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Resistant gram-negative infections in a pediatric intensive care unit: a retrospective study in a tertiary care center

Bir üniversite hastanesi çocuk yoğun bakım biriminde dirençli gram-negatif enfeksiyonların değerlendirilmesi

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Abstract

Aim: Healthcare-associated infections cause increased morbidity and mortality in intensive care units. In this study, it was aimed to compare infections with multi-drug resistance and extended drug resistance, while evaluating the characteristics of resistant Gram-negative infections in the pediatric intensive care unit in our university hospital.

Material and Methods: In this study, pediatric patients who were found to have Gram-negative infections during hsopitalization in the pediatric intensive care unit in our faculty between January 2011 and December 2015, were evaluated retrospectively.

Results: One thousand thirty patients were internalized in our unit in the study period. The incidence for healthcare-associated infection was found as 17.2% and the incidence density was found as 32.7 per 1000 patient days. The incidence for healthcare-related infection per 1000 device days and the rate for device use were calculated as 66.9 and 0.59, respectively. One hundred thirty Gram-negative infection episodes were found in 79 patients whose median age was 22 (1–205) months. The most common infections included ventilator-related pneumonia (n=78, 60%) and bloodstream infections (n=38, 29.2%). The most common causative agents included *Pseudomonas aeruginosa* (n=50, 38.5%), *Kleibsiella pneumonia* (n=32, 24.6%) and *Acinetobacter baumannii* (n=28, 21.5%). Among *A. baumannii* isolates, the rates for resistance against piperacillin-tazobactam and meropenem were found as 96.4% and 89.3%, respectively. Empirical use of carbapenems, aminoglycosides, and fluoroquinolones, the presence of total parenteral nutrition and history of Gram-negative bacterial infections prior to pediatric intensive care unit admission were significantly more common among extended-drug Gram-negative bacterial infections. The late mortality rate was found to be higher in presence of ex-

Öz

Amaç: Sağlık bakımı ilişkili enfeksiyonlar yoğun bakım birimlerinde yüksek hastalık ve ölüme neden olmaktadır. Bu çalışmada, üniversite hastanemiz çocuk yoğun bakım birimindeki dirençli gram negatif enfeksiyonların özellikleri değerlendirilirken; çok ilaca dirençli ve genişletilmiş ilaç direnci olan enfeksiyonların karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler: Bu çalışmada Ocak 2011–Aralık 2015 yılları arasında, fakültemiz çocuk yoğun bakım biriminde yatışı sırasında gram negatif enfeksiyon saptanan çocuk hastalar geriye dönük olarak değerlendirildi.

Bulgular: Çalışma döneminde birimimize 1 030 hasta yatırıldı; sağlık bakımı ilişkili enfeksiyon sıklığı %17,2, sıklık yoğunluğu 1 000 hasta günü başına 32,7 idi. 1 000 cihaz günü başına sağlık bakımı ilişkili enfeksiyon sıklığı ve cihaz kullanım oranı sırasıyla 66,9 ve 0,59 olarak hesaplandı. Yaş ortancası 22 (1–205) ay olan 79 hastada, 130 gram negatif enfeksiyon atağı saptandı. En sık saptanan enfeksiyonlar, ventilatör ilişkili pnömoni (n=78, %60) ve kan akım enfeksiyonu (n=38, %29,2) idi. En sık etkenler *Pseudomonas aeruginosa* (n=50, %38,5), *Kleibsiella pneumonia* (n=32, %24,6) ve *Acinetobacter baumannii* (n=28, %21,5) idi. *A. baumannii* izolatları arasında piperasilin-tazobaktam ve meropenem direnci sırası ile %96,4 ve %89,3 saptandı. Ampirik karbapenem, aminoglikozid ve florokinolon kullanımı, total parenteral nütrisyon varlığı, yoğun bakım öncesi geçirilmiş gram negatif enfeksiyon öyküsü anlamlı olarak daha yüksekti. Geç dönem ölüm hızı genişletilmiş ilaç direnci varlığında daha yüksek saptandı. Geçirilmiş gram negatif enfeksiyon öyküsü, genişletilmiş ilaç direnci açısından bağımsız

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tended drug resistance. History of Gram-negative infection was found to be an independent risk factor in terms of extended drug resistance.

Conclusion: Healthcare-associated infections are an important health problem and it is important for infection control committees of hospitals to determine and apply strategies according to hospital colonization in prevention.

