1)	15/52 (28.8)	-
Michele Malagola	Italy	18/24 (76)	80/162 (49)	24/80 (30)	8/80 (10)
Worawut Choeyprasert	Thailand	2/9 (18)	33/215 (15.3)	9/33 (27.3)	-
Michael J. Satlin	USA	-	306	39/306 (12.7)	-
Paola Perez	Colombia	-	-	6/46 (13)	-
Sebastian Scheich	Germany	-	20/184 (10.9)	3/20 (15)	-
Hyeah Choi	South Korea	40/107 (37.4)	380	107/380 (28.1)	-
Esma Eryilmaz-Eren	Turkey	-	68/553 (12.3)	39/68 (57.3)	-
Andrea J. Zimmer	USA	-	343	86/343 (25)	-

MDR – multidrug resistance; **ESBL** – extended-spectrum beta-lactamases.

The findings of our review showed that there was no statistically significant difference between the prevalence of bacterial BSI and *E.coli*-related BSI in HSCT patients in different parts of the world, and in some cases, the prevalence rate in Asian countries was reported to be lower than in European and American countries. This could be because the bacteria identification techniques in Asian countries may be weak and unable to detect. Maybe it is because today, with the development and improvement in molecular diagnostic techniques, different countries have become closer to each other in microbial diagnosis. However, the existence of differences in reports can be related to the site of infection, clinical samples, operator precision, diagnostic phenotypic methods, type of molecular techniques used, and geographical region.

Findings of the current review indicated the BSI caused by *E. coli* between 15-80%.[3,4] The high rate of prevalence of ESBL strains indicates an alarming increase in these strains, which must be taken seriously. This high trend is in accordance with the data obtained from other studies.[3,17] In addition, the data extracted from other studies showed that mortality caused by ESBL strains is higher compared to that cause by sensitive strains, which indicates a need for immediate

intervention and targeted treatment to prevent mortality in HSCT patients, who are more susceptible to BSI caused by MDR strains.[1,5,10,18,19]

The bloodstream infections caused by ESBLs became more important because studies from Asian and European countries reported a high prevalence.

Based on the results obtained from this review, resistance to ciprofloxacin, cefepime, and third- and fourth-generation cephalosporins was reported to be the highest, with a prevalence of 100%, and the lowest was against amikacin, with a prevalence of 13-38%. Also, resistance against fluoroquinolones was between 53-92%. These results indicated a very high resistance to antibiotics such as third generation cephalosporins and fluoroquinolones, and as a result, limit the choice of antibiotics for the treatment of BSI in patients undergoing HSCT, because American Society of Clinical Oncology/Infectious Diseases Society of America (ASCO/IDSA) recommends the use of fluoroquinolones for adult patients with immunosuppression associated with cancer at high risk of febrile neutropenia.[20] In addition, it should be noted that in hematological malignancies, the use of broad-spectrum antibiotic prophylaxis against Gram-negative bacteria, including *E. coli*, led to subsequent BSI with multidrug-resistant and ESBL pathogens.[3]

As presented, a high resistance against all antibiotics used in these studies was reported, and the interesting thing is that only a study conducted by M. Yemişen et al. reported a low resistance to all antibiotics used.[21] High resistance to fluoroquinolones has been reported by Michele Malagola et al.,[9] and Davide Mattei et al.,[2] which are used as prophylaxis in patients undergoing HSCT to prevent bacteremia. Resistance to carbapenems has also been reported to be high, as Moghnieh et al.,[22] and Wang et al.[23] reported a resistance between 75-83%, while Zeng et al. reported a resistance of about 16%.[15] This level of resistance is alarming; infection with carbapenemase-producing Enterobacteriaceae (KPC) strains has been reported to be 2%, while infection-related mortality has been reported to be 64%.[9] The difference in the level of antibiotic resistance can be due to reasons such as: the antibiogram method, geographical region, type of clinical sample, the amount of antibiotic use in each region, health and control measures against the spread of resistant strains, the amount of antibiotic use in agriculture and animal husbandry, and the antibiotic pressure due to the use of broad-spectrum antibiotics in each region.[7]

It is important to investigate BSI caused by *E. coli* because the studies conducted in recent decades showed that the trend of infection has changed from Gram-positive microorganisms to Gram-negative bacteria, including *E. coli*.[12,24] Inappropriate empirical therapy can be one of the reasons for drug resistance, which has subsequently led to an increase in BSI with MDR and ESBL strains[4], where a high mortality rate due to *E. coli*-related BSI, as reported by several studies, prove this claim.[23]

The most important limitation of this study was the lack of access to some articles, for which we contacted the authors but received no response. Another limitation was that languages other than English were not used for searching.

