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Original Article

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Bacteremia in Hematopoietic Stem Cell Recipients Receiving Fluoroquinolone Prophylaxis: Incidence, Resistance, and Risk Factors

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ABSTRACT

Background: Bacteremia is a common complication in hematopoietic stem cell transplant (HSCT) recipients. Prophylactic fluoroquinolone is recommended and used in these individuals. Breakthrough infections can occur with fluoroquinolone-resistant strains. We aimed to identify the incidence, resistance, and risk factors for bacteremia in HSCT recipients receiving fluoroquinolone prophylaxis.
Materials and Methods: This retrospective study was performed on patients who received fluoroquinolone prophylaxis and underwent autologous and allogeneic HSCT between 2015 and 2019. The incidence of bacteremia, comorbidity, treatment, and invasive procedures was compared in these patients with and without bacteremia.
Results: There were 553 patients included in the study, 68 (12.3%) had bacteremia. The incidence of bacteremia is 8.2% of autologous HSCT recipients and 18.4% of allogeneic HSCT recipients. The significant risk factors associated with bacteremia were steroid-using (odds ratio [OR]:13.83, 95% confidence interval [CI]: 2.88 - 66.40), higher Charlson Comorbidity Index (CCI)-mean (OR: 1.57, 95% CI: 1.15 - 2.16), diabetes mellitus (OR: 4.29, 95% CI: 1.11 - 16.48) in autologous HSCT, steroid-using (OR: 6.84, 95% CI: 1.44 - 32.33), longer duration of neutropenia (OR: 1.05, 95% CI: 1.01 - 1.09) using central venous catheter (OR: 7.81, 95% CI: 1.00 - 61.23) in allogeneic HSCT. Seventy-three pathogens were isolated from a total of 68 bacteremia episodes. The most commonly occurring agents were *Escherichia coli, Klebsiella pneumoniae* and *Enterococcus* spp. Resistance to fluoroquinolones was 87.2%, 70.0% and 60.0% among these strains, respectively.
Conclusion: High CCI, diabetes mellitus, use of steroids and long-term neutropenia and use of central venous catheters were significantly associated with the breakthrough bacteremia in HSCT recipients receiving fluoroquinolone prophylaxis. Fluoroquinolone prophylaxis may reduce the incidence of bacteremia but may select strains resistant to fluoroquinolone.

Keywords: Fluoroquinolone; Hematopoietic stem cell recipients; Bacteremia

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INTRODUCTION

Bacteremia is one of the main causes of morbidity and mortality in hematopoietic stem cell transplantation (HSCT) recipients [1]. Depending on the protocol used for transplantation and the duration of neutropenia, its incidence increases as much as 20.0% of autologous HSCT recipients and 40.0% in allogeneic HSCT recipients [2-4]. This may lead to delays in chemotherapy and increased costs of antimicrobial treatment for target organisms. Oral fluoroquinolone prophylaxis has been demonstrated to decrease the incidence of febrile neutropenic episodes and mortality in neutropenic patients [5]. Prophylaxis with fluoroquinolones is recommended because of their activity against both Gram-positive and Gram-negative microorganisms and their high oral bioavailability [6]. Although there was no significant difference in mortality in HSCT recipients, it was determined that the incidence of bloodstream infections and febrile neutropenia decreased [7, 8].

Despite these benefits of prophylaxis, increased resistance to fluoroquinolones is a concern [9]. Resistance in our region is to reach a 50.0% level for *Enterobacteriaceae*, and this is a condition that should be considered in quinolone prophylaxis [10].

In this study, we aimed to identify the incidence, resistance and risk factors for bacteremia in HSCT recipients receiving fluoroquinolone prophylaxis.

MATERIALS AND METHODS

1. Patients

This retrospective study was conducted in a tertiary hospital with a 38-bed hematology unit and a 37-bed HSCT unit. Adult patients (>18 years of age) undergoing HSCT for the first time between January 2015 and December 2019 and using fluoroquinolone prophylaxis in the neutropenic period were included. The clinical characteristics, transplantation protocols, comorbidities, Charlson Comorbidity Index (CCI) and microbiological data of the patients were obtained from hospital data processing system records. Recurrent infections were excluded.

