Original Article

Gram-negative bacilli causing infections in an intensive care unit of a tertiary care hospital in Istanbul, Turkey

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Abstract

Introduction: This study aimed to demonstrate the changing epidemiology of infecting microorganisms and their long-term resistance profiles and to describe the microbiological point of view in anti-infective management of intensive care unit (ICU) patients.

Methodology: A total of 5,690 isolates of Gram-negative bacilli were included in this study. Antibiotic susceptibility was tested using the disk diffusion method and Vitek 2 system. Chi-square tests were used for hypothesis testing.

Results: The most frequently isolated organisms were *A. baumannii* (37.3%), *P. aeruginosa* (30.3%), *Enterobacter* spp. (10.4%), *E. coli* (10.4%), and *Klebsiella* spp. (8.9%). *A. baumannii* was the most frequently isolated organism from the respiratory tract (43.4%); the susceptibility rates for imipenem and meropenem decreased to 7% and 6% ($p < 0.0001$), respectively. The percentage of multidrug-resistant (MDR) *A. baumannii* isolates continuously increased from 18.7% in 2004 to 69% in 2011 ($p < 0.0001$), whereas MDR *P. aeruginosa* isolates increased from 1.5% to 22% ($p < 0.0001$). Carbapenem-resistant *Klebsiella* isolates emerged in 2010 and increased to 20% in the next year. The rates of ESBL-producing *Enterobacteriaceae* in the ICU was very high in 2011 – 50% for *E. coli* and 80% for *Klebsiella* strains.

Conclusion: The most common isolated Gram-negative bacillus in our study was *A. baumannii* and that the prevalence of MDR isolates has increased markedly over. Accordingly, the comparison of antibiotic resistance of other pathogens in 2004 and 2011 displayed an increasing trend. These data imply the urgent need for new and effective strategies in our hospital and in the region.

Key words: Gram-negative bacilli; Antibiotic resistance; ICU; MDR

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Introduction

Gram-negative bacilli (GNB) are a common cause of sepsis, pneumonia, and urinary tract infections in intensive care unit (ICU) patients [1-3]. Hospitalized patients in these areas often suffer from a debilitating physical condition, deficiencies of the immune system, and severe infectious complications including nosocomial infections requiring intense antibiotic therapy for long periods. These types of infections are not only difficult to treat, but also have a significant adverse economic impact on the healthcare system in terms of costs, increased length of hospital stay, morbidity, and mortality [3-5]. Antibiotic resistance among GNB are increasing continuously and this issue must be dealt with as a major worldwide issue [6-9]. As variations do exist among different countries and hospitals, the local resistance data is essential for appropriate initial therapy of ICU infections [10]. The aim of this study was to report the changing epidemiology of ICU pathogens and their long-term resistance profiles, and to provide a microbiological point of view in anti-infective management of ICU patients.

Methodology

Data was collected between January 2004 and December 2011 at the 21-bed mixed ICU of Haydarpasa Numune Education and Research Hospital (HNH), which has a 725 bed capacity. Patients who acquired infections after 48 hours of ICU admission were included in this study; diagnosis was made according to Centers for Disease Control and Prevention guidelines [11]. Ethical approval was granted from The Haydarpasa Numune Education and

Research Hospital Ethical Committee (HNEAH-KAEK/27).

The clinical isolates of GNB recovered from tracheal aspirate, blood, and urine samples were analyzed, identified using standard microbiological techniques, and differentiated to species level by BBL Enteric/Nonfermenter ID Kit (Becton Dickinson, Franklin Lakes, USA) and Vitek2 system (bioMérieux, Marcy l'Etoile, France). Consecutive, non-duplicate, and clinical GNB isolates were collected.

Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) criteria and microbroth dilution assay with the Vitek 2 system (bioMérieux, Marcy l'Etoile, France). The following antibiotics (Oxoid Disc) were tested: ampicillin/sulbactam, piperacillin/tazobactam, ceftriaxone, ceftazidime, cefoperazone/sulbactam, cefepime, gentamicin, amikacin, ciprofloxacin, levofloxacin, imipenem, and meropenem. Colistin entered the market in Turkey in 2009. The isolates were classified as susceptible, intermediate, or resistant according to the breakpoints established by the CLSI [12]. Breakpoints of cefoperazone/sulbactam were interpreted according to cefoperazone. Quality control was performed by testing *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Klebsiella pneumoniae* ATCC 700603. Extended-spectrum ß-lactamase (ESBL) producers were detected using the CLSI double disk diffusion method. *A. baumannii* and *P. aeruginosa* were classified as multidrug-resistant (MDR) by non-susceptibility to at least one agent in three or more antibiotic classes [13].

Chi-square tests were used for hypothesis testing using SPSS version 11.0; OR and 95% confidence intervals was calculated using EPI-INFO version 3.5.1 for statistical analysis. Differences were considered statistically significant at p-values < 0.05.

Results

A total of 5,690 isolates of GNB were identified between 2004 and 2011. Respiratory tracts (4,351, 76.5%), blood cultures (690, 12.1%) and urine (649, 11.4%) were the major sources of the isolates (Table 1). The organisms most frequently isolated were *A. baumannii* (2,124, 37.3%), *P. aeruginosa* (1,736, 30.3%), *Enterobacter* spp. (594, 10.4%), *E. coli* (592, 10.4%), and *Klebsiella* spp. (509, 8.9%).

Table 1. Distribution of isolates among samples

Samples	2004	2005	2006	2007	2008	2009	2010	2011	Total
Respiratory tract	267	379	447	511	535	785	755	672	**4,351**
Blood	30	45	73	105	112	129	98	98	**690**
Urine	102	102	91	64	72	85	72	61	**649**
Total	**399**	**526**	**611**	**680**	**719**	**999**	**925**	**831**	**5,690**

Table 2. Distribution of GNB isolates among samples between 2004 and 2011

Organisms most frequently isolated	Samples	2004	2005	2006	2007	2008	2009	2010	2011	Total
	Res.tract	53	128	244	207	267	356	339	295	**1,889**
A. baumannii	Blood	4	9	21	25	27	36	27	25	**174**
	Urine	6	8	3	9	10	12	8	5	**61**
	Res.tract	105	146	98	186	164	279	223	192	**1,393**
P. aeruginosa	Blood	6	9	11	27	24	31	19	12	**153**
	Urine	46	44	31	12	13	14	17	13	**190**
	Res.tract	45	47	57	45	40	47	52	43	**376**
***Enterobacter* spp.**	Blood	12	9	17	22	28	21	14	11	**134**
	Urine	11	11	8	17	15	12	6	4	**84**
	Res.tract	25	38	15	49	40	52	33	28	**280**
E. coli	Blood	2	2	4	17	14	19	14	12	**84**
	Urine	28	30	36	19	27	38	28	22	**228**
	Res.tract	8	14	16	17	22	49	102	104	**332**
***Klebsiella* spp.**	Blood	3	8	11	11	14	20	22	32	**121**
	Urine	5	2	6	5	6	8	11	13	**56**
	Res.tract	31	6	17	7	2	2	6	10	**81**
Others	Blood	3	8	9	3	5	2	2	6	**65**
	Urine	6	7	7	2	1	1	2	4	**30**
Total		**399**	**526**	**611**	**680**	**719**	**999**	**925**	**831**	**5,690**

