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ORIGINAL ARTICLE

Epidemiology and antimicrobial resistance among commonly encountered bacteria associated with infections and colonization in intensive care units in a university-affiliated hospital in Shanghai

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Background/Purpose: The aim of this study was to classify intensive care unit (ICU) bacterial strains as either ICU-acquired or ICU-on-admission and to compare their epidemiological and antibiogram characteristics.
Methods: The study was performed in a 1300-bed university-affiliated hospital from January 1, 2006 to December 31, 2010. Based on the time of ICU admission, ICU isolates were classified as ICU-acquired strains (appearing more than 48 hours after admission) or ICU-on-admission strains (appearing 48 hours or less from admission). The microbiological data before ICU admission, the microbiological data, and susceptibility testing were compared between the ICU-acquired and ICU-on-admission bacterial isolates.
Results: The most common ICU-acquired strains were *Acinetobacter baumannii* (19.5%), *Pseudomonas aeruginosa* (15.6%), *Stenotrophomonas maltophilia* (11.5%), *Staphylococcus aureus* (10.7%), *Enterococcus* spp. (10.6%), and *Klebsiella pneumoniae* (9.7%). There were significant differences between ICU-acquired and ICU-on-admission isolates in the susceptibility rates of Gram-negative bacteria to antibiotics, especially the susceptibility of *A. baumannii* to imipenem [23.8% (ICU-acquired) vs. 44.4% (ICU-on-admission), $p < 0.001$] and meropenem (24.1% vs. 37.8%, $p < 0.001$), and the susceptibility of *P. aeruginosa* to imipenem (39.3% vs. 76.1%,

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$p < 0.001$) and meropenem (58.5% vs. 76.1%, $p < 0.05$). Furthermore, decreased susceptibility rates of *A. baumannii* and *P. aeruginosa* to carbapenems were correlated with an extended ICU stay ($p < 0.05$).

Conclusion: Because of decreasing susceptibility rates of pathogens (especially ICU-acquired strains) and a significant correlation with the length of ICU stay, intensivists should consider a patient's time of ICU admission and previous microbiological data and should distinguish ICU-acquired strains from non-ICU-acquired strains so as to initiate optimized empirical antibiotic therapy against ICU-acquired infections.

Introduction

Nosocomial infection has become an important worldwide public health problem and increases morbidity, mortality, and cost during a patient's hospital stay.[1–4] The prevalence of infections acquired in intensive care units (ICUs) is even higher than it is in general wards because of the severity of diseases, prolonged ICU and hospital stays,[5] immunosuppression of ICU patients, and greater number of interventions with invasive devices such as central-line catheters, invasive mechanical ventilations, Foley urine catheters.[6,7]

An ICU-acquired infection is defined as an infection occurring more than 48 hours after an ICU admission.[8] In a recent multicenter study involving 71 adult ICUs, 7.4% of the 9493 patients had an ICU-acquired infection.[9] ICU-acquired infections commonly include a central line-associated bloodstream infection (CLBSI, 40%), catheter-associated urinary tract infection (CAUTI, 31%), ventilator-associated pneumonia (VAP, 20%), and surgical site infection (SSI, 9%).[10,11] These ICU-acquired infections are the most common complications for patients during ICU stays and contribute to significant morbidity and mortality.[12]

Local epidemiological data and antibiograms are useful for optimized empirical antibiotic therapy for severe ICU-acquired infections. Antimicrobial susceptibility of pathogens can vary markedly between hospitals and different units within the same hospital. It is therefore necessary to monitor prevalence and antimicrobial susceptibility patterns to modify antimicrobial hospital policy, especially in ICUs. However, since many ICU admissions are the result of substantial infections,[9,13,14] most epidemiological studies on ICU-acquired bacterial strains include strains obtained outside the ICU. They thus have a bias with respect to actual antibiotic resistant patterns. Few epidemiological data are available on the prevalence, distribution, and antibiogram of ICU-acquired and ICU-on-admission strains (excluding "ICU" strains that are actually non-ICU strains).

The aim of this study was to classify ICU strains as ICU-acquired or ICU-on-admission, based on the length of time from the ICU admission [greater than 48 hours (ICU-acquired) or up to 48 hours from admission (ICU-on-admission)]. The microbiological data was classified before ICU admission. The epidemiological and antibiogram characteristics were compared.

Methods

Hospital settings

The study was performed at Ruijin Hospital (Shanghai, China), a 1300-bed university-affiliated hospital, from January 1, 2006 to December 31, 2010. Ruijin Hospital has three ICUs: a 12-bed surgical ICU (SICU) in which surgical intensive care patients and postoperative patients are cared for; a 10-bed respiratory ICU (RICU) in which general intensive care patients, especially patients with respiratory dysfunction, are cared for; and an 18-bed emergency ICU (EICU) in which most patients had been admitted from the emergency department.