Keywords: Children, intensive care unit, resistant gram-negative infections

risk etmeni olarak bulundu.

Çıkarımlar: Sağlık bakımı ilişkili enfeksiyonlar önemli bir sağlık sorunudur ve önlemede mümkünse her hastanenin kendi enfeksiyon kontrol kurulunun hastane kolonizasyonuna göre stratejiler belirleyip uygulaması önemlidir.

Anahtar sözcükler: Çocuk, dirençli gram negatif enfeksiyonlar, yoğun bakım birimi

Introduction

Healthcare-associated infections (HAIs) lead to increased morbidity and mortality in intensive care units (ICUs) (1). Many factors including frequent contact with healthcare workers, long-term hospitalization in ICUs, frequent invasive procedures, and the presence of comorbidities increase the risk of HAIs, especially including cases caused by resistant causative agents (2). Despite an increase in resistant nosocomial infections, studies in the area of new antibiotic development are not sufficient (3). In addition, studies reporting the pharmacokinetic characteristics and reliability of newly developed antibacterial agents in children are considerably limited. Therefore, management of resistant infections is especially difficult in pediatric intensive care units (PICU).

Generally, more than one-third of HAIs are caused by Gram-negative microorganisms including mainly multidrug resistant (MDR) agents (4). This frequency reaches 70% in ICUs (5). The United States of America (USA) Centers for Disease Control and Prevention (CDC) has called attention to the marked increase in imipenem and fluoroquinolon-resistant *P. aeruginosa*, carbapenem-resistant *A. baumannii*, and third-generation cephalosporin and carbapenem-resistant Enterobacteriaceae species (4). One of the most important reasons for this is undoubtedly inappropriate antibiotic use. For antibiotics to be used efficiently for adequate time peirods, physicians should know of the antibacterial resistances in their own units. Although there are studies related to adult ICUs in this area, data involving PICUs are limited.

In this study, it was aimed to evaluate the clinical and laboratory characteristics of resistant Gram-negative infections (GNI), antibiotic resistances, and treatment responses in the pediatric ICU in our university hospital, and to compare GNIs that had multi-drug resistance and extended drug resistance.

Material and Methods

Pediatric intensive care unit and active survaillance

Pediatric patients who were found to have resistant GNI during hospitalization in the PICU in a tertiatry care university hospital between January 2011 and December 2015 were included in this study. In the study period, 1030 patients were hospitalized in the PICU; the incidence of HAIs was found as 17.2% and the incidence density was found as 32.7 per 1000 patient days. One hundred thirty GNI episodes were found in 79 patients (female=30, 38%) wose median age was 22 (1–205) months (Table 1). Two GNI episodes were found in 43 (54.4%) patients and 3 GNI episodes were found in 4 patients (5.1%). The HAI incidence per thousand material days and the rate of material use were found as 66.9 and 0.59, respectively.

Table 1. The patients' clinical characteristics

	n	%
Total number of patients	79	
Age (months), median (range)	22 (1–125)	
Sex		
Female	30	38
Male	49	62
Underlying disease	58	73.4
Neurologic disease	22	27.8
Metabolic disease	13	16.4
Chronic liver disease	7	8.9
Chronic heart disease	5	6.3
Malignancy	3	3.8
Chronic lung disease	3	3.8
Primary immunodeficiency	2	2.5
Chronic renal failure	2	2.5
Diabetes mellitus	1	1.3
Hospitalization time in PICU (days), median (range)	35 (3–201)	
PRISM score during hospitalization in PICU, median (range)	9 (2–40)	
Early mortality rate	9	11.3
Late mortality rate	21	26.6

PICU: Pediatric intensive care unit; PRISM: Pediatric risk of mortality score

The PICU in our clinic includes six beds and gives service to complicated patients aged between 1 month and 18 years. There are two rooms each including three beds. There is no isolation room in our unit. The patient-nurse ratio is 2:1.

Since January 2010, active surveillance has been conducted in our PICU by a nurse and a specialist of pediatric infectious diseases who are employed by the Hospital Infection Control Committee (HICC). In this context, HAIs are regularly recorded and reported to the HICC monthly.

