Journal of Medical Sciences 2022, 3(2) 123-130 **Araştırma Makalesi** / Research Article
https://doi.org/10.46629/JMS.2022.84

Risk Factors for Antibiotic Resistance and Mortality in Nosocomial Gram-negative Bloodstream Infections: A Retrospective Study

Nozokomiyal Gram-negatif Kan Dolaşımı Enfeksiyonlarında Antibiyotik Direnci ve Mortalite için Risk Faktörleri: Retrospektif Bir Çalışma

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Abstract

Aim: The current increase in the rate of nosocomial infection caused by the drug-resistant and multi-drug resistant (MDR) Gram-negative bacteria rendered the current treatment options insufficient. In this case-control study, we aimed to determine the risk factors for drug-resistance, multi-drug resistance and mortality in nosocomial bloodstream infections (NBSIs).

Material and Methods: The study included one hundred consecutive patients aged 18 years and over with nosocomial bloodstream infections caused by Gram-negative bacteria. Twenty-nine patients with multi-drug-resistant Gram-negative bacteremia constituted the case group, and 71 patients without MDR constituted the control group. Forty-four patients who ended up with mortality formed the case group, and 56 patients who recovered formed the control group.

Results: Acinetobacter baumannii was isolated as the most common causative microorganism. The mean age in the group with MDR bacteria-caused NBSI was significantly higher than in the non-MDR group (p=0.02). Older age (Odds ratio [OR] = 1.0; 1.0-1.1; p=0.047), acute renal failure (ARF) (OR= 12.8; 2.7-58.7; p=0.001), use of cephalosporins within the last month (OR= 15.8; 2.3-107.6; p=0.005), and A. baumannii as the causative agent (OR=6.1; 1.6-23.8; p=0.008) were independent risk factors for development of MDR bacteria-caused NBSI. In patients with Gram-negative bacteremia; malignancy (OR=7.7; 2.4-24.4; p <0.001), high Eastern Cooperative Oncology Group (ECOG) score (OR=2.9; 1.3-6.5; p=0.009), and high Acute Physiological and Chronic Health Evaluation II (APACHE II) score (OR=1.2; 1.1-1.3; p=0.001) were found to be independent risk factors for mortality.

Discussion and Conclusion: The findings of the present study revealed that advanced age, acute renal failure, and use of cephalosporins within the last month were independent risk factors for multidrug resistance in nosocomial Gram-negative bacteremia. The findings§ also revealed that malignancy, high ECOG and APACHE II scores were independent risk factors for mortality in patients with nosocomial Gram-negative bacteremia. Avoidance of empiric use of broad-spectrum cephalosporins may limit resistance. In addition, considering existing risk factors when initiating empiric therapy may prevent poor prognosis.

Keywords: Nosocomial bloodstream infection, Gram-negative bacteria, multidrug-resistance, MDR.

Öz

Amaç: Dirençli ve çok ilaca dirençli (MDR) Gram negatif bakterilerin neden olduğu nozokomiyal enfeksiyon oranındaki mevcut artış, günümüzdeki tedavi seçeneklerini yetersiz kılmıştır. Bu vaka-kontrol çalışmasında nozokomiyal kan dolaşımı enfeksiyonlarında (NKDE) ilaç direnci, çoklu ilaç direnci ve mortalite için risk faktörlerini belirlemeyi amaçladık.

Gereç ve Yöntem: Çalışmaya Gram-negatif bakterilerin neden olduğu nozokomiyal kan dolaşım enfeksiyonu olan 18 yaş ve üstü, yüz ardışık hasta dahil edildi. MDR Gram-negatif bakteriyemili 29 hasta vaka grubunu, MDR'si olmayan 71 hasta kontrol grubunu oluşturdu. Mortalite ile sonuçlanan 44 hasta vaka grubunu, iyileşen 56 hasta ise kontrol grubunu oluşturdu.

Bulgular: Acinetobacter baumannii en sık etken mikroorganizma olarak izole edilmiştir. MDR bakteri kaynaklı NKDE olan grupta yaş ortalaması, MDR olmayan gruba göre anlamlı olarak daha yüksekti (p=0.02). İleri yaş (Odds oranı [OR] = 1.0; 1.0-1.1; p=0.047), akut böbrek yetmezliği (ABY) (OR= 12.8; 2.7-58.7; p=0.001), son bir ay içinde sefalosporin kullanımı (OR= 15.8; 2.3-107.6; p=0.005) ve etkenin A. baumannii olması (OR=6.1; 1.6-23.8; p=0.008), MDR için bağımsız risk faktörleriydi. Gram negatif bakteriyemili hastalarda; malignite (OR=7.7; 2.4-24.4; p <0.001), yüksek Eastern Cooperative Oncology Group (ECOG) skoru (OR=2.9; 1.3-6.5; p=0.009) ve Acute Physiology And Chronic Health Evaluation II (APACHE II) skoru (OR=1.2; 1.1-1.3; p=0.001) mortalite için bağımsız risk faktörleri olarak bulundu.

Tartışma ve Sonuç: Bu çalışmanın bulguları nozokomiyal Gram negatif bakteriyemide ileri yaş, akut böbrek yetmezliği ve son bir ay içinde sefalosporin kullanımının MDR için bağımsız risk faktörleri olduğunu ortaya koydu. Bulgular ayrıca hastane kaynaklı Gram negatif bakteriyemili hastalarda malignite, yüksek ECOG ve APACHE II skorlarının mortalite için bağımsız risk faktörleri olduğunu ortaya koydu. Geniş spektrumlu sefalosporinlerin ampirik kullanımından kaçınılması direnci sınırlayabilir. Buna ilaveten ampirik tedavi başlanırken mevcut risk faktörlerinin göz önünde bulundurulması kötü prognozu önleyebilir.

Anahtar kelimeler: Nozokomiyal kan dolaşımı enfeksiyonu, Gram negatif bakteri, çoklu ilaç direnci, MDR.

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Introduction

Nosocomial bloodstream infections are one of the main challenges we encounter in the intensive care units (ICUs), and it can cause morbidity and mortality. In addition, the general use of antibiotics may increase infection by drug-resistant bacteria, which are related to mortality (1). Although various effective strategies such as the use of prophylactic antibiotics have been implemented, the prevalence of nosocomial bloodstream infection (BSI) remains high and further protective approaches to nosocomial bloodstream infection in ICU need to be established. The risk factors for the development of nosocomial bloodstream infection include inappropriate use of antibiotics, drug-resistant and multidrug-resistance (MDR) (2).

The nosocomial infections develop in 10-15% of the hospitalized patients, surpassing the 20% in developing countries. The nosocomial bloodstream infections (NBSIs) have a crucial place among the nosocomial infection, particularly in the ICUs. The bloodstream infections comprised the 14% of all hospital infections. The 55-60% of the nosocomial bloodstream infection develop due to the Gram-positive bacteria, while 35-40% develop due to the Gram-negative bacteria (3,4).

The Gram-negative bacteria are responsible for 30-40% of the nosocomial bloodstream infection cases. The mortality in the nosocomial bloodstream infection was reported roughly as between 5-58%. The rapid progression and high mortality rate of nosocomial bloodstream infection based on Gram-negative bacteria made them keep their importance (5-7). Another feature of the Gram-negative bacteria that enables them to be important in nosocomial infections is the drug-resistance associated with wide and inappropriate antibiotic usage. The increase in the drug resistance results in the failure of the antibiotic therapy that was started as empirical in the period of hospitalization, and this causes an increase in morbidity and mortality rates. For preventing the development of resistance, it is required to make infection control policies,to apply regular and efficient surveillance programs and to prevent the wide and inappropriate antibiotic usage (8,9).

The current increase in the rate of nosocomial infection caused by the drug-resistant and MDR Gram-negative bacteria rendered the current treatment options insufficient. For this reason, in our case-control study, we aimed to determine the risk factors for drug-resistant, MDR and mortality in nosocomial bloodstream infections.

Material and Methods

This case-control study was approved by the local ethics committee (B.30.2.ODM0.20.08/2022), was planned retrospectively, and was conducted at Ondokuz Mayis University, Samsun, Turkey. The procedures were followed in accordance with the ethical standards of Ondokuz Mayis University and the Helsinki Declaration.

Consecutive 100 patients older than 18 years and diagnosed with nosocomial bloodstream infection caused by Gram-negative bacteria in our tertiary care hospital between Jun 2004 and December 2005 were included in the study. For each of the patients, only the first bacteraemic episode was taken for the study. Data were obtained from patients with Gram-negative bacteria growth in one or more blood cultures of patients with symptoms of systemic infection such as fever, chills and / or hypotension, 48-72 hours after hospitalization or within ten days after discharge. Bloodstream infection was divided into primary and secondary. Bacteremias occurring without another infection focus primary BSI; bacteremias originating from a detectable infection site as a source of bacteremia were defined as secondary BSI. Bacteremia due to catheter was evaluated in primary BSI. The focus of bacteremia was divided into two categories as low risk and high risk. The urinary system, catheter, and soft tissue were defined as the "low-risk bacteremia focus on associated with ≤30% mortality, while the lower respiratory system, abdomen, unknown focus was defined as the "high-risk bacteremia focus on associated with mortality >30%.

The case group consisted of 36 patients with drug-resistant Gram-negative bacteria-caused NBSI whereas the control group consisted of 64 patients with drug-susceptible Gram-negative bacteria-caused NBSI. The drug resistance was defined as resistance to 3rd generation cephalosporins for Enterobactericeae spp., S. maltophilia and A. baumannii and resistant to either one of piperacillin, ciprofloxacin, ceftazidime and imipenem/meropenem for Pseudomonas aeruginosa (10).

A total of 29 patients had MDR Gram-negative bacteria-caused NBSI as the case group, while the control group included 71 patients with non-MDR Gram-negative bacteria-caused NBSI.

The multiple resistant bacteremia was defined as resist-

ant to 3rd generation cephalosporins for Enterobacteriaceae spp.; resistant to at least three of the broad spectrum cephalosporins, carbapenem, aminoglycoside, quinolone and broad spectrum penicillin for P. aeruginosa, S. maltophilia, A. baumannii. The MDR bacteremia was also accepted as drug-resistant bacteremia. The polymicrobial bacteremia was also defined as the isolation of various microorganisms in addition to Gram-negative bacteria in the blood culture (10).

The 30rd day mortality was used as the major outcome variable. The case group for mortality was comprised of 44 patients that resulted in mortality while the control group was comprised of 56 patients that lived in the 30rd day after the bacteremia.

The inappropriate antimicrobial treatment was defined as use of antimicrobial agent to which a pathogen is resistant or delay in starting appropriate treatment (11).

Clinical and laboratory data were collected at the time of admission including age, gender, cause of admission (surgery or internal), hospitalization in the ICUs, comorbid diseases, the number of patients in the room and the presence of companions, invasive procedures applied, presence of invasive devices, the treatments received before bacteremia. The prognosis of the patient was evaluated with the Acute Physiology Age Chronic Heath Evaluation (APACHE II) score and Eastern Cooperative Oncology Group (ECOG) score for each patient.

All statistical analyzes in the study were done using SPSS 25.0 software (IBM SPSS, Chicago, IL, USA). Descriptive data are given as numbers and percentages. In terms of categorical variables, comparisons between groups were made with Pearson's Chi Square test and Fisher's Exact Test. Whether continuous variables are suitable for normal distribution was confirmed by the Kolmogorov-Smirnov Test. The risk factors were evaluated with chi- square test or Fisher's Exact test for categorical data, and Student t test or Mann-Whitney U test for non-categorical data. Multiple variable analyses were performed using logistic regression analyses. The results were evaluated within the 95% confidence interval, and $p<0.05$ values were considered significant. Bonferroni correction was made where appropriate.

Table 1. Hospitalization and follow-up characteristics of patients with nosocomial drug-resistant Gram-negative bacteremia [n (%)].

	Susceptible (n=64)	Resistant (n=36)	p
Female	30 (46.9)	14 (38.9)	NS
Male	34 (53.1)	22 (61.1)	NS
Age	56 (min-max: 18-86)	59 (min-max: 19-79)	NS
Hospitalizasyon to internal medicine service	42 (65.6)	23 (63.9)	NS
Hospitalization to surgical service	22 (34.4)	13 (36.1)	NS
Hospitalization to intensive care unit	3 (4.7)	11 (30.6)	**0.001**
Admission diagnosis			
WBT	2 (3.1)	4 (11.1)	NS
Malignancy	23 (35.9)	8 (22.2)	NS
Surgery	13 (20.3)	9 (25)	NS
Internal	26 (40.6)	15 (41.6)	NS
Bedtime*	18 (min-max:3-150)	14 (min-max:3-106)	NS
Number of patients in the room			NS
1 patient	6 (9.3)	5 (13.8)	NS
2 patients	19 (29.6)	8 (22.2)	NS
≥3 patients	39 (60.9)	23 (63.8)	NS
The presence of the companion	41 (64.1)	18 (50)	NS
Share the same room**	37 (57.8)	27 (75)	NS
APACHEII	15 (±4.92 SD)	15 (±5.97 SD)	NS
ECOG	3 (±2.22 SD).	4 (±3.90 SD)	**0.016**

* Hospitalization date before bacteremia, ** Share the same room with the patient known to be infected with resistant Gram-negative bacteria. WBT: Whole body trauma, ECOG: Eastern Cooperative Oncology Group, APACHE II: the Acute Physiology Age Chronic Heath Evaluation, NS: Not significant

Table 2. Risk factors for drug resistance and MDR in patients with nosocomial Gram-negative bacteremia [n (%)].

	MDR (n=29)	Non-MDR (n=71)	p	%95 CI	OR	p
Female	12 (41)	32 (45.1)	>0.05			
Male	17 (58.6)	39 (54.9)	>0.05			
Advanced age	65 (min-max:19-79)	55 (min-max:18-86)	**0.02**	1.0-1.1	1.0	**0.047**
ARF	8 (27.6)	4 (5.6)	**0.005**	2.7-58.7	12.8	**0.001**
Previous antibiotic usage	18 (62.1)	23 (32.4)	**0.012**			
Use of cephalosporins	6 (20.7)	3 (4.2)	**0.016**	2.3-107.6	15.8	**0.005**
Use of carbapenems	7 (24.1)	6 (8.5)	**0.049**			
APACHE II	16.90 (±6.39 SD)	14.52 (±4.84 SD)	**0.046**			
ECOG	3 (min-max: 2-4)	3 (min-max: 2-4)	>0.05			
Agents						
Esherichia coli	7 (24.2)	22 (30.9)	NS			
Klebsiella pneumoniae	3 (10.3)	15 (21.1)	NS			
Enterobacter cloacae	2 (6.9)	3 (4.2)	NS			
Enterobacter aerogenes	1 (3.5)	3 (4.2)	NS			
Acinetobacter baumannii	11 (37.9)	7 (9.9)	**0.002**	1.6-23.8	6.1	**0.008**
Pseudomonas aeruginosa	3 (10.3)	12 (16.9)	NS			
Stenotrophomonas maltophilia	2 (6.9)	3 (4.2)	NS			
Other		6 (8.6)	NS			
Polymicrobial bacteremia	4 (13.8)	9 (12.7)	NS			
Bacteremia source			NS			
Low risk	10 (34.5)	30 (42.3)	NS			
High risk	19 (65.5)	41 (57.7)	NS			

MDR: Multi-drug resistant, CI: Confidence interval, OR: Odds ratio, ARF: Acute renal failure, ECOG: Eastern Cooperative Oncology Group, APACHE II: the Acute Physiology Age Chronic Heath Evaluation, NS: Not significant.

Results

A total of 56% of those enrolled in the study were male, the median age was 57 (IQR: 16, min-max.:18-86) years.

The rate of patients with drug-resistant bacteria-caused NBSI was significantly higher in the intensive care unit than the rate of those hospitalized in other services (p=0.001). The mean ECOG score of resistant bacteria breeders was found to be significantly higher than those with susceptible bacteria (p=0.016). The group with drug-resistant bacteria-caused NBSI was similar to the group with drug-susceptible bacteria-caused NBSI in terms of gender, malignancy, admission to internal or surgical wards, duration of hospitalization before bacteremia, number of patients in the room, sharing the same room with those with resistant bacteria growth in culture, and average APACHE score (p> 0.05 for each) (Table 1).

The mean age in the group with MDR bacterial growth was significantly higher than in the non-MDR group (p=0.02). Older age was an independent risk factor for MDR (p=0.047; OR: 1.0; 1.0-1.1). Patients with acute renal failure had significantly higher rate of MDR bacterial growth than those without ARF (p=0.005). It was determined that ARF was an independent risk factor for MDR bacterial growth, and increased the risk 12.8 times (OR; 2.7-58.7; p=0.001). The rates of the patients with use of carbapenem (p=0.049) and overall antibiotics (p=0.012) were significantly higher in those with MDR bacteria-caused NBSI. The rate of the patients with MDR bacteria-caused NBSI was detected in those who were given cephalosporins within the last month was found to be significantly higher than those who were not given cephalosporin (p=0.016). It was found that cephalosporin administration was an independent risk factor for MDR bacterial growth and increased the risk 15.8 times (OR; 2.3-107.6; p=0.005). The rate of patients with growth of MDR bacteria in those with A. baumannii growth was significantly higher than those with growth of different species of bacteria (p=0.005). A. baumannii growth was found to be an independent risk factor for MDR bacterial growth and increased the risk 6.1 times (OR; 1.6-23.8; p=0.008). The mean APACHE score was found to be significantly higher in those with MDR bacterial growth compared to the non-MDR group (Table 2).

In patients with Gram-negative bacteremia, the mortality rate was significantly higher in those with malignancy than those without malignancy (p=0.002). Malignancy was found to be an independent risk factor for mortality and increased the risk 7.7 times (OR; 2.4-

Table 3. Risk factors for mortality in patients with nosocomial Gram-negative bacteremia [n (%)].

	Dead (n=44)	Survived (n=56)	p	95% CI	OR	p
Age (year)	57.7 (±13.1SD)	55.4 (±16.8 SD)	NS			
Malignancy	27 (61.4)	16 (28.6)	**0.002**	2.4-24.4	7.7	**<0.001**
Drainage	9 (20.5)	2 (3.6)	**0.01**			
Emergent surgery	9 (20.5)	2 (3.6)	**0.01**			
Chemotherapy	15 (34.1)	6 (10.7)	**0.009**			
Transfusion of blood and blood products	22 (50)	13 (23.2)	**0.01**			
High-risk bacteremia source	35 (79.5)	25 (44.6)	**0.001**			
ECOG	3 (min-mak2-4)	3 (min-max: 2-4)	**0.002**	1.3-6.5	2.9	**0.009**
APACHE II	17 (min-mak9-35)	13 (min-max: 6-26)	**<0.001**	1.1-1.3	1.2	**0.001**

ECOG: Eastern Cooperative Oncology Group, APACHE II: the Acute Physiology Age Chronic Heath Evaluation, NS: Not significant.

24.4; p <0.001). Median ECOG score in the patients who died was found to be significantly higher than the surviving patients. High ECOG score was found to be an independent risk factor for mortality and increased the risk 2.9 times (OR; 1.3-6.5; p=0.009). Median APACHE II score in patients who died was found to be significantly higher than in surviving patients. High APACHE II score was found to be an independent risk factor for mortality and increased the risk 1.2 times (OR; 1.1-1.3; p=0.001). Mortality rates were significantly higher in patients with drainage (p=0.01), emergency operations (p=0.01), chemotherapy (p=0.009), transfusion of blood and blood products (p=0.01), and high-risk bacteremia sources (p=0.001) was found to be high (Table 3).

There were not any statistical differences between the patient groups with mortality and cure, regarding the applications of mechanical ventilation, tracheostomy, endotracheal tube, central venous catheterization, thorax tube, internal urine catheter, emergency or elective invasive intervention and elective surgery.

Discussion

Nosocomial infections are important because of leading to high morbidity and mortality rates. They also cause increasing costs. Nosocomial infections caused by the antibiotic-resistant microorganisms also increase the mortality rate (11). In cases of infections caused multidrug-resistant bacteria, therapeutic options are limited and the treatment may be ineffective. Gram-negative bacteria are isolated more commonly in the ICUs nosocomial bloodstream infection. The precautions about the frequent and inappropriate antibiotic usage is one of the key factors in preventing the development of resistance (12-14). Therefore, in the present study, we aimed to identify risk factors for drug-resistant, MDR and mortality.

The ECOG score shows the patient's consciousness and self-care, and higher score means worse clinical condition (15). In the present study, the mean ECOG score was found to be significantly higher in the cases that drug-resistant bacteria were detected than those that the susceptible species were determined. In addition, The rate of patients that growth of resistant bacteria was detected in the intensive care unit was significantly higher than the rate of those hospitalized in other services. These findings show that the risk of developing resistant Gram-negative bacteria-induced bacteremia is significantly higher in patients admitted to the intensive care unit and associated with poor consciousness.

Older patients become susceptible to infection due to increased comorbidity, more healthcare, and age-related changes in host defense consisting of immune-nonimmune mechanisms (16). In the present study, the mean age was found to be significantly higher in the group with MDR bacteria-caused NBSI compared to those with non-MDR bacteria-caused NBSI, and advanced age was found to be an independent risk factor for development of NBCI caused by MDR bacteria, and acccordingly for MDR bacteremia.

Cellular and humoral immune response is impaired in uremic patients (17). One of the most common complications in ARF is infection, and mortality rate in ARF cases are reported between 39-71% (18). In the present study, among the comorbidities, the rate of patients with NBSI caused by MDR bacteria was

found to be significantly higher in those with only acute renal failure compared to those without ARF, and it was found that ARF was an independent risk factor for MDR bacteria-caused NBSI with a 12.8-fold increased risk. However, these findings were different from other reports in the literatüre (19-21). Besides, ARF wasn't found as a risk factor for mortality, similar to other studies (22). However, Kalil et al. (23) found AFR as a risk factor for MDR bacteria-caused nosocomial infection, similar to the present study. These findings show that the risk of developing bacteremia due to MDR Gram-negative bacteria increases significantly in patients with ARF.

In the present study, the rate of patients with MDR bacteria-caused NBSI was found to be significantly higher in those who used antibiotics within the last month. In addition, the rate of patients with MDR bacterial growth in those who were given cephalosporins was found to be significantly higher than those who were not given cephalosporin, and it was found that cephalosporin use was an independent risk factor for development of MDR bacteria-caused NBSI and increased the risk 15.8 times. In addition, rates of patients with MDR bacteria-caused NBSI were significantly higher in those who used carbapenem. All these findings show that the risk of developing MDR Gram-negative bacteria-induced bacteremia is significantly increased in patients recently used antibiotics, especially in those who had severe infection requiring treatment with cephalosporins or carbapenem.

A. baumannii is the most common cause of ventilator-associated pneumonia and bloodstream infection. This may be due to the fact that A. baumannii can intensively colonize the patient, environment and the equipment used in the hospital. Therefore, it was reported that A. baumannii isolates cause infections and nosocomial outbreaks with MDR patterns more frequently in hospitals and ICUs (24,25). In the present study, the species with the highest MDR rate was found to be A. baumannii (37%) and 61.1% of these isolates were found to be MDR. In the present study, the rate of patients with MDR bacteria-caused NBSI was found to be significantly higher in those with A. baumannii-caused NBSI compared to those with different the other bacterial causative agents, and A. baumannii was found to be an independent risk factor for development of MDR bacteria-caused NBSI with a 6.1-fold increased risk. These findings show that is mostly responsible for MDR Gram-negative bacteremia cases.

In the present study, the mean APACHE score was found to be significantly higher in patients with MDR bacterial growth compared to the non-MDR group. This finding shows that, according to APACHE II scoring, the possibility of developing bacteremia due to MDR bacteria increases significantly in patients with severe clinical condition.

In the present study, in patients with Gram-negative bacteremia; the mortality rate was found to be significantly higher in those with malignancy than those without malignancy, and malignancy was found to be an independent risk factor for mortality and increased the risk 7.7 times. This finding indicates that malignancy is the main factor determining the risk in terms of mortality even in the case of Gram-negative bacteremia, and in this sense, it remains important. This indicates that the prognosis is significantly unfavorable if Gram-negative bacteremia develops in patients with malignancy.

Determining the patient's consciousness and general clinical picture provides important data in terms of predicting the prognosis (15). In the present study, the median ECOG score in the patients who died was found to be significantly higher than the patients who survived, and it was found that the high ECOG score was an independent risk factor for mortality and increased the risk 2.9 times. In addition, the median APACHE II score in the patients who died was found to be significantly higher than the surviving patients, and the high APACHE II score was found to be an independent risk factor for mortality and increased the risk 1.2 times. In the present study, the patients with high ECOG scores and the high APACHE II risk scores also support the comorbid diseases and comorbid conditions, as well as the physiological functions of the patients. Patients with high ECOG scores are more exposed to contact that may pose a risk for transmission with resistant hospital flora, considering their general condition; this increases the risk of infection with resistant bacteria. This may lead to mortality by causing the performance of patients who require continuous support to decrease further. All these findings show that the development of Gram-negative bacteremia significantly worsens the prognosis in patients with insufficient awareness, self-care and / or severe general condition.

The clinical condition of the patients poses an important risk in terms of development of bacteremia and mortality (12). In the present study, mortality rates

were found to be significantly higher in patients with drainage, emergency operations, chemotherapy, transfusion of blood and blood products, and high risk sources of bacteremia. These findings show that the development of Gram-negative bacteremia significantly increases the mortality rate in those who have poor general health and have conditions that require various invasive or severe treatment.

Poorly initiated empirical antibiotic therapy is a natural consequence of bloodstream infection caused by drug-resistant or MDR Gram-negative bacteria. Inappropriately initiated antibiotic treatment in the present study did not pose a risk for mortality, similar to other studies (10,19). However, contrary to the present study, it has been shown in several studies that inappropriate antibiotic treatment is associated with high mortality in severe infections caused by drug-resistant bacteria (19). This could be related to carrying out appropriate antibiotic treatment in line with effective surveillance studies.

Conclusion

The findings of the present study show that advanced age, acute renal failure, and use of cephalosporins within the last month were independent risk factors for development of MDR Gram-negative bacteremia. The findings also show that malignancy, high ECOG and APACHE II scores were independent risk factors for mortality in patients with nosocomial Gram-negative bacteremia.

The effects of patient's underlying disease and the severity of the disease, the comorbid state, the microbiological factors and the focus of the infection can explain the different results. In addition, sampling size and effective surveillance in the studies together with feedback to clinicians are also factors affecting the current outcome.

Regarding the risk factors mentioned in the present study, the precautions about the frequent and inappropriate antibiotic usage, especially the empiric usage of broad spectrum cephalosporins might limit the increasing antimicrobial resistance. In the planning of the treatment for patients with advanced age, those with severe renal dysfunction, those receiving broad spectrum cephalosporin treatment before the bacteremia, and those in intensive care unit, the treatment should be started considering the fact that the causative agent may be resistant, to prevent the bad prognosis due to the failure of the empirical therapy, the elongation of the hospitalization period and the high cost.

Limitations

There were some limitations in the present study. Since molecular methods could not be performed in the present study, the relatedness of the isolates could not be determined. That might cause statistical bias. However, the distribution of the patients in terms of the dates they were hospitalized was so wide that we consider this negative effect might be very limited.

Received Date/Geliş Tarihi: 18.12.2021
Accepted Date/Kabul Tarihi: 31.03.2022

Kaynaklar

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