Definitions

ICU isolates were classified as either ICU-acquired strains or ICU-on-admission strains. An ICU-acquired strain was defined as a bacterial species that was obtained more than 48 hours after the patient's ICU admission,[15] whereas an ICU-on-admission isolate was defined as a bacterial species that was obtained within 48 hours after the patient's ICU admission.

An extensively drug-resistant (XDR) pathogen was defined as a pathogen isolate that was resistant to all currently available systemic antibiotics such as cephalosporins, aztreonam, carbapenems, aminoglycosides, fluoroquinolones, and sulbactam (except for polymyxin B).[16]

Patients

Patients younger than 18 years old, patients whose ICU stay was either less than 72 hours or longer than 3 months, and patients readmitted to any ICU within 3 months were excluded from the comparison of the epidemiological and antibiogram characteristics of ICU-acquired and ICU-on-admission isolates.

Microbiological data and susceptibility testing

For patients admitted to ICU and then once weekly during their ICU stays, urine specimens and specimens from sputum or endotracheal tube aspirates were regularly collected and cultured for bacteria and fungi. Sputum, endotracheal aspirates, oral swabs, urine, blood,

catheters, and drainage samples were collected, based on clinical indications of infections during patients' ICU stays. All bacteria isolated were included in the study.

Data for *in vitro* susceptibility testing were collected from the microbiological laboratory during a 5-year period (2006—2010). The identification of bacterial species was performed according to the criteria of the American Society for Microbiology (ASM) and *in vitro* susceptibility testing was performed according to the breakpoint definitions of the Clinical and Laboratory Standards Institute (CLSI, Wayne, PA). Antibacterial susceptibility testing for the most commonly used antibiotics for a given microorganism was routinely performed for all potential pathogens isolated from any sample site. This testing was not repeated when a microorganism was isolated more than once in the same patient within 4 days. All isolates for which antibacterial susceptibility testing had been performed were recorded in a computer database. The database excluded redundancies of strains (i.e., the same microorganism with the same antibiotic susceptibility pattern detected in a separate isolate from the same patient). Antibiograms were retrospectively calculated for each year from 2006 to 2010 for the most frequent Gram-positive and Gram-negative bacteria and for the most commonly prescribed antibiotics in the institution. The following microorganisms were selected because of their prevalence and because of the relevance of their susceptibility pattern in the choice of empirical antibacterial therapy: *Pseudomonas aeruginosa* (amikacin, gentamicin, ciprofloxacin, piperacillin, piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, cefaperazone/sulbactam); *Acinetobacter baumannii* (amikacin, gentamicin, trimethoprim-sulfamethoxazole, ciprofloxacin, piperacillin, piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, cefaperazone/sulbactam); and *Staphylococcus aureus* (oxacillin, vancomycin, linezolid, teicoplanin). Antibiograms were extracted for the whole institution, for the three ICUs (i.e., SICU, RICU, and EICU), and for the ICU-acquired strains and for the ICU-on-admission strains.

Statistical analysis

Data are presented by number of isolates and their percentages. Comparative analysis was performed by using the chi-square test for categorical variables. Two-tailed tests were performed with the significance set at p less than 0.05. The software used for analysis was SPSS 17.0 (SPSS Inc., Chicago, IL, USA) with Bonferroni corrections for multiple tests.

Results

Comparison of epidemiological and antibiogram characteristics between ICU and hospital-wide settings

Prevalence and distribution of the clinical isolates

For the whole hospital, 24,764 strains were isolated during the study period; 9116 (36.8%) were Gram-positive strains, and 15,648 (63.2%) were Gram-negative strains. The most common isolates were *Escherichia coli* (21.9%), *S. aureus* (11.4%), *Klebsiella pneumoniae* (9.4%), *P. aeruginosa* (9.0%), and *A. baumannii* (8.5%). Among the 2711 ICU strains, 28.8% were Gram-positive strains and 71.2% were Gram-negative strains. The most commonly isolated strains were *A. baumannii* (17.7%), *P. aeruginosa* (14.6%), *S. aureus* (12.3%), *Stenotrophomonas maltophilia* (11.4%), and *K. pneumoniae* (9.1%) (Table 1).