Table 3. Trends in antibiotic resistance among various GNB between 2004 and 2011

		Resistance rates (%)									
Pathogen	**Antibiotic**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**p**	**Trend**
A. baumannii	Imipenem	21.9	35.2	64.9	50.2	71.1	76.0	89.0	92.9	< 0.0001	↑
	Meropenem	23.4	28.3	64.9	50.2	65.1	81.9	92.0	94.2	< 0.0001	↑
	Ampicilin-sulbactam	48.4	20.0	98.1	83.0	79.9	85.9	97.1	95.1	< 0.0001	↑
	Gentamicin	71.9	49.7	82.1	80.1	55.9	53.0	38.0	63.1	< 0.0001	↓
	Amikacin	37.5	30.3	50.0	44.8	57.9	75.0	75.9	70.2	< 0.0001	↑
	Ceftazidime	98.4	91.0	99.3	97.1	95.7	98.0	98.1	99.1	0.427[a]	-
	Cefoperazone-sulbactam	1.6	4.1	5.2	9.1	25.0	58.9	79.9	92.0	< 0.0001	↑
	Ciprofloxacin	92.2	61.4	73.1	55.6	65.1	90.1	90.1	98.2	< 0.0001	↑
	Levofloxacin	90.6	66.9	67.2	63.9	71.1	85.9	88.0	96.9	< 0.0001	↑
P. aeruginosa	Imipenem	24.8	24.1	25.0	50.2	30.8	46.0	62.2	48.8	< 0.0001	↑
	Meropenem	24.8	21.1	22.9	50.2	41.8	51.2	56.0	46.1	< 0.0001	↑
	Piperacilin-tazobactam	47.8	48.2	35.7	42.2	22.9	44.1	57.9	56.2	0.004	↑
	Gentamicin	73.2	71.9	70.7	72.0	42.8	71.9	50.2	31.8	< 0.0001	↑
	Amikacin	1.9	3.0	27.9	32.0	19.9	48.1	20.8	23.0	0.254	-
	Ceftazidime	33.8	74.9	85.7	82.2	79.6	96.0	91.9	53,0	0.001	↓
	Ciprofloxacin	72.0	71.9	67.9	64.0	62.7	71.9	59.1	47.9	< 0.0001	↑
	Levofloxacin	82.8	74.9	84.3	54.2	75.6	84.0	69.1	59.0	0.001	↑
***Klebsiella* spp.**	Imipenem	0	0	0	0	0	0	5.0	20.0	-	*
	Meropenem	0	0	0	0	0	0	7.0	19.0	-	*
	Piperacilin-tazobactam	18.8	20.8	18.2	21.2	64.3	63.6	79.3	75.8	< 0.0001	↑
	Gentamicin	18.8	20.8	15.2	21.2	11.9	18.2	30.4	44.3	< 0.0001[b]	↑
	Amikacin	12.5	16.7	15.2	15.2	33.3	14.3	24.4	28.9	0.043[b]	↑