2. Ethics statement

The clinical study was approved by ethics committee of the Kayseri City Hospital (Date: 25.06.2020 Number: 107). Since it was a retrospective file screening study, consent was not obtained from the patients.

3. Institutional protocol for allogeneic or autologous HSCT

The patients were followed up in a single-room unit using a high-efficiency particulate filter. Central nutrition and drug infusion were performed with a central catheter (central venous or Hickman catheter or port). Granulocyte colony-stimulating factor administration was started on the day of transplantation and continued until engraftment.

4. Infection control procedures and prophylaxis

Patients gargle with 0.2% chlorhexidine gluconate solution every 12 hours from the start of the conditioning chemotherapy until the mucositis resolves.

Infection prophylaxis and management; All patients were given acyclovir as antiviral prophylaxis from the start of chemotherapy to engraftment. Oral fluconazole tablet

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was used as antifungal prophylaxis in autologous HSCT recipients, oral suspension or posaconazole tablet was used in allogeneic HSCT recipients. All HSCT recipients were given prophylaxis with oral moxifloxacin 400 mg/day or levofloxacin 500 mg/day to prevent bacterial infections until neutropenia was resolved or neutropenic fever. Surveillance cultures (stool, urine, throat, nose, rectal, and blood) were performed from all patients at the hospitalization.

5. Microbiological protocol

If the patient had a fever >38.3°C once or >38°C on two consecutive measurements within the first 100 days post-transplant, a blood culture was obtained prior to administration of empirical antimicrobial therapy. A 10 ml blood sample was drawn from a peripheral venous vein and incubated in a BacT/ALERT® 3D (BioMérieux Inc., Durham, NC, USA) blood culture vial. Microorganisms grown within five days were recorded.

An organism other than coagulase-negative Staphylococci (CNS) was considered a cause of bacteremia when it grew in one or more vials. CNS were accepted as causative agents if they grew in two different blood cultures with the same antibiotic sensitivity pattern. A combination of a Vitek 2 system (BioMérieux, Marcyl'Étoile, France) and traditional methods was used to identify the species and reveal the resistance pattern, according to the recommendations of the European Committee for Antimicrobial Susceptibility Testing (EUCAST).

6. Statistical analyses

Statistical analysis was performed using the SPSS 22.0 version (IBM Corp., Armonk, NY, USA) package program. Categorical variables were expressed as numbers and percentages, and Chi-square or Fisher's Exact Test analysis was used for comparisons. Shapiro-Wilks test was performed to determine whether continuous variables showed normal distribution. Parametric data; mean ± standard deviation was shown as mean ± standard deviation, while intergroup significance was determined using the Student's *t*-test. Non-parametric data are; median (min - max) and intergroup significance were determined using the Mann Whitney *U* test. In all analyses, $P < 0.05$ was considered statistically significant. Variables that *P*-value ≤0.05 were included in the multivariate logistic regression analysis and variables with a *P*-value of <0.05 in the analysis were determined as risk factors for bacteremia.

RESULTS

1. Patient Characteristics

HSCT was performed on a total of 553 patients and used fluoroquinolone prophylaxis during the peri-transplantation period between January 2015 and December 2019. The mean age of the patients was 48.4 (± 14.6), range (17 - 82). Totally, 61.8% of patients were male. The most common hematologic malignancies were multiple myeloma (36.5%), acute myeloid leukemia (21.9%), and non-Hodgkin lymphoma (13.6%), respectively. Autologous HSCT was performed in 59.7% of patients and allogeneic HSCT in 40.3%. As antibacterial prophylaxis, 89.9% of the patients had received levofloxacin, and 10.1% had received moxifloxacin. The mean neutropenia duration was 15.1 (± 7.6) range (4 - 60) days. The most common comorbidity was hypertension (15.1%), and the mean CCI of all patients was 3.1 (± 1.8), range (0 - 11). The clinical characteristics of the patients are presented in **Table 1**.