When isolates were stratified according to specimen type, the epidemiology and distributions were significantly different among the different specimen types and between the hospital and ICU isolates of the same specimen type. For the whole institution, *A. baumannii*, *P. aeruginosa*, *K. pneumoniae,* and *S. aureus* were the most commonly isolated pathogens in respiratory tract samples, whereas *E. coli, Enterococcus faecalis,* and *E. faecium* were common in urine and bile samples. *E. coli, S. epidermidis,* and *K. pneumoniae* were the top three pathogens obtained from

Table 1 Isolate numbers and prevalence of clinical isolates in the hospital and intensive care unit settings

Bacteria	Isolate no. (%)				
	Hospital (n = 24,764)	ICU (n = 2711)	RICU (n = 705)	SICU (n = 1225)	EICU (n = 781)
Gram-positive isolates					
Staphylococcus aureus	2,826 (11.4%)	332 (12.3%)	82 (11.3%)	144 (11.8%)	106 (13.6%)
CNS	2761 (11.1%)	168 (6.2%)	47 (6.7%)	78 (6.4%)	43 (5.5%)
Enterococcus faecalis	1673 (6.8%)	73 (2.7%)	17 (2.4%)	39 (3.2%)	17 (2.2%)
Enterococcus faecium	945 (3.8%)	166 (6.1%)	20 (2.8%)	109 (8.9%)	37 (4.7%)
Gram-negative isolates					
Escherichia coli	5414 (21.9%)	217 (8.0%)	27 (3.8%)	128 (10.4%)	61 (7.8%)
Klebsiella pneumoniae	2320 (9.4%)	246 (9.1%)	77 (10.9%)	94 (7.7%)	75 (9.6%)
Acinetobacter baumannii	2115 (8.5%)	481 (17.7%)	138 (19.6%)	187 (15.3%)	156 (20.0%)
Pseudomonas aeruginosa	2230 (9.0%)	397 (14.6%)	117 (16.6%)	166 (13.6%)	114 (14.6%)
Stenotrophomonas maltophilia	1058 (4.3%)	309 (11.4%)	101 (14.3%)	135 (11.0%)	73 (9.3%)
Enterobacter	689 (2.8%)	86 (3.2%)	21 (3.0%)	47 (3.8%)	18 (2.3%)
Proteus	449 (1.8%)	26 (1.3%)	7 (1.0%)	12 (1.0%)	7 (0.9%)

CNS = coagulase-negative staphylococci; EICU = emergency intensive care unit; ICU = intensive care unit; RICU = respiratory intensive care unit; SICU = surgical intensive care unit.

blood samples. For ICU settings, *A. baumanii* was predominant in the respiratory tract, in catheters, and in blood samples. *Enterococcus faecium*, *E. coli*, and *P. aeruginosa* were common in urine samples from ICU patients. A significant decreasing trend was observed in the prevalence of *S. aureus* and *A. baumannii* in the RICU during the analysis. *S. aureus* decreased from 15.5% to 3.8% and *A. baumannii* decreased from 27.7% to 7.8% (Fig. 1).

Comparison of antibiograms for hospital-wide and ICU settings

During the 5-year period for either the ICU or the hospital, a trend of decreasing antibiotic susceptibility was present in commonly separated strains ($p < 0.001$). There were also significant differences between the ICU and the hospital antibiograms (Table 2). For multidrug-resistant bacteria, there was a significant difference between the hospital and ICU settings in the prevalence of MRSA [67.3% (hospital) vs. 94.3% (ICU), $p < 0.001$]; XDR *A. baumannii* (26.5% vs. 39.1%, $p < 0.001$); and XDR *P. aeruginosa* (7.6% vs. 11.8%, $p < 0.01$) (Table 3).

Comparison of epidemiological and antibiogram characteristics between ICU-acquired and ICU-on-admission isolates

Prevalence and distribution of ICU isolates

There were 1094 patients enrolled and 2324 ICU strains analyzed. Of the analyzed strains, 1746 (75.1%) were ICU-acquired strains and 578 (24.9%) were ICU-on-admission strains. The most common ICU-acquired strains were *A. baumannii* (19.5%), *P. aeruginosa* (15.6%), *S. maltophilia* (11.5%), *S. aureus* (10.7%), *Entercoccus* spp. (10.6%), and *K. pneumoniae* (9.7%). However, the most common ICU-on-admission strains were *P. aeruginosa* (19.6%), *A. baumannii* (15.6%), *K. pneumoniae* (13.3%), *Enterococcus* spp. (12.4%), *S. aureus* (10.6%), and *E. coli* (7.6%). The prevalence and distribution of ICU-acquired and ICU-on-admission isolates were similar among the various specimen types. For the ICU-acquired strains, *A. baumannii* notably remained the leading pathogen in all specimen types, except urine samples. For blood samples, *A. baumannii*, S. *aureus*, and *K. pneumoniae* were the dominant isolated pathogens.