	Ceftazidime	81.3	83.3	90.9	93.9	76.2	88.3	90.4	80.5	0.305[b]	-
	Ceftriaxone	93.8	91.7	90.9	97.0	78.6	88.3	92.6	89.9	0.854[c]	-
	Cefepime	50.0	58.3	69.7	90.9	76.2	31.2	90.4	79.9	0.035[d]	↑
	Cefoperazone-sulbactam	31.3	25.0	21.2	24.2	50.0	44.2	60.0	59.1	< 0.0001	↑
	Ciprofloxacin	37.5	79.2	63.6	66.7	54.8	22.1	26.7	63.8	0.132	-
	Levofloxacin	31.3	70.8	57.6	72.7	81.0	18.2	16.3	77.2	0.838	-
***Enterobacter* spp.**	Imipenem	0	0	0	0	0	0	0	0	-	-
	Meropenem	0	0	0	0	0	0	0	0	-	-
	Piperacilin-tazobactam	38.2	31.3	25.6	57.1	55.4	48.8	63.9	41.4	< 0.0001	↑
	Gentamicin	16.2	13.4	18.3	22.6	18.1	33.8	19.4	36.2	0.002	↑
	Amikacin	10.4	7.5	12.2	11.9	21.7	7.5	19.4	10.3	0.252	-
	Ceftazidime	50.0	62.7	53.7	44.0	71.1	67.5	77.4	62.1	0.002	↑
	Ceftriaxone	54.4	65.7	52.4	65.5	91.6	72.5	77.8	70.7	< 0.0001	↑
	Cefepime	54.4	58.2	46.3	46.4	57.8	42.5	73.6	58.6	0.161	-
	Cefoperazone-sulbactam	14.7	28.4	22.0	23.8	44.6	43.8	47.2	29.3	< 0.0001	↑
	Ciprofloxacin	20.6	25.4	35.4	53.6	48.2	45.0	15.3	29.3	0.618	-
	Levofloxacin	22.1	32.8	28.8	46.4	55.4	42.5	13.9	29.3	0.767	-
E. coli	Imipenem	0	0	0	0	0	0	0	0	-	-
	Meropenem	0	0	0	0	0	0	0	0	-	-
	Piperacilin-tazobactam	20.0	24.3	41.8	22.4	9.9	31.2	32.0	25.8	0.478	-
	Gentamicin	20.0	15.7	50.9	36.5	32.1	44.0	26.7	27.4	0.173	-
	Amikacin	7.3	1.4	10.9	5.9	9.9	3.7	4.0	6.5	-	*
	Ceftazidime	76.4	70.0	70.9	57.6	82.7	74.3	61.3	51.6	0.040	↑
	Ceftriaxone	78.2	71.4	78.2	60.0	82.7	75.2	62.7	53.2	0.016	↑
	Cefepime	61.8	68.6	70.9	56.5	75.3	73.4	58.7	50.0	0.262	-
	Cefoperazone-sulbactam	3.6	7.1	10.9	14.1	14.8	20.2	22.7	21.0	< 0.0001	↑
	Ciprofloxacin	58.2	61.4	69.1	49.4	74.1	67.0	54.7	51.6	0.577	-
	Levofloxacin	54.5	41.4	76.4	69.4	75.3	62.4	54.7	50.0	0.914	-