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Table 1. Demographic and clinical characteristics of hematopoietic stem cell transplantation recipients

Characteristics	Total N = 553 (%)	Autologous N = 330 (%)	Allogeneic N = 223 (%)
Gender (F/M)	211/342 (38.2/61.8)	119/211 (36.1/63.9)	92/131 (41.3/58.7)
Age mean (± SD), years	48.4 (± 14.6)	52.6 (± 12.9)	42.1 (± 14.7)
Hematological cancer diagnosis			
Multiple myeloma	202 (36.5)	200 (60.6)	2 (0.9)
Acute myeloid leukemia	121 (21.9)	-	121 (54.3)
Non-Hodgkin lymphoma	75 (13.6)	71 (21.5)	4 (1.8)
Hodgkin lymphoma	49 (8.9)	43 (13.0)	6 (2.7)
Acute lymphoblastic leukemia	32 (5.8)	1 (0.3)	31 (13.9)
Myelodysplastic syndrome	20 (3.6)	-	20 (9.0)
Myelofibrosis	14 (2.5)	-	14 (6.3)
Aplastic anemia	15 (2.7)	-	15 (6.7)
Germ cell tumor	10 (1.8)	10 (3.0)	-
Diffuse large B cell lymphoma	9 (1.6)	9 (2.7)	-
Others	15 (2.7)	5 (1.5)	10 (4.5)
Conditioning Regimen	179 (32.0)	-	179 (80.3)
Graft *vs.* host disease (GVHD)	20 (3.6)	-	20 (9.0)
Grade of GVHD median (min - max)	2 (1 - 4)	-	2 (1 - 4)
Steroid	35 (6.3)	11 (3.3)	24 (10.8)
Steroid dose (methylprednisolone, mg/kg, day) median (min - max)	1 (1 - 5)	1 (1 - 5)	1 (1 - 5)
Duration of neutropenia mean (± SD), day	15.1 (± 7.6)	12.0 (± 4.9)	19.7 (± 8.6)
Prophylaxis			
Moxifloxacin/Levofloxacin	56/497 (10.1/89.9)	28/302 (8.5/91.5)	28/195 (12.6/87.4)
Comorbidities			
Charlson comorbidity index mean (± SD)	3.1 (± 1.8)	3.1 (± 1.7)	3.1 (± 1.8)
Hypertension	98 (15.2)	71 (21.5)	27 (12.1)
Diabetes mellitus	67 (12.1)	36 (10.9)	31 (13.9)
Coronary arter disease	58 (10.5)	37 (11.2)	21 (9.4)
Chronic obstructive pulmonary disease	31 (5.6)	24 (7.3)	7 (3.1)
Chronic kidney disease	39 (7.1)	20 (6.1)	19 (8.5)
Human immunodeficiency virus	1 (0.01)	-	1 (0.3)
Invasive Procedures			
Hemodialysis	28 (5.1)	11 (3.3)	17 (7.6)
Total parenteral nutrition	139 (25.1)	79 (23.9)	60 (26.9)
Central venous catheter	474 (85.7)	287 (87.0)	187 (83.9)
Port catheter	22 (4.0)	10 (3.0)	12 (5.4)
Hickman catheter	57 (10.3)	33 (10.0)	24 (10.8)

F, female; M, male; SD, standart deviation.