Conclusions

There is a high prevalence of *E. coli*-related BSI and subsequent mortality, especially by MDR and ESBL strains in patients undergoing HSCT, due to their greater susceptibility to infection. Essential measures are required to prevent the spread of microbial resistance. These measures can include monitoring colonization of patients, hand washing, avoiding arbitrary prescription of antibiotics, room isolation, personal protective equipment, proper use of disinfectants, non-use of broad-spectrum antibiotics, and prompt empirical antibiotic treatment.

Considering the challenge of BSI caused by MDR strains including *E. coli* in this group of patients, the use of alternative compounds such as plant extracts and nanoparticles should be considered.

Author contributions statement: FJ conceptualized the study; PA carried out the search process; MGS interpreted the findings; KB edited and revised the manuscript. All authors read and approved the final version of the manuscript.

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References

1. Mert D, Ceken S, Iskender G, et al. Epidemiology and mortality in bacterial bloodstream infections in patients with hematologic malignancies. J Infect Dev Ctries. 2019;13:727-35. https://doi.org/10.3855/jidc.11457
2. Mattei D, Baretta V, Mazzariol A, et al. Characteristics and outcomes of bloodstream infections in a tertiary-care pediatric hematology-oncology unit: a 10-year study. J Clin Med. 2022;11:880. https://doi.org/10.3390/jcm11030880
3. Haddad S, Jabbour JF, Hindy JR, et al. Bacterial bloodstream infections and patterns of resistance in patients with haematological malignancies at a tertiary centre in Lebanon over 10 years. J Glob Antimicrob Resist. 2021;27:228-35. https://doi.org/10.1016/j.jgar.2021.09.008
4. Puerta-Alcalde P, Cardozo C, Marco F, et al. Changing epidemiology of bloodstream infection in a 25-years hematopoietic stem cell transplant program: current challenges and pitfalls on empiric antibiotic treatment impacting outcomes. Bone Marrow Transplant. 2020;55:603-12. https://doi.org/10.1038/s41409-019-0701-3
5. Bow EJ. Fluoroquinolones, antimicrobial resistance and neutropenic cancer patients. Curr Opin Infect Dis. 2011;24:545-53. https://doi.org/10.1097/QCO.0b013e32834cf054
6. Ali N, Adil S, Shaikh MU. Bloodstream and central line isolates from hematopoietic stem cell transplant recipients: data from a developing country. Transpl Infect Dis. 2014;16:98-105. https://doi.org/10.1111/tid.12176
7. Cao W, Guan L, Li X, et al. Clinical analysis of bloodstream infections during agranulocytosis after allogeneic hematopoietic stem cell transplantation. Infect Drug Resist. 2021:185-92. https://doi.org/10.2147/IDR.S280869
8. Castagnola E, Bagnasco F, Mesini A, et al. Antibiotic resistant bloodstream infections in pediatric patients receiving chemotherapy or hematopoietic stem cell transplant: factors associated with development of resistance, intensive care admission and mortality. Antibiotics. 2021;10:266. https://doi.org/10.3390/antibiotics10030266
9. Malagola M, Rambaldi B, Ravizzola G, et al. Bacterial blood stream infections negatively impact on outcome of patients treated with allogeneic stem cell transplantation: 6 years single-centre experience. Mediterr J Hematol Infect Dis. 2017;9:e2017036.
10. Hosseini SMJ, Naeini NS, Khaledi A, Daymad SF, Esmaeili D. Evaluate the relationship between class 1 integrons and drug resistance genes in clinical isolates of *Pseudomonas aeruginosa*. Open Microbiol J. 2016;10:188-96. https://doi.org/10.2174/1874285801610010188
11. Jafarabadi M, Khaledi A. *Escherichia coli* bloodstream infections and associated antibiotic resistance pattern in hematological malignancy populations, a global systematic review. EJMO. 2024;8:15-23. https://doi.org/10.14744/ejmo.2024.79645
12. Mikulska M, Del Bono V, Raiola AM, et al. Blood stream infections in allogeneic hematopoietic stem cell transplant recipients: reemergence of Gram-negative rods and increasing antibiotic resistance. Biol Blood Marrow Transplant. 2009;15:47-53. https://doi.org/10.1016/j.bbmt.2008.10.024
13. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int J Health Policy Manag. 2014;3:123-8. https://doi.org/10.15171/ijhpm.2014.71
14. Macesic N, Morrissey C, Cheng A, Spencer A, Peleg AY. Changing microbial epidemiology in hematopoietic stem cell transplant recipients: increasing resistance over a 9 - year period. Transpl Infect Dis. 2014;16:887-96. https://doi.org/10.1111/tid.12298
15. Zeng Q, Xiang B, Liu Z. Profile and antibiotic pattern of blood stream infections of patients receiving hematopoietic stem cell transplants in Southwest China. Infect Drug Resist. 2022:2045-54. https://doi.org/10.2147/IDR.S358926
16. Choeyprasert W, Hongeng S, Anurathapan U, Pakakasama S. Bacteremia during neutropenic episodes in children undergoing hematopoietic stem cell transplantation with ciprofloxacin and penicillin prophylaxis. Int J Hematol. 2017;105:213-20. https://doi.org/10.1007/s12185-016-2113-0
17. Trecarichi EM, Tumbarello M, Spanu T, et al. Incidence and clinical impact of extended-spectrum-β-lactamase (ESBL) production and fluoroquinolone resistance in bloodstream infections caused by *Escherichia coli* in patients with hematological malignancies. J Infect. 2009;58:299-307. https://doi.org/10.1016/j.jinf.2009.02.002
18. Liang T, Xu C, Cheng Q, Tang Y, Zeng H, Li X. Epidemiology, risk factors, and clinical outcomes of bloodstream infection due to extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in hematologic malignancy: a retrospective study from Central South China. Microb Drug Resist. 2021;27:800-8. https://doi.org/10.1089/mdr.2020.0033
19. Mohsenzadeh M, Abtahi-Eivary SH, Pirouzi A, Khaledi A, Rahimi M. A systematic review and meta-analysis of urinary tract infection, frequency of IS elements and MDR isolates retrieved from adult patients. Gene Rep. 2020;20:100707. https://doi.org/10.1016/j.genrep.2020.100707