The p value in the table shows the result of the Chi-square test linear-by-linear Association
The Chi-square test statistic is calculated for all years that have expected frequencies ≥ 5
[a]The Chi-square test statistic is calculated for years between 2007-2011
[b]The Chi-square test statistic is calculated for years between 2005-2011
[c]The Chi-square test statistic is calculated for years between 2009-2011
[d]The Chi-square test statistic is calculated for years between 2006-2011
*The Chi-square test statistic is not calculated as all years had expected frequencies < 5

Figure 1. Resistance rates of *A. baumannii*

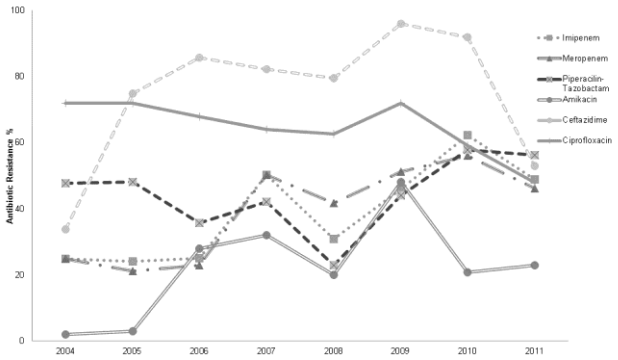

Figure 2. Resistance rates of *P. aeruginosa*

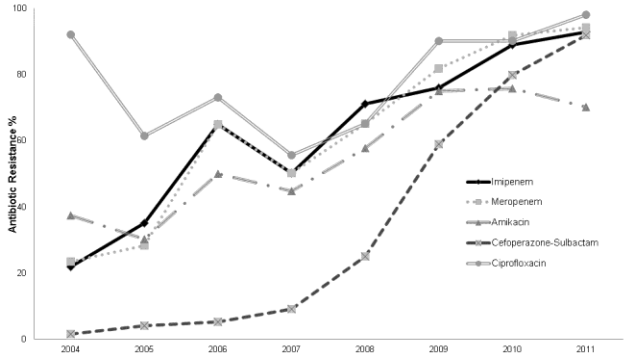

Table 4. Comparison of 2004 and 2011 antibiotic resistance of *A. baumannii*

Antibiotic	Resistance (%) 2004	Resistance (%) 2011	p value	OR	95% CI
IMP	21.9	92.9	< 0.0001	0.02	0.04-0.11
MEM	23.4	94.2	< 0.0001	0.02	0.04-0.11
AK	37.5	70.2	< 0.0001	0.26	0.21-0.52
CES	1.6	92.0	< 0.0001	0.00	0.00-0.03
CIP	92.2	98.2	0.021	0.22	0.17-0.68

IMP: imipenem; MEM: meropenem; AK: amikacin; CES: cefoperazone-sulbactam; CIP: ciprofloxacin
Statistical analyses were calculated using EPI-INFO version 3.5.1

Table 5. Comparison of 2004 and 2011 antibiotic resistance of *P. aeruginosa*

Antibiotic	Resistance (%) 2004	Resistance (%) 2011	p value	OR	95% CI
IMP	24.8	48.8	< 0.0001	0.35	0.22-0.39
MEM	24.8	46.1	< 0.0001	0.39	0.42-0.75
TZP	47.8	56.2	0.106	0.71	0.65-1.04
AK	1.9	23.0	< 0.0001	0.07	0.04-0.36
CAZ	33.8	53.0	< 0.0001	0.45	0.48-0.81
CIP	72.0	47.9	< 0.0001	2.79	1.40-2.46

IMP: imipenem; MEM: meropenem; TZP: tazobactam-piperacilin; AK: smikacin; CAZ: ceftazidime; CIP: ciprofloxacin
Statistical analyses were calculated using EPI-INFO version 3.5.1

A. baumannii was the most commonly isolated organism from respiratory tracts (1,889, 43.4%) and blood cultures (174, 25.2%), while *E. coli* was the most frequently isolated organism from urine (228, 35.1%) (Table 2).

There was a significant increasing trend in the percentage of *A. baumannii* isolated from the respiratory tract, while a decreasing trend in the percentage of *P. aeruginosa* was observed when counts of 2004 to 2011 were compared (Chi-square: 15,796 $p < 0.0001$). The antimicrobials tested and the percentages of isolates determined to be resistant are listed in Table 3. All of *A. baumannii* and *P. aeruginosa* isolates were susceptible to colistin.

A. baumannii

Rates of resistance to most antibiotics were significantly increased among *A. baumannii* during the study period (Table 3, Figure 1). The susceptibility of imipenem and meropenem in *A. baumannii* isolates markedly dropped from 78.1% and 76.6% to 7.1% and 5.8%, respectively. A similar decline in susceptibility was observed for amikacin. Gentamicin and fluoroquinolone resistance rates had fluctuations, while ceftazidime showed no difference. The comparison of the resistance rates in the first year (2004) and in the last year (2011) showed a remarkable increase for imipenem, meropenem, amikacin, and cefoperazone-sulbactam, as seen in Table 4. The percentage of MDR isolates continuously increased from 18.7% (2004) to 69% (2011) ($p < 0.0001$).

P. aeruginosa

The resistance for imipenem, meropenem, and amikacin for *P. aeruginosa* isolates increased, as seen in Figure 2 and Table 3. The imipenem resistance rate was higher in 2010 (62.2%) compared to the previous study years. Piperacillin-tazobactam had fluctuations in susceptibility. Interestingly, the increasing resistance rates to ceftazidime dropped from 96% in 2009 to 53% in 2011. Gentamicin and fluoroquinolone resistance rates fluctuated but decreased in 2011. When 2004 was compared to 2011 for piperacillin-tazobactam, no difference other than ciprofloxacin was observed, as shown in Table 5. The percentage of MDR isolates increased from 1.5% in 2004 to 22% in 2011 ($p < 0.0001$).