2. Incidence and risk factors of bacteremia

There were 68 patients (12.3%) with bacteremia over the study period. The incidence of bacteremia was 12.2% in all patients, 8.2% of autologous HSCT recipients and 18.4% in allogeneic HSCT recipients. Risk factors of bacteremia in autologous and allogeneic HSCT recipients were presented in **Table 2**. In autologous HSCT patients, steroid-using was used more frequently in the bacteremia group (P <0.001). Patients in the bacteremia group had a higher CCI [(mean ± SD) 5.6 ± 2.8 *vs.* 2.9 ± 1.4, P <0.001)], prevalence of diabetes mellitus (DM) [48.1% *vs.* 10.9%, P <0.001], and chronic kidney disease (P <0.001) than non-bacteremia [25.9% *vs.* 6.1%]. Among invasive procedures, the central venous catheter was used more frequently in patients with bacteremia (P <0.001). The most common hematological malignancy in patients with non-bacteremia was multiple myeloma (P = 0.013).

In allogeneic HSCT recipients, consolidation therapy and steroid were used more frequently in the bacteremia group (P <0.001, P = 0.003, respectively). Graft versus host disease was more common in patients with bacteremia (P = 0.004). Patients with bacteremia had a longer duration of neutropenia than patients without bacteremia [(mean ± SD) 24.4 ± 11.3

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Table 2. Risk factors for bacteremia in autologous and allogeneic hematopoietic stem cell recipients received fluoroquinolone prophylaxis

Characteristics	Autologous				Allogeneic			
	Non-bacteremia n = 303 (%)	Bacteremia n = 27 (%)	*P*-value	OR (95% CI)	Non-bacteremia n = 182 (%)	Bacteremia n = 41 (%)	*P*-value	OR (95% CI)
Gender (F/M)	108/195 (35.6/64.4)	11/16 (40.7/59.3)	0.677		75/107 (41.1/58.9)	17/24 (58.5/41.5)	1.000	
Age mean (± SD), year	52.6 (± 13.0)	52.6 (± 11.8)	0.983		41.8 (± 15.0)	43.5 (± 13.3)	0.516	
Hematological cancer diagnosis								
Multiple myeloma	190 (62.7)	10 (37.0)	**0.013**		2 (1.1)	-	1.000	
Acute myeloid leukemia	-	-			97 (53.3)	24 (58.5)	0.605	
Non-Hodgkin lymphoma	61 (20.1)	10 (37.0)	0.051		3 (1.6)	1 (2.4)	0.559	
Hodgkin lymphoma	37 (12.2)	6 (22.2)	0.141		6 (3.3)	-	0.596	
Acute lymphoblastic leukemia	1 (0.3)	-	1.000		26 (14.3)	5 (12.2)	1.000	
Myelodysplastic syndrome					16 (8.8)	4 (9.8)	0.769	
Myelofibrosis					12 (6.6)	2 (4.9)	1.000	
Aplastic anemia					11 (6.0)	4 (9.8)	0.486	
Germ cell tumor	9 (3.0)	1 (3.7)	0.579					
Diffuse large B cell lymphoma	7 (2.3)	2 (7.4)	0.162					
Others	5 (1.7)	-	1.000		9 (4.9)	1 (2.4)	0.693	
Therapies								
Conditioning regimen					149 (81.9)	30 (73.2)	0.276	
Graft versus host disease (GVHD)					11 (6.0)	9 (22.0)	**0.004**	
Grade of GVHD median (min - max)					1 (1 - 3)	2 (1 - 4)	0.175	
Steroid	5 (1.7)	6 (22.2)	**<0.001**	13.8 (2.9 - 66.4)	11 (6.0)	13 (31.7)	**<0.001**	6.8 (1.4 - 32.3)
Steroid dose (methylprednisolone, mg/kg, day), median (min - max)	1 (1 - 5)	1.5 (1 - 2)	1.000		1 (1 - 5)	2 (1 - 5)	0.280	
Duration of Neutropenia mean (± SD), day	12.1 (± 5.1)	11.8 (± 1.2)	0.760		18.6 (± 7.5)	24.4 (± 11.3)	**0.003**	1.0 (1.0 - 1.1)
Prophylaxis								
Moxifloxacin/Levofloxacin	23/280 (7.6/92.4)	5/22 (18.5/81.5)	0.065		23/159 (12.6/87.4)	5/36 (12.2/87.8)	1.000	
Comorbidities								
Charlson comorbidity index mean (± SD)	2.9 (± 1.4)	5.6 (± 2.8)	**<0.001**	1.6 (1.1 - 2.2)	3.0 (± 1.8)	4.0 (± 1.8)	**0.003**	
Hypertension	66 (21.8)	5 (7.0)	0.811		23 (12.6)	4 (9.8)	0.793	
Diabetes mellitus	23 (7.6)	13 (48.1)	**<0.001**	4.3 (1.1 - 16.5)	18 (9.9)	13 (31.7)	**0.001**	
Coronary arter disease	32 (10.6)	5 (18.5)	0.206		18 (9.9)	3 (7.3)	0.773	
Chronic obstructive pulmonary disease	21 (6.9)	3 (11.1)	0.431		6 (3.3)	1 (2.4)	1.000	
Chronic kidney disease	13 (4.3)	7 (25.9)	**<0.001**		13 (7.1)	6 (14.6)	0.128	
Human immunodeficiency virus	-	1 (3.7)	0.082		-	-		
Invasive Procedures								
Hemodialysis	10 (3.3)	1 (3.7)	1.000		16 (8.8)	1 (2.4)	0.324	
Total parenteral nutrition	68 (22.4)	11 (40.7)	0.056		53 (29.1)	7 (17.1)	0.124	
Central venous catheter	260 (85.8)	27 (9.4)	**0.034**		147 (80.8)	40 (97.6)	**0.005**	7.8 (1.0 - 61.2)
Port catheter	10 (3.3)	-	1.000		12 (6.6)	-	0.130	
Hickman catheter	33 (10.9)	-	0.091		23 (12.6)	1 (2.4)	0.089	