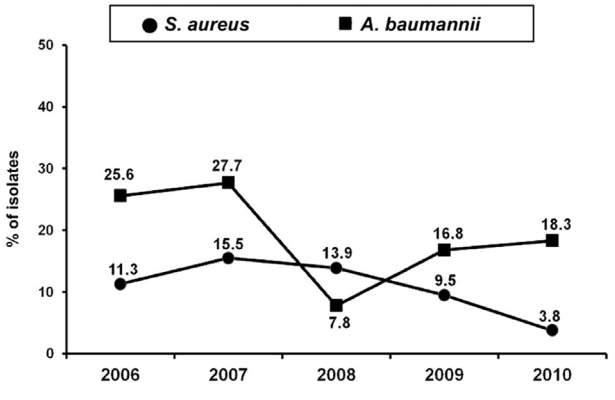

Figure 1. Prevalence of *Staphylococcus aureus* and *Acinetobacter baumannii* in the RICU.

Comparison of antibiograms between ICU-acquired and ICU-on-admission isolates

There were no significant differences in the antibiograms of the Gram-positive strains (including *S. aureus* and *Enterococcus* spp.) between ICU-on-admission and ICU-acquired groups. For the following commonly isolated Gram-negative strains, the antibiograms of were compared between the two groups of isolates: *A. baumannii*, *P. aeruginosa*, *K. pneumoniae*, and *E. coli* (Table 2). Differences in the susceptibility of *A. baumannii* to amikacin, ceftazidime, cefepime, imipenem, meropenem was observed between ICU-acquired and ICU-on-admission strains. For *P. aeruginosa*, the susceptibility to amikacin, imipenem, and meropenem differed significantly. Differences also existed in the susceptibility of *K. pneumoniae* to cefoperazone/sulbactam and piperacillin/tazobactam and in the susceptibility of *E. coli* to ceftazidime. When the three ICUs were analyzed separately, the susceptibility rates of *A. baumannii* and *P. aeruginosa* to carbapenems tended to be lower in the ICU-acquired isolates (data not shown).

Since the susceptibility rates significantly decreased in the ICU-acquired strains (compared to the rates of ICU-on-admission isolates)—especially for *A. baumannii* and *P. aeruginosa* to carbapenems—the relationships between the susceptibility rates of *A. baumannii* and *P. aeruginosa* to carbapenems and the length of ICU stay were further investigated by dividing the time of hospitalization into three periods: 48 hours or less, from 48 hours to 7 days, and more than 7 days. Fig. 2 illustrates the relationships between the susceptibility rates and the ICU length of stay. Decreased susceptibility rates of *A. baumannii* and *P. aeruginosa* to carbapenems were correlated with a prolonged ICU stay ($p < 0.05$). An analysis of sputum specimens showed that the susceptibility rate of *P. aeruginosa* to meropenem decreased as a patient's ICU length of stay increased (Fig. 3).

Stratifications according to the site of sampling such as sputum or endotracheal aspiration, oral swab, urine, blood, catheters, bile, drainage showed no differences in susceptibility between ICU-on-admission and ICU-acquired strains, with the exception of the susceptibility of *A. baumannii* to gentamicin [27.8% (ICU-on-admission) vs. 16.7% (ICU-acquired), $p < 0.05$] and trimethoprim-sulfamethoxazole (25.3% vs. 14.9%, $p < 0.05$); the susceptibility of *P. aeruginosa* to amikacin (92.4% vs. 77.8%, $p < 0.01$) and imipenem (69.6% vs. 40.6%, $p < 0.01$); the susceptibility of *K. pneumoniae* to cefoperazone/sulbactam (92.3% vs. 57.8%, $p < 0.01$); and the susceptibility of *E. coli* to ceftazidime (84.6% vs. 54.7%, $p < 0.05$) and ciprofloxacin (30.8% vs. 7.5%, $p < 0.05$) for sputum or endotracheal aspiration cultures.

The proportions of the multidrug-resistant strains were compared between the ICU-on-admission and ICU-acquired groups. No vancomycin-resistant *Enterococci* (VRE) were observed during the study period. Between the ICU-acquired and ICU-on-admission strains, no significant differences were found in the proportions of MRSA, XDR *A. baumannii*, and XDR *P. aeruginosa* or in the proportions of extended spectrum beta-lactamase (ESBL)-producing *K. pneumoniae* and *E. coli* (Table 3).