Enteric Gram negative bacilli

The most active agents against *E. coli* and *Enterobacter* spp. were imipenem and meropenem; their susceptibility profiles remained stable over the eight years and no resistant isolate was detected. Until 2009, there were no isolates resistant to carbapenems for *Klebsiella* spp. (Table 3), but the resistance rate was 20% in 2011. Amikacin and gentamicin showed good *in vitro* activity against *E. coli*, but resistance rates for *Klebsiella* spp. increased. The resistance rates of *E. coli* to ciprofloxacin and levofloxacin were around 40%-50% during the study period, and reached to a peak level of 75% in 2008. The susceptibility patterns of ciprofloxacin and levofloxacin for *Klebsiella* isolates had fluctuations, but decreased significantly in the last year. Decreases in the percentage of isolates susceptible to ciprofloxacin were also seen with *Klebsiella* spp. (62.5% to 36.2%) and *Enterobacter* spp. (79.4% to 70.7%). Cefoperazone/sulbactam and piperacillin/tazobactam showed higher activity against *E. coli* and *Enterobacter* spp. than against *Klebsiella* spp. High rates of resistance to third-generation cephalosporins were observed among isolates of *Enterobacteriaceae*. The percentage of ESBL-producing *Klebsiella* strains remained remarkably high (above 80%) in 2004 through 2011; the percentage of ESBL-producing *E. coli* strains also remained high but fluctuated and decreased from 75.8% to 50%.

Discussion

This eight-year surveillance study aimed to evaluate the antibiotic resistance patterns and changes among GNB recovered from ICU patients with infections in a Turkish hospital. An active patient surveillance database for hospital infections in targeted clinics has been maintained since 2003 in our hospital. We found that more than three-quarters of GNB isolates were recovered from clinical respiratory specimens in the ICU (Tables 1, 2). The remaining quarter of the microbiological samples included blood and urine specimens. Lockhart *et al*. reported that source of the GNB isolates from ICU patients in hospitals in the United States were as follows: the respiratory tract (52.1%), urine (17.3%), and blood (14.2%) [2]. In a study from China, the authors found that most of the GNB isolates (61.2%) were from the respiratory tract [14].

In our study, *A. baumannii* and *P. aeruginosa* were the most common microorganisms isolated from ICU patients, similar to what has described by the Turkish hospital infection surveillance system [15]. The spectrum of pathogens in ICUs may change from country to country with time and by hospital, type of ICU, and specific patient population [15-20].

During the eight-year period, isolation of *A. baumannii*, which was the most common agent from respiratory tract samples, increased remarkably. We previously documented that most of the healthcare associated infections in our ICU were ventilator-associated pneumonia caused by *A. baumannii* [21]. The most frequent GNB isolated from respiratory tract samples differ greatly among hospitals in Turkey [15,22].

The high resistance rates may be associated with antibiotic abuse and prolonged ICU stays [23]. Our data indicate an alarming pattern of antibiotic resistance in the majority of ICU isolates. The most dramatic change was observed for *A. baumannii*; the isolates showed an increasing trend of resistance to most antibiotics. No antibiotic tested in this study was effective enough to produce > 30% susceptibility for *A. baumannii* isolates except colistin. Accordingly, the resistance for imipenem, meropenem, and amikacin increased over time. On the other hand, *P. aeruginosa* resistance rates were lower overall than *A. baumannii* resistance rates for the antibiotics tested. In 2011, the resistance rate of *P. aeruginosa* to piperacillin/tazobactam slightly increased, while ciprofloxacin resistance decreased compared to 2004.