OR, odds ratio; CI, confidence interval; F, female; M, male; SD, standard deviation.

days *vs.* 18.6 ± 7.5 days, $P = 0.003$]. Patients in the bacteremia group had a higher CCI [(mean ± SD) 4.0 ± 1.8 *vs.* 3.0 ± 1.8, $P = 0.003$], prevalence of DM [31.7% *vs.* 9.9%, $P = 0.001$], than non-bacteremia and central venous catheter were used more frequently in patients with bacteremia ($P = 0.005$).

In multivariate analysis, steroid using (odds ratio [OR]: 13.83, 95% confidence interval [CI]: 2.88 - 66.40, $P = 0.001$), higher CCI mean (OR: 1.57, 95% CI: 1.15 - 2.16, $P = 0.005$), DM (OR: 4.29, 95% CI: 1.11 - 16.48, $P = 0.034$) were identified as the significant risk factors for bacteremia in autologous HSCT recipients; steroid use (OR: 6.84, 95% CI: 1.44 - 32.33, $P = 0.015$), longer duration of neutropenia (OR: 1.05, 95% CI: 1.01 - 1.09, $P = 0.013$), a central venous catheter (OR: 7.81, 95% CI: 1.00 - 61.23, $P = 0.049$) were identified allogeneic HSCT recipients.

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Table 3. Isolates and susceptibility rates to antibiotics