Table 2 Susceptibility rates of hospital-wide, ICU, ICU-acquired, and ICU-on-admission isolates

	Susceptibility rate (%)			
	Hospital	ICU	ICU-acquired	ICU-on-admission
Acinetobacter baumannii	$n = 2115$	$n = 481$	$n = 340$	$n = 90$
Amikacin	48.6	25.4*	23.2	35.6**
Trimethoprim-sulfamethoxazole	37.6	15.9*	11.2	24.4**
Ciprofloxacin	37.4	14.2*	12.1	20.0
Piperacillin/tazobactam	39.5	16.0*	15.3	22.2
Cefaperazone/sulbactam	61.4	48.0*	41.5	50.0
Ceftazidime	41.8	16.4*	14.1	27.8**
Cefepime	41.4	17.6*	13.2	25.6**
Imipenem	55.8	31.8*	23.8	44.4**
Meropenem	55.1	31.2*	24.1	37.8**
Pseudomonas aeruginosa	$n = 2230$	$n = 397$	$n = 272$	$n = 113$
Amikacin	76.1	77.0	80.9	89.4**
Ciprofloxacin	68.5	67.7	71	64.6
Piperacillin/tazobactam	74.3	64.1	68.4	69.9
Ceftazidime	73.7	60.7*	67.3	69.9
Cefepime	74.3	67.0	73.2	69.9
Imipenem	66.2	48.1*	39.3	76.1**
Meropenem	71.0	57.2*	58.5	76.1**
Klebsiella pneumoniae	$n = 2320$	$n = 246$	$n = 169$	$n = 77$
Amikacin	88.3	73.3*	79.3	83.1
Ciprofloxacin	64.0	41.2*	52.7	49.4
Piperacillin/tazobactam	78.0	48.3*	56.8	71.4**
Ceftazidime	66.7	36.9*	66.3	66.2
Cefepime	66.8	36.3*	71.6	75.3
Imipenem	99.5	98.3	100.0	100.0
Meropenem	99.5	98.3	98.2	100.0
Escherichia coli	$n = 5414$	$n = 217$	$n = 145$	$n = 44$
Amikacin	79.4	79.4	78.6	79.5
Ciprofloxacin	31.3	12.4*	15.2	20.5
Piperacillin/tazobactam	78.6	71.8	74.5	65.9
Ceftazidime	46.4	27.5*	68.3	50.0**
Cefepime	46.4	26.1*	60.7	50.0
Imipenem	89.2	99.3*	100.0	100.0
Meropenem	89.2	98.9*	100.0	95.5

ICU = intensive care unit.
*$p < 0.001$, for comparisons between hospital-wide and ICU isolated strains.
**$p < 0.05$, for comparisons between ICU-acquired and ICU-on-admission strains.

Discussion

S. aureus remained the most commonly isolated Gram-positive bacteria hospital-wide and in the three ICUs. There was a trend of decreasing annual prevalence in the ICU isolates. This decreasing prevalence of *S. aureus* was significant in the RICU. The prevalence of *S. aureus* remained stable from 2006 to 2008 in the RICU, ranging from 11.3% to 15.47%. However, the prevalence decreased significantly to 9.4% in 2009 and 3.8% in 2010. In 2008,

Table 3 Prevalence of multidrug-resistant bacteria in hospital-wide, ICU, ICU-acquired, and ICU-on-admission isolates

	Indicated resistant isolate no./Total isolate no. (%)			
	Hospital	ICU	ICU-acquired	ICU-on-admission
Methicillin-resistant *Staphylococcus aureus*	1902/2826 (67.3)	313/332 (94.3)*	187/187 (100)	61/62 (98.4)
XDR *Acinetobacter baumannii*	561/2115 (26.5)	188/481 (39.1)*	154/340 (45.2)	32/90 (35.6)
XDR *Pseudomonas aeruginosa*	170/2230 (7.6)	47/397 (11.8)*	24/272 (8.8)	0/113 (0)
ESBL-producing *Klebsiella pneumoniae*	455/2320 (19.6)	80/246 (32.5)*	48/169 (28.4)	19/77 (25.0)
ESBL-producing *Escherichia coli*	2350/5414 (43.4)	100/217 (46.0)*	55/145 (37.9)	22/44 (50.0)

ICU = intensive care unit; ESBL = extended spectrum beta-lactamase; XDR = extensively drug-resistant.
*$p < 0.01$, for comparisons between hospital-wide and ICU isolated strains.