The resistance of *A. baumannii* to commonly used antibiotics has become a widespread and serious problem in ICUs of Turkey [21]. Carbapenem resistance in *A. baumannii* was seen in three-fourths of the isolates, while *P. aeruginosa* was reported to be resistant in one-third of the strains according to the Turkish National Hospital Infection Surveillance Network Report [15]. Other Turkish investigators have reported relatively lower rates of resistance (50%-87%) to carbapenems in *A. baumannii* [24-27]. Other studies reported similar resistance rates of *P. aeruginosa* [24,25]. In contrast to our results, the resistance rates of *A. baumannii* and *P. aeruginosa* are low in many developed countries [2,17]. *P. aeruginosa* and *A. baumannii* isolated from centers in the United States in the MYSTIC program (1999–2008) were characterized by higher susceptibilities to meropenem 85.4% and 45.7%, respectively [28]. The susceptibility results from MYSTIC Europe 2007 were also higher than our rates [29]. Treatment options for carbapenem-resistant *A. baumannii* infections are limited, and agents such as empirical colistin are now being considered in our ICU.

We observed a significant increase in resistance trend to ceftazidime, ceftriaxone, piperacillin-tazobactam, and cefoperazone-sulbactam among *Enterobacteriacea* isolates, but amikacin was broadly active. One of the most important observations from our study was the decrease of ciprofloxacin susceptibility for *Enterobacteriacea* over the study period. Overall fluoroquinolone usage is strongly linked to the emergence of fluoroquinolone resistance among GNB, and once established, resistance rates increase with increased usage [2]. Except for some *Klebsiella* strains, all enteric GNB were susceptible to carbapenems. Carbapenem-resistant *Klebsiella* spp. isolates emerged in 2010 in our ICU and have increased to 20%. Leblebicioglu *et al*. reported a 6% resistance rate to carbapenems [25]. These observations are consistent with the results of other surveillance studies from Turkey [15,24], and suggest that carbapenems are still effective against *Enterobacteriaceae*; nevertheless, consideration should be given to carbapenamase-producing isolates, owing to their emergence and dissemination potential. In fact, the increased use of carbapenems to combat the growing prevalence of multidrug resistance, particularly ESBL-producing strains, shows early signs of eroding carbapenem effectiveness [30,31].

An alarming finding is the increase in resistance to third-generation cephalosporins and the increasing prevalence of ESBL-producing *Enterobacteriaceae*. Our rates for ESBL-production were 50% for *E. coli* and 80% for *Klebsiella* spp. in 2011. These observations are consistent with the results of other recent surveillance studies from Turkish hospitals and developing countries [7,32,33]. In contrast, the prevalence of ESBL-producing *E. coli* and *K. pneumoniae* in Sweden was 3.9% and 14.3% respectively [34]. The rate for *K. pneumoniae* was 8% in the Netherlands [31].

MDR increased to 92% of *A. baumanni* and 45% of *P. aeruginosa* isolates at the end of the study period. Accordingly, the increasing prevalence of MDR GNB in our ICU was disturbing**.** This trend towards increasing rates of MDR GNB has also been observed in several other studies of more limited scope than ours [26,30,35]. The reason that MDR and ESBL-production rates are higher in our ICU is not exactly clear. Test isolates were not routinely available to us for ancillary molecular characterization of either resistance determinants or clonal relationships. Considering the status of antibiotic abuse in Turkey, the continuation of the present trend of resistance to antibiotics among GNB seems inevitable.

Conclusion

Our study showed that the prevalence of resistance was quite problematic in the ICU. The most

frequently isolated GNB was *A. baumannii,* which shows a high MDR phenotype. Only colistin is an effective treatment. The extraordinary resistance rates seen in the ICU may be associated with deficiencies in infrastructure, understaffing, antibiotic abuse, and the prolonged ICU stays of patients. Thus, collaboration between ICU doctors and infectious diseases specialists is of great importance in Turkey [36]. The lack of any new compounds in the near future indicates that national, regional, and local surveillance efforts are imperative to provide clinicians with information for choosing empirical therapy. We believe these surveillance studies are helpful for planning more effective infection control policies and rational antibiotic therapy, and can reduce infection-related costs, morbidity, and mortality.

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