20. Taplitz RA, Kennedy EB, Bow EJ, et al. Antimicrobial prophylaxis for adult patients with cancer-related immunosuppression: ASCO and IDSA clinical practice guideline update. J Clin Oncol. 2018;36:3043-54. https://doi.org/10.1200/JCO.18.00374
21. Yemişen M, Balkan İİ, Salihoğlu A, et al. The changing epidemiology of bloodstream infections and resistance in hematopoietic stem cell transplantation recipients. Turk J Hematol. 2016;33:216-22. https://doi.org/10.4274/tjh.2014.0378
22. Moghnieh R, Abdallah D, Awad L, et al. Bacteraemia post-autologous haematopoietic stem cell transplantation in the absence of antibacterial prophylaxis: a decade's experience from Lebanon. Infection. 2018;46:823-35. https://doi.org/10.1007/s15010-018-1200-y
23. Wang L, Wang Y, Fan X, Tang W, Hu J. Prevalence of resistant Gram-negative bacilli in bloodstream infection in febrile neutropenia patients undergoing hematopoietic stem cell transplantation: a single center retrospective cohort study. Medicine. 2015;94:e1931. https://doi.org/10.1097/MD.0000000000001931
24. Gudiol C, Garcia-Vidal C, Arnan M, et al. Etiology, clinical features and outcomes of pre-engraftment and post-engraftment bloodstream infection in hematopoietic SCT recipients. Bone Marrow Transplant. 2014;49:824-30. https://doi.org/10.1038/bmt.2014.37
25. Niyazi D, Stoeva T. In vitro activity of ceftazidime-avibactam against 3rd generation cephalosporin and carbapenem resistant Gram-negative bacteria obtained from blood and fecal samples of hematopoietic stem cell transplanted patients. Acta Microbiol Bulg. 2023;39:78-82. https://doi.org/10.59393/amb23390111
26. Choi H, Ahn H, Lee R, Cho S-Y, Lee DG. Bloodstream infections in patients with hematologic diseases: causative organisms and factors associated with resistance. Infect Chemother. 2022;54:340-52. https://doi.org/10.3947/ic.2022.0069
27. Eryilmaz-Eren E, Izci F, Ture Z, Sagiroglu P, Kaynar L, Ulu-Kilic A. Bacteremia in hematopoietic stem cell recipients receiving fluoroquinolone prophylaxis: incidence, resistance, and risk factors. Infect Chemother. 2022;54:446-55. https://doi.org/10.3947/ic.2022.0005
28. Zimmer AJ, Stohs E, Meza J, et al. Bloodstream infections in hematologic malignancy patients with fever and neutropenia: are empirical antibiotic therapies in the United States still effective? Open Forum Infect Dis. 2022;9:ofac240. https://doi.org/10.1093/ofid/ofac240
29. Sava M, Bättig V, Gerull S,. Bloodstream infections in allogeneic haematopoietic cell recipients from the Swiss Transplant Cohort Study: trends of causative pathogens and resistance rates. Bone Marrow Transplant. 2023;58:115-8. https://doi.org/10.1038/s41409-022-01851-y
30. Puerta-Alcalde P, Chumbita M, Charry P, et al. Risk factors for mortality in hematopoietic stem cell transplantation recipients with bloodstream infection: points to be addressed by future guidelines. Transplant Cell Ther. 2021;27:501.e1-6. https://doi.org/10.1016/j.jtct.2021.03.017
31. Ogura S, Kimura M, Takagi S, et al. Characteristics of gram-negative bacteremia during febrile neutropenia among allogeneic hematopoietic stem cell transplant recipients on levofloxacin prophylaxis. Eur J Clin Microbiol Infect Dis. 2021;40:941-8. https://doi.org/10.1007/s10096-020-04096-z
32. Perez P, Patiño J, Estacio M, Pino J, Manzi E, Medina D. Bacteremia in pediatric patients with hematopoietic stem cell transplantation. Hematol Transfus Cell Ther. 2020;42:5-11. https://doi.org/10.1016/j.htct.2019.05.006
33. Ferreira AM, Moreira F, Guimaraes T, et al. Epidemiology, risk factors and outcomes of multi-drug-resistant bloodstream infections in haematopoietic stem cell transplant recipients: importance of previous gut colonization. J Hosp Infect. 2018;100:83-91. https://doi.org/10.1016/j.jhin.2018.03.004
34. Gjaerde LI, Moser C, Sengeløv H. Epidemiology of bloodstream infections after myeloablative and non - myeloablative allogeneic hematopoietic stem cell transplantation: a single - center cohort study. Transpl Infect Dis. 2017;19:e12730. https://doi.org/10.1111/tid.12730
35. Satwani P, Freedman JL, Chaudhury S, et al. A multicenter study of bacterial blood stream infections in pediatric allogeneic hematopoietic cell transplantation recipients: the role of acute gastrointestinal graft-versus-host disease. Biol Blood Marrow Transplant. 2017;23:642-7. https://doi.org/10.1016/j.bbmt.2017.01.073
36. Scheich S, Reinheimer C, Brandt C, et al. Clinical impact of colonization with multidrug-resistant organisms on outcome after autologous stem cell transplantation: a retrospective single-center study. Biol Blood Marrow Transplant. 2017;23:1455-62. https://doi.org/10.1016/j.bbmt.2017.05.016
37. Stoma I, Karpov I, Milanovich N, Uss A, Iskrov I. Risk factors for mortality in patients with bloodstream infections during the pre-engraftment period after hematopoietic stem cell transplantation. Blood Res. 2016;51:102-6. https://doi.org/10.5045/br.2016.51.2.102
38. El-Mahallawy H, Samir I, Fattah RA, Kadry D, El-Kholy A. Source, pattern and antibiotic resistance of blood stream infections in hematopoietic stem cell transplant recipients. J Egyp Natl Canc Inst. 2014;26:73-7. https://doi.org/10.1016/j.jnci.2013.12.001
39. Kwon JC, Kim SH, Choi JK, et al. Epidemiology and clinical features of bloodstream infections in hematology wards: one year experience at the catholic blood and marrow transplantation center. Infect Chemother. 2013;45:51-61. https://doi.org/10.3947/ic.2013.45.1.51