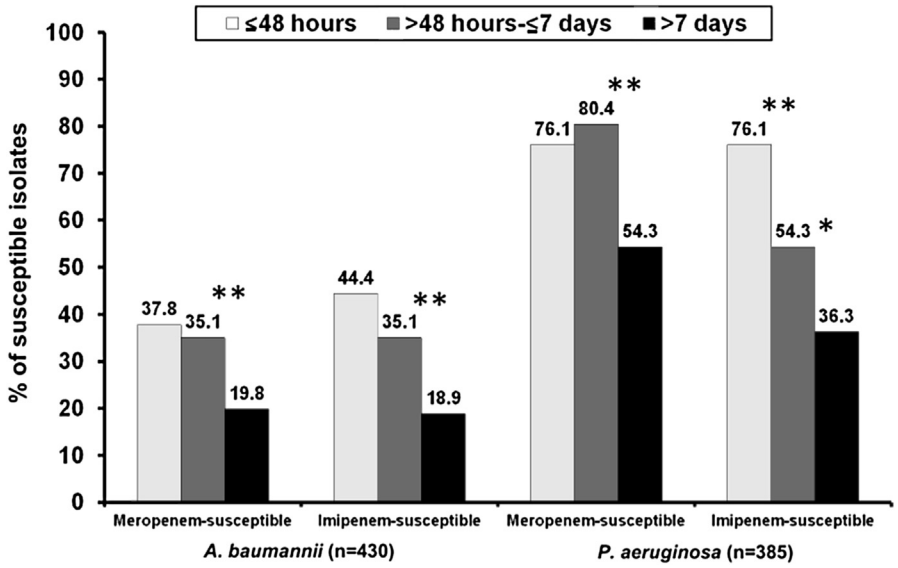

Figure 2. Relationship between length of ICU stay and susceptibility rates of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* to carbapenems. *$p < 0.05$, for comparisons between 48 hours or less, from 48 hours up to 7 days, or more than 7 days. **$p < 0.01$, for comparisons between 48 hours or less, from 48 hours up to 7 days, or more than 7 days.

chlorhexidine decontamination was introduced in the RICU, and contact isolation precautions and appropriate hand hygiene were implemented to prevent cross-transmission. Thus, these comprehensive interventions may have decreased the prevalence of *S. aureus*.

Similar distributions and prevalence of Gram-positive strains were observed; however, the distribution of Gram-negative bacteria differed significantly between the hospital-wide and ICU isolates. *E. coli* was the most commonly isolated Gram-negative strain in the hospital, whereas nonfermentative bacteria, especially *A. baumannii* and *P. aeruginosa*, were the predominant ICU strains[17]. When ICU isolates were further stratified as ICU-on-admission or ICU-acquired strains, the epidemiology and distribution of the isolates were similar. However, for the ICU-acquired strains, *A. baumannii* remained the leading pathogen in all specimen types, including sputum, oral swabs, urine, blood, catheters, bile, and drainage.

Although further stratification of the ICU isolates into ICU-acquired strains added little information to the prevalence and distribution of ICU settings, the results of the present analysis showed significant differences between ICU and hospital-wide antimicrobial susceptibility rates, and between presumably ICU-acquired and ICU-on-admission antibiograms. The comparison revealed similar susceptibility rates among Gram-positive strains, whereas

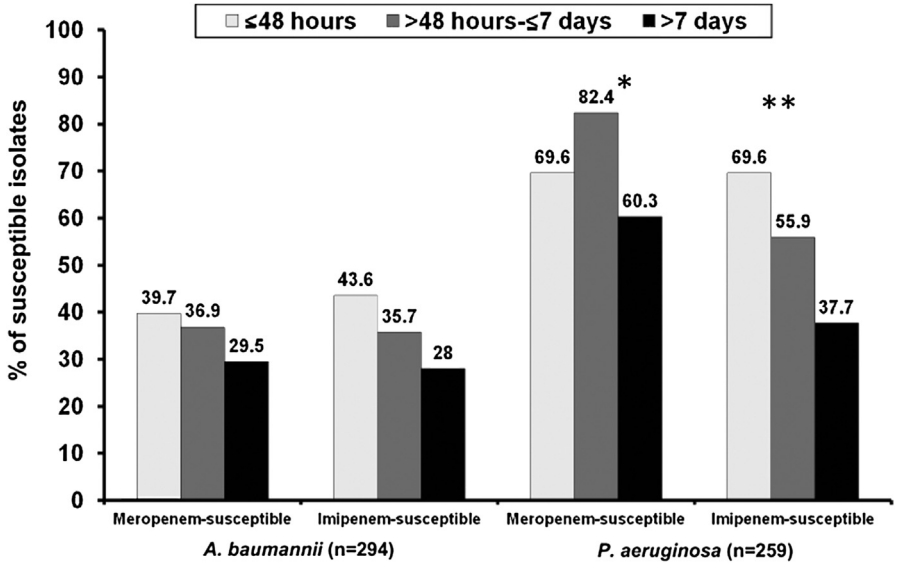

Figure 3. Relationship between susceptibility rates of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* from sputum samples to carbapenems and the length of ICU stay. *$p < 0.05$, for comparisons between either 48 hours or less, from 48 hours up to 7 days, or more than 7 days. **$p < 0.01$ for comparisons between either 48 hours or less, from 48 hours up to 7 days, or more than 7 days.