In our unit, the primary approach is to initiate treatment with anti-pseudomonal penicillin or cephalosporin when a GNI is suspected. If culture remains negative after the first 48–72 hours, aminoglycoside is added to treatment or carbanepem treatment is initiated. Emprical fluoroquinolon, colistin or combination treatment are not preferred unless the patient carries high risk in terms of resistant GNI. During initiation and adjustment of antibiotic treatment, the resistance status specified with surveillance in our unit, the presence of agent with extended drug resistance (EDR) and the colonization status of the host are determinative.

Data collection

Data related to the patients [age, sex, underlying disease, hopsitalization time before PICU, previous GNI, history of antibiotic and immunosupressive drug use, Pediatric Mortality Risk Scoring (PRISM) during hospitalization in the PICU, presence of central venous catheter (CVC), presence of urinary catheter and total parenteral nutrition, and type and time of mechanical ventilation (MV) (intubation/tracheostomy)] were recorded retrospectivley from patient files and the computer system by way of predetermined standard questionnaires.

Definitions

The diagnosis of HAI was made by a nurse and a specialist of pediatric infectious diseases who were employed by the HICC in the scope of active surveillance according to the HICC criteria (6).

Infections that developed 48 hours after hospitalization in the PICU, and had no manifestation at the time of hospitalization or in the incubation period, were considered as HAIs. The incidence of HAIs (%) was calculated using the formula "(HAI number/number of hospitalized patients) x 100" and the HAI incidence density was calculated using the formula "(HAI number/patient days) x 1000". The incidence density was defined as "(HAI episode number/patient days) x 1000". The total patient days and the number of days when materials including central venous catheter, endotracheal tube, and urinary catheter were used, were recorded. The HAI incidence per material use day and the material usage rate were calculated using the formulas "(HAI episode number/material usage days) x1000" and "total material usage days/total patient days)," respectively.

The presence of resistance to one agent in at least 3 antimicrobial categories each was defined as 'MDR,' and the presence of sensitivity to antibacterial agents in one or two categories was considered 'EDR.'

Use of systemic antibiotics for 72 hours or longer in 30 days prior onset of infections was expressed as 'prior antibiotic use.' Mortality in the first 7 days after the infection episode was recorded as 'early mortality rate' and mortality arising from any reason in 30 days was recorded as 'late mortality rate.'

Laboratory data

Complete blood count, transaminase levels, renal function tests, C-reactive protein (CRP), and procalcitonin (PCT) concentrations, and complete urinalysis, which were routinely ordered during the follow-up of the patients, were recorded. Microbiologic culture results and antibiogram sensitivities for blood obtained from catheters or peripheral blood, for tracheal aspirate obtained from endotracheal tubes or tracheostomy cannullae in patients on MV and for urine and other body fluids, were recorded.

Microbiologic examination

Samples of respiratory tract and sterile body fuilds were primarily examined using Gram staining. The tracheal aspirate samples were cultured in 5% sheep blood agar (Becton Dickinson, Germany) and chocholate agar (Oxoid, England) and incubated for 24–48 hours in a 5% CO_2 setting. When they were cultured in Mac Conkey agar (Oxoid, England), they were incubated for 24–48 hours at normal atmospheric conditions. Blood cultures were studied using a BACTEC 9120 (Becton Dickinson, USA) system. When a positive signal in favour of growth was obtained, they were cultured in 5% sheep blood agar and chocolate agar.

Urine samples were inoculated in chromogenic agar (BD CHROMagar Orientation Medium, Germany) and incubated for 24–48 hours at normal atmospheric conditions. Sterile body fluids were inoculated in 5% sheep blood agar, Schaedler agar (Oxoid, England), and meat broth (Oxoid, England) and anaerobic conditions were provided by way of a GasPak system (Becton Dickinson, USA).

The pathogens that were isolated were defined by way of traditional methods (Gram staining, catalase, oxidase, DNase, use of carbohydrate, urease, use of citrate, lysine decarboxilase, Voges-Proskauer, movement, and indol tests). Antimicrobial sensitivity tests were performed in Mueller Hinton agar (Oxoid, England) using the Kirby Bauer disc method in accordance with the recommendations of the Clinical Laboratory Standarts Institute (CLSI). Appropriate antibiotic discs were used for Enterobacteriaceae, Gram-negative rods (BD BBL, Sensi-Disc, USA).

The gradient test (E test, bioMeriéux, France) was studied for minimal inhibitor concentration and the results were evaluated according to the CLSI criteria (7).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc; Chicago, IL, USA) Verion 21 package program. Normality was tested using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Data are expressed as median, minimum-maximum, frequency and percentage. Measuremental data that did not show normal distribution were compared using the Mann-Whitney U test in independent groups. Categorical data were evaluated using the Chi-square and Fisher's exact test. The significance limit was set at $p<0.05$.