40. Mikulska M, Del Bono V, Bruzzi P, et al. Mortality after bloodstream infections in allogeneic haematopoietic stem cell transplant (HSCT) recipients. Infection. 2012;40:271-8. https://doi.org/10.1007/s15010-011-0229-y

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Supplementary Table 1. Antimicrobial resistance of *E. coli* in the current review

First author	*E. coli* n	Antibiotics Resistance pattern n/%									
		CIP	TZP	FEP	Third- and fourth-generation cephalosporins	Carbapenems	Fluoroquinolones	SXT	CAZ	CRO	AM
M. Yemişen		4/13 (30.8)	3/13 (23)	2/13 (15.4)	-	-	-	-	3/13 (23)	3/13 (23)	5/13 (38.5)
A.M. Ferreira	8	8/8	0	5	-	-	-	-	-	-	-
Rima Moghnieh	6	6/6 (100)	5/6 (83.3)	6/6 (100)	6/6 (100)	5/6 (83.3)	-	4/6 (66.7)	-	-	-
Michele Malagola	24	-	-	-	-	0	22 (92)	-	-	-	-
Qiang Zeng	25	-	-	-	-	4/25 (16)	-	-	-	-	-
L. Wang	36	-	-	-	-	27/36 (75)	-	-	-	-	-
Weijie Cao	15	12/15 (80)	5/15 (33.3)	7/15 (46.7)	-	-	-	13/15 (86.7)	8/15 (87.1)	12/15 (80)	2/15 (13.3)
Davide Mattei	30	-	-	-	9/30 (30)	0	16/30 (53.3)	-	-	-	-

CIP – ciprofloxacin; **CAZ** – ceftazidime; **CRO** – ceftriaxone; **TZP** – piperacillin/tazobactam; **FEP** – cefepime; **SXT** – sulfamethoxazole/trimethoprim; **AM** – amikacin.