important differences existed among Gram-negative strains,[18] especially *A. baumannii*, *P. aeruginosa*, *K. pneumoniae*, and *E. coli*. These findings may guide the choice of empirical antibiotic therapy when clinicians are confronted with an ICU-acquired infection, although these data are limited to certain clinical situations and specific for the hospital and ICUs where the data were collected.[19]

Few epidemiological data are available on antibiograms that compare ICU-acquired and ICU-on-admission acquired strains (excluding "ICU" strains that actually are non-ICU strains). The present study tried to distinguish presumably ICU-acquired isolates from ICU-on-admission isolates, based on the length of time from the admission the isolate appeared (48 hours or less from admission or after 48 hours from admission, respectively) and based on previous microbiological data before the patient's transfer to the ICU. By doing this, the susceptibility rates were found to be much lower to certain antibiotics in some Gram-negative ICU-acquired strains (especially for *A. baumannii* and *P. aeruginosa* to carbapenems), compared to the susceptibility rate of ICU-on-admission strains. Decreased susceptibility rate of *A. baumannii* and *P. aeruginosa* to carbapenems furthermore was correlated with a prolonged ICU stay ($p < 0.05$) when the ICU stay were further divided as follows: within 48 hours, from 48 hours to 7 days, and from 7 days or more.

The global spread of carbapenem-resistant *P. aeruginosa* and *A. baumannii* is of great concern,[11,20] given that carbapenems are often used to treat these infections in the ICU. The significantly low susceptibility of ICU-acquired strains to carbapenems may be related to the increasing use of carbapenems in ICUs, although the actual use of carbapenems unavailable at this time in our study. According to Lamoth et al.,[21] the use of carbapenems is particularly high in the ICU[22] [e.g., 22 defined daily doses (DDDs) of imipenem and meropenem vs., 4.5 DDDs of piperacillin/tazobactam per 100 bed-days]. The clinical use of carbapenems may continue to increase with prolonged ICU stays.

Inadequate initial antimicrobial treatment in serious infections increases mortality. Achieving adequate treatment is increasingly difficult because of the increasing prevalence of multidrug-resistant (MDR) pathogens. As previously noted, the failure to recognize the presence of MDR pathogens results in inadequate antibiotic therapy. This oversight leads to increased mortality. This vicious cycle can promote the increasing use of wide-spectrum antibiotics and increasing resistance to these antibiotics. Carbapenems continue to provide a valuable weapon as bacterial resistance to the other classes of antibiotics increases[23]; however, reports on carbapenem-resistant bacteria such as *A. baumannii* and *P. aeruginosa* should increasingly draw the attention of clinicians and microbiologists since resistance to carbapenems may lead to the failure of initial empirical antibiotic therapy in severe ICU-acquired infections and thereby increase the morbidity and mortality.

Because of the increasing difficulty in choosing initial empirical antibiotics against possible MDR or XDR pathogens, clinical interventions for infection control may play an important role in decreasing the prevalence of MDR pathogens,[24] and thereby break the vicious cycle. The decreasing trend in the prevalence of *A. baumannii* in the RICU may be the result of a multifaceted intervention to reduce XDR *A. baumannii* colonization and infection since 2008. The interventions included implementing contact isolation precautions and appropriate hand hygiene, active surveillance, cohorting patients who were colonized or infected with XDR *A. baumannii*, and environmental cleaning. Apisarnthanarak et al.[16] also conducted a multifaceted intervention to control XDR *A. baumannii* infection, and the efficacy of the intervention was supported by the dramatically decreasing prevalence of XDR *A. baumannii* in longterm follow-up. At least 38% of all nosocomial infections in the ICU may result from cross-transmission. The real frequency may be even higher since the susceptibility rates of these nonfermentative organisms in an ICU are much lower in countries with limited resources than in developed countries.[25] Reducing the incidence of these MDR pathogens with multifaceted interventions may be crucial in improving the outcomes of ICU-acquired infections in developing countries.