Ethics committee approval was obtained from Istanbul Medical Faculty Ethics Committee for this study (2017/485). Patient consent was not obtained because this study, which was adjusted in accordance with the Helsinki principles, was conducted retrospectively.

Results

The demographic and clinical characteristics of the patients are shown in Table 1. One hundred thirty GNI episodes were found in 79 patients (female=30, 38%) whose median age was found as 22 (range, 1–205) months. Two GNI episodes were found in 43 patients (54.4%) and 3 GNI episodes were found in 4 patients (5.1%). The incidence of HAIs was found as 17.2% and the incidence density was 32.7 per 1000 patient days. The incidence of HAIs per 1000 material days and the rate of material use were found as 66.9 and 0.59, respectively.

Among a total of 130 GNI episodes, 45.3% (n=59) were MDR infections and 27.6% (n=3) were EDR infections. The patients' median hospitalization time in the PICU was found as 35 (range, 3–201) days. An underlying chronic disease was present in 58 (78.4%) patients. No significant difference was found when the presence of primary disease was compared in terms of GNI resistance (MDR/EDR).

The most common GNIs were found to be ventilator-associated pneumonia (VAP) (n=78, 60%) and blood-stream infections (BSI) (n=38, 29.2%). Catheter-associated infection (CAI) (n=9, 6.9%) and urinary tract infection (UTI) (n=4, 3.1%) were found less commonly. Peritonitis was found in one patient. The distribution of GNIs by culture specimens is shown in Table 2.

No GNIs were found that were resistant to all drugs. No significant difference could be found between MDR and EDR GNIs in terms of laboratory criteria (Table 2).

The distribution of the microorganisms by culture specimens is shown in Table 3 and their antibacterial resistances are shown in Table 4.

Various combination treatments including mainly meropenem+amikacin (n=25, 19.2%) were used during treatment of Gram-negative infections in 73.1% of the cases (Table 1).

When the characteristics of MDR and EDR GNIs were compared, the presence of hospitalization for more than 15 days before the PICU was found to be significantly more common and the median hospitalization time in the PICU was found to be significantly longer in EDR-GNIs ($p=0.001$ and $p=0.005$, respectively). The frequencies for emprical use of karbapenem, aminoglycoside, and fluoroquinolone, the presence of total parenteral nutrition, and history of GNI prior to the PICU were found to be significanly higher in EDR-GNIs ($p=0.005$, $p=0.004$, $p=0.02$, $p=0.004$, and $p<0.001$, respectively). A higher rate of EDR was found in *A. baumannii* species ($p<0.001$) in contrast to *P. aeruginosa* ($p=0.01$). There was no difference between the groups in terms of early mortality, but late mortality was found to be higher in EDR-GNIs ($p=0.022$).

In the comparison of the categorical data, the variables that were found to be statistically significant ($p<0.05$) were evaluated with logistic regression analysis. Past history of GNI, a hospitalization period of >15 days prior to the PICU, and growth of *A. baumannii* were found to be independent risk factors in terms of EDR-GNIs (Table 5).

Mortality was observed in 9 (11.3%) cases in 7 days after the development of an HAI. In these patients, the median age was found as 31 months and the median PRISM score was 12 (range, 4–40). Chronic disease was present in four patients; the most common HAI was VAP (n=5).

Discussion

Infections are the main reason of mortality in non-coronary ICUs (1). In an international study, the prevalence

Table 2. Comparison of the clinical characteristics of resistant Gram-negative infections