Frequency of microorganisms, n (%)	AMP/SAM (%)	CIP/LVX/MXF (%)	CRO/CAZ (%)	FEP (%)	TZP (%)	IPM/MEM (%)	AMK (%)	CST (%)	TMP/SMX (%)	MET (%)	VAN (%)
Gram-negatives, 57 (80.2)											
Escherichia coli, 39 (53.4)	13/30 (43.3)	5/39 (12.8)	23/33 (63.6)	10/25 (40.0)	13/24 (54.2)	18/19 (94.7)	26/27 (96.3)	-	2/5 (40.0)		
Klebsiella pneumoniae, 10 (13.7)	2/8 (25.0)	3/10 (30.0)	3/9 (33.3)	2/3 (66.7)	4/8 (50.0)	4/8 (50.0)	6/9 (66.7)	2/3 (66.7)	1/5 (20.0)		
Enterobacter spp., 3 (4.1)	1/3 (33.3)	3/3 (100.0)	2/2 (100.0)	-	-	-	3/3 (100.0)	-	-		
Pseudomonas aeruginosa, 2 (2.7)	-	0/2 (0.0)	2/2 (100.0)	2/2 (100.0)	2/2 (100.0)	2/2 (100.0)	2/2 (100.0)	2/2 (100.0)	-		
Stenotrophomonas maltophilia, 2 (2.7)	-	1/2 (100.0)	2/2 (100.0)	-	-	-	-	-	2/2 (100.0)		
Acinetobacter spp., 1 (1.4)	1/1 (100.0)	1/1 (100.0)	-	1/1 (100.0)	-	1/1 (100.0)	-	1/1 (100.0)	-		
Gram-positives, 16 (19.8)											
Enterococcus spp., 10 (13.7)	2/9 (22.2)	4/10 (40.0)	-	-	-	-	-	-	-	-	9/10 (90.0)
Coagulase negative *staphylococcus* 4 (5.5)	2/4 (50.0)	2/4 (50.0)	-	-	-	-	-	-	-	1/4 (25.0)	4/4 (100.0)
Staphylococcus aureus, 2 (2.7)	1/1 (50.0)	1/1 (50.0)	-	-	-	-	-	-	-	2/2 (100.0)	2/2 (100.0)

AMP, ampicillin; SAM, ampicillin-sulbactam; CIP, ciprofloxacin; LVX, levofloxacin; MXF, moxifloxacin; CRO, ceftriaxone; CAZ, ceftazidime; FEP, cefepime; TZP, piperacillin-tazobactam; IPM, imipenem/cilastatin; MEM, meropenem; AMK, amikacin; CST, colistin; TMP/SMX, trimethoprim-sulfamethoxazole, MET, methicillin; VAN, vancomycin.

3. Causative organisms and antimicrobial resistance

The distribution and antimicrobial susceptibility of 73 strains isolated from 68 patients with bacteremia are shown in **Table 3**. In four patients, more than one bacteria were isolated from blood cultures. Gram-negative bacteria was 80.2% of all isolates, and Gram-positive bacteria was 19.8%. The most frequently isolated Gram-negative pathogen was *Escherichia coli* (53.4%), and Gram-positive pathogen was *Enterococcus* spp. (13.7%). The frequency of non-fermenter Gram-negatives was 6.8%. The susceptibility of the isolates to antibiotics is presented in **Table 3**. There was 87.2% resistance against fluoroquinolones in *E. coli*, 70.0% in *K. pneumoniae*, and 60.0% in *Enterococcus* spp. 50% in *S. aureus.* Resistance to third-generation cephalosporins was 36.4% in *E. coli* strains, and only a strain was resistant to carbapenems. Resistance to third-generation cephalosporin was 66.7% in *K. pneumoniae* strains. All *Staphylococcus* spp. strains were resistant to methicillin. In *Enterococcus* spp., vancomycin resistance was found only in one strain (10.0%).

DISCUSSION

In this study, we found that breakthrough bacteremia was observed in 68 patients (12.3%) among 553 patients undergoing allogeneic and autologous HSCT with fluoroquinolone prophylaxis. Using steroids, longer neutropenia duration, higher CCI, DM and using central venous catheter were significantly associated with the occurrence of breakthrough bacteremia in HSCT recipients receiving fluoroquinolone prophylaxis. Of isolated bacteria, Gram-negatives (80.2%) were identified more predominantly. Quinolone resistance in *E. coli* was found to be 87.2%.