This study has several limitations. First, it was a single-center study. Since susceptibility rates vary among hospitals and units, the results may not be representative and reproducible in other institutions. Second, this study included clinical data (not listed here) such as demographic data, underlying diseases, mechanical ventilation days, catheter days, and duration of ICU stay; however, individual risk factors for infections with resistant microorganisms were not analyzed. We further plan to investigate and analyze the epidemiology of ICU-acquired infections, risk factors, and outcomes. In addition, the 48-hour cutoff point was chosen in accordance with the Centers for Disease Control standard definitions of nosocomial infections,[25] and the 7-day cutoff was chosen in accordance with the study by Jean et al.[20] However, incubation periods may vary by the type of pathogen or by a patient's underlying conditions, which make distinguishing between cases of ICU-acquired and ICU-on-admission colonization and infections difficult.

In conclusion, variability exists in the prevalence and distribution of clinical isolated strains and in the susceptibility rates of clinical isolates between hospital-wide and ICU settings. Because of the decreasing susceptibility rates of pathogens to antibiotic treatment (especially ICU-acquired strains) and because of a significant correlation between the susceptibility rates of *A. baumannii* and *P. aeruginosa* to carbapenems with ICU length of stay, intensivists should consider the amount of time from a patient's ICU admission and the patient's previous microbiological data, and the patient's length of ICU stay, and distinguish between ICU-acquired strains and "ICU" strains that are actually non-ICU strains when initiating appropriate empirical antibiotic therapy against ICU-acquired infections.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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References

1. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *JAMA* 1995;**274**:639—44.
2. Sánchez-Velázquez LD, Ponce de León Rosales S, Rangel Frausto MS. The burden of nosocomial infection in the intensive care unit: effects on organ failure, mortality and costs. A nested case-control study. *Arch Med Res* 2006;**37**:370—5.
3. Geffers C, Sohr D, Gastmeier P. Mortality attributable to hospital-acquired infections among surgical patients. *Infect Control Hosp Epidemiol* 2008;**29**:1167—70.
4. Aranaz-Andrés JM, Aibar-Remón C, Vitaller-Murillo J, Ruiz-López P, Limón-Ramírez R, Terol-García E, et al. Incidence of adverse events related to health care in Spain: results of the Spanish National Study of Adverse Events. *J Epidemiol Community Health* 2008;**62**:1022—9.
5. Zhang YL, Yang YB, Wang NP, Chen JH. Infection analysis on intensive care units patients. *Chin J Nosocomiol* 2003;**13**: 120—3 [article in Chinese].
6. Ak O, Batirel A, Ozer S, Çolakoğlu S. Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: a prospective cohort study. *Med Sci Monit* 2011;**17**:PH29—34.
7. Routsi C, Pratikaki M, Platsouka E, Sotiropoulou C, Nanas S, Markaki V, et al. Carbapenem-resistant versus carbapenem-susceptible Acinetobacter baumannii bacteremia in a Greek intensive care unit: risk factors, clinical features and outcomes. *Infection* 2010;**38**:173—80.
8. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988;**16**:128—40.
9. Malacarne P, Langer M, Nascimben E, Moro ML, Giudici D, Lampati L, et al. Building a continuous multicenter infection surveillance system in the intensive care unit: findings from the initial data set of 9,493 patients from 71 Italian intensive care units. *Crit Care Med* 2008;**36**:1105—13.
10. Hidron AI, Edwards JR, Patel J, Horan TC, Sievert DM, Pollock DA, et al. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006—2007. *Infect Control Hosp Epidemiol* 2008;**29**:996—1011.
11. Doyle JS, Buising KL, Thursky KA, Worth LJ, Richards MJ. Epidemiology of infections acquired in intensive care units. *Semin Respir Crit Care Med* 2011;**32**:115—38.
12. Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al. Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. *Crit Care* 2011;**15**. R100.
13. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006;**34**:344—53.
14. Malacarne P, Boccalatte D, Acquarolo A, Agostini F, Anghileri A, Giardino M, et al. Epidemiology of nosocomial infection in 125 Italian intensive care units. *Minerva Anestesiol* 2010;**76**: 13—23.
15. Falagas ME, Karveli EA, Siempos II , Vardakas KZ. Acinetobacter infections: a growing threat for critically ill patients. *Epidemiol Infect* 2008;**136**:1009—19.
16. Apisarnthanarak A, Pinitchai U, Thongphubeth K. A multifaceted intervention to reduce pandrug-resistant *Acinetobacter* baumannii colonization and infection in 3 intensive care units in a Thai tertiary care center: a 3-year study. *Clin Infect