Variable (n)	DR-GNI		EDR-GNI		p
	n	%	n	%	
Total number of episodes	59/130 (45.3)		36/130 (27.7)		
Hospitalization time prior to PICU >15 days	34	57.6	32	88.9	**0.001**[a]
PRISM score during hospitalization in PICU, median (range)	9 (2–21)		7.5 (2–19)		0.62c
Hospitalization time in PICU (days), median, (range)	38 (9–190)		50.5 (3–201)		**0.005**[c]
Use of antibiotic in the last 30 days	58	98.3	36	100	0.62[b]
Empirical use of antibiotics					
Carbapenem	45	76.3	35	97.2	**0.005**[b]
Third-generation cephalosporin	49	83.1	30	83.3	0.97[a]
Aminoglycoside	48	81.4	36	100	**0.004**[b]
Anti-pseudomonal penicillin	44	74.6	32	88.9	0.07[b]
Fluoroquinolone	13	22	16	44.4	**0.02**[a]
Presence of invasive intervention					
Intubation/MV	59	100	35	97.2	0.37[b]
Central venous catheter	59	100	36	100	–
Total parenteral nutrition	37	62.7	32	88.9	**0.004**[b]
Urinary catheterization	54	91.5	35	97.2	0.25[b]
Tracheostomy	21	35.6	15	41.7	0.55[a]
Surgical drain	7	11.9	5	13.9	0.77[a]
Hemodiafiltration	14	23.7	13	36.1	0.19[a]
PEG	7	11.9	6	16.7	0.35[a]
Surgery	22	37.3	19	52.8	0.21[a]
History of GNI prior to PICU	26	44.1	30	83.3	**<0.001**[c]
Laboratory measurements, median, (range)					
Number of white blood cells (cell/μL)	12.310 (4250–26.800)		1300 (3100–28.200)		0.47[c]
Absolute neutrophil count (cell/μL)	4300 (850–18.760)		6450 (410–21.300)		0.72[c]
C-reactive protein (mg/L)	89 (24–421)		128 (31–389)		0.22[c]
Procalcitonin (mcg/L)	1.5 (0.15–4.1)		1.6 (0.5–5.2)		0.19[c]
MV time (days), median, (range)	19 (3–54)		24.5 (3–83)		0.056[c]
Microorganism					
P. aeruginosa	26	44.1	7	19.4	**0.01**[a]
A. baumannii	6	10.2	22	61.1	**<0.001**[a]
K. pneumonia	17	28.8	6	16.7	0.18[a]
Early mortality rate	4	6.7	5	13.9	0.25[b]
late mortality rate	8	13.6	12	33.3	**0.022**[a]

MDR: Multidrug resistance; PICU: Pediatric intensive care unit; EDR: Expanded drug resistance; GNI: Gram-negative infection; MV: Mechanical ventilation; PEG: Percutaneous endoscopic gastrostomy; PRISM: Pediatric risk of mortality score; [a]Chi-square test; [b]Fisher's exact test; [c]Mann-Whitney U test

of ICU-associated HAI was found as 18.9% (2.3–49.2%), though there was a difference between regions (8). Similarly, the rate of HAIs was found as 51% in the EPIC II point prevalence study, which involved 1265 ICUs from 76 countries (9). Infection rates are higher in developing countries, including our country (1). In a multi-center study published recently by Leblebicioğlu et al. (10), the rates of device-associated HAI in our country were found to be above the International Nosocomial Infection Control Consortium report and USA National Health Safety Network data. The frequency of HAIs was found as 17.2% in our study, in accordance with the literature.

Table 3. Distribution of the agents by culture specimens

	Total		*P. aeruginosa*		*K. pneumonia*		*A. baumannii*		*E. coli*		*S. maltophilia*		Other	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Blood	38	29.2	9	7	16	12.3	8	6.1	2	1.5	1	0.8	2	1.5
TAC	78	60	39	30	10	7.7	17	13.2	3	2.3	5	3.8	4	3.0
Catheter	9	6.9	2	1.5	5	3.8	1	0.8	1	0.8	–	–	–	–
Urine	4	3.1	–	–	1	0.8	1	0.8	2	1.5	–	–	–	–
Peritoneal fluid	1	0.8	–	–	–	–	1	0.8	–	–	–	–	–	–

TAC: Tracheal aspirate culture

Table 4. Antibacterial sensitivities of the microorganisms

Antibiotics	*P. aeruginosa*		*K. pneumonia*		*A. baumannii*		*E. coli*	
	n	%	n	%	n	%	n	%
AMP-SUL	40	80	26	81.3	27	96,4	7	87.5
Ceftriaxone	45	90	28	87.5	28	100	7	87.5
Ceftazidime	34	68	24	75	28	100	6	75
Cefepime	30	60	23	71.9	28	100	3	37.5
PIP-TAZ	36	72	22	68.8	27	96.4	5	62.5
SEF-SUL	26	52	21	65.6	22	78.6	5	62.5
Ciprofloxacin	25	50	16	50	26	92.9	4	50
Amikacin	32	64	21	65.6	27	96.4	5	62.5
Gentamicin	29	58	22	68.8	23	82.1	5	62.5
Netilmicin	17	34	14	43.8	20	71.4	1	12.5
Meropenem	21	42	15	46.9	25	89.3	3	37.5
Imipenem	18	36	11	34.4	23	82.1	1	12.5
Levofloxacin	11	22	6	18.8	19	67.9	0	0
Colistin	2	4	0	0	3	10.7	0	0
Tigecycline	*	*	*	*	1/22 (4.5)		*	*