Bacteremia is the most common infection in neutropenic episodes and the HSCT period. Bacterial BSI affect approximately 5.0 – 10.0% of autologous and 20.0 - 30.0% of allogeneic HSCT recipients, with significant variations between centers and between patients undergoing different transplantation procedures, and type of conditioning regimens [1-4,

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11-13]. Few studies in the literature have studied bacteremia risk factors in HSCT recipients receiving quinolone prophylaxis. Blennow et al. reported that the incidence of bacteremia was 21.0% in allogeneic HSCT recipients receiving ciprofloxacin prophylaxis. Age, donor age, diagnosis (all leukemia *vs.* others), donor (unrelated *vs.* related), and human leukocyte antigen match (match *vs.* mismatch) were risk factors for blood stream infection [4].

It has been reported that high CCI and DM is a bacteremia caused by resistant bacteria in patients with hematological malignancies. Similarly, comorbidities and a high CCI may increase the risk of bacteremia in HSCT recipients [14, 15]. According to our multivariate analysis results, high CCI and DM are associated with an increased risk of bacteremia. This result may have arisen due to steroids, especially in diabetic patients, disrupting blood glucose regulation. In HSCT recipients, steroid use is one factor that increases the risk of bacteremia in previous studies [16, 17]. In our study, steroids were associated with an increased risk of bacteremia in autologous and allogeneic HSCT recipients.

In the study of Busca et al. [18] evaluating allogeneic HSCT recipients, long neutropenia duration was reported as an independent risk factor for bacteremia. In our study, according to the literature, the mean neutropenia duration (24.3 days) in allogeneic HSCT recipients with bacteremia was longer than those without (18.6 days), and this difference was statistically significant.

According to the literature, the central venous catheter increases the risk of bacteremia [19]. In our allogeneic HSCT recipient patients, this risk was 7.8 fold. Infection control measures and bundles, especially catheter care, are essential at this point [16].

It is known that bacteremia risk is reduced in HSCT recipients with quinolone prophylaxis [3, 11]. There is concern that fluoroquinolone for prophylaxis will result in the selection of resistant strains, especially in Gram-negative bacteria [20]. Results have been reported in the literature that it may increase the rate of colonization or infection with quinolone-resistant bacteria in HSCT recipients or neutropenic patients [21, 22]. However, there are also reports that it will not affect quinolone resistance [23]. Although there are reports of patients receiving quinolone prophylaxis in the epidemiology of our country, there are very limited data on HSCT recipients. Quinolone resistance was found in half of the Gram-negative agents that cause bacterial infections in HSCT recipients in the first six months in a European study in which data from our country were also taken [24]. In another study evaluating bloodstream infections in pediatric hematology/oncology patients in our country, the quinolone resistance of *E. coli* and *K. pneumoniae* was 75% and 55.6%, respectively [25]. A total of 73 bacterial organism agents were isolated in our study, and approximately 78.1% of them were Gram-negative. Quinolone resistance was about 87.2% in *E. coli* strains and 70% in *K. pneumoniae*.

Enterococcus spp. is seen with increasing frequency among bacterial bloodstream infection agents in patients with hematological malignancies and HSCT recipients. A study showed that the isolation of *Enterococcus* spp. increased significantly after the initiation of quinolone prophylaxis [26, 27]. In previous studies conducted in our region, resistance rates of *Enterococcus* spp. strains to quinolones were seen to vary between 15.0 - 72.0% [28, 29]. In our study, quinolone resistance was found in 60.0% of the strains obtained from patients who received quinolone prophylaxis and developed enterococcal bacteremia. Therefore, it is not possible to say that the use of quinolone prophylaxis causes an additional increase in the rate of resistance to quinolones in enterococci.

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The most important limitation was the retrospective design of the study. As well, the study was conducted at a single center. Consequently, it can only reflect data from a center and a restricted geographic area.

In conclusion, we examined, incidence, resistance and risk factors in HSCT recipients receiving fluoroquinolone prophylaxis in this study. Our bacteremia incidence was 12.0% and central venous catheter, steroid use, DM, high CCI, and long duration of neutropenia were found to increase the risk of bacteremia. Quinolone resistance in bacteria causing bacteremia was more than 50.0%.

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