*Not studied; AMP-SUL: Ampicillin-sulbactam; PIP-TAZ: Piperacillin tazobactam; SEF-SUL: Cefoperazone sulbactam

Table 5. Evaluation of independent risk factors according to logistic regression analysis in terms of development of resistance

	p	OR	95% CI
Hospitalization time prior to PICU >15 days	0.007	4.9	2.08–78.51
Past GNI before PICU	0.005	13.52	2.15–84.82
Growth of *A. baumannii*	0.002	24.27	3.12–188.6

PICU: Pediatric intensive care unit; GNI: Gram-negative infection

The use of invasive medical devices and surgical interventions increases the risk of HAI. The most common HAIs include VAP, catheter-associated BSIs, UTIs, and BSIs (11). Similarly, the most common infections included VAP and BSI in our study. Catheter-associated UTI was found with a rate that was far below the rates reported previously (12). This may be related with the geater use of diapers and lower use of catheters due to low median age of our patients. The prevalence of VAP was found to be relatively high because most of our patients had chronic disease.

In a comprehensive study conducted by Eraksoy et al. (13) in which antimicrobial sensitivity was evaluated, the most

common resistant Gram-negative agents were *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii*. Although the rates are different in other studies, the most common agents are similar (14–16). In our study, the frequency of *E. coli* was found to be markedly lower compared with the reported rates.

According to the 2007 Meropenem Yearly Susceptibility Test Information Collection (MYSTIC), the sensitivity of *P. aeruginosa* isolates to piperacillin-tazobactam (PIP-TAZ) is considerably high in our country (13). However, PIP-TAZ resistance was found to be considerably high (72%) among *P. aeruginosa* species in our study. Similarly, cefepim and meropenem resistances were also higher. This appears to be related to the fact that our patients were chronic patients, were being hospitalized for longer periods, and the rate of patients who received short-term postoperative care was very low because our clinic is a reference center. Due to these factors, our rates of emprical use of PIP-TAZ might have been high and our strategy to discontinue treatment in a short period might have been insufficient. In this context, it would not be appropriate to reflect our clinic's resistance pattern to the whole country.

Treatment of resistant GNIs is especially difficult for pediatricians. Antibiotics including fluoroquinolone, colistin, and tigecycline are not used in pediatric patients except for obligatory conditions. In addition, Tigecycline, which is a rescuer for physicians caring for adults, has not been approved for use in children (17). During our follow-up, no significant adverse effects were observed in a 43-month-old patient with metabolic disease who was treated with a colistin-tigecycline combination and developed EDR, *A. baumannii*-associated VAP. This patient was treated successfully. Although it has been stated in a few publications related to use of tigecycline in children in the literature that it might be safe, further comprehensive studies are needed (18, 19). Similarly, one should also avoid emprical colistin treatment in children because of its adverse effects. Although the rate of colistin resistance was low in our study, the mortality rate was found to be high in our patients who used colistin. Undoubtedly, these patients had mutiple factors including the EDR agent and the presence of underlying chronic disease.

As the the hospitalization time increases, exposure to invasive interventions and antimicrobial drugs prolongs. Similarly, the rates for hospitalization longer than 15 days, prolonged PICU stay, use of TPN, history of GNE, and use of broad-spectrum antibiotics were found to be high in patients with EDR-GNIs in our study, as expected. Therefore, narrow-spectrum agents should be preferred to prevent antibiotic resistance, especially in patients with prolonged ICU hospitalization. The antibiotic spectrum should be narrowed according to the culture results and treatment should be discontinued appropriately in the shortest time.

In conclusion, antibiotic management politics should be conducted dynamically in addition to precautions in order to decrease mortality and morbiditiy rates related to HAIs. Although this study is a retrospective study and involves a limited number of patients, it is valuable in that it reflects the PICU data in a university hospital. Further studies especially related to PICUs should be conducted throughout our country.

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Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Istanbul Medical Faculty (2017/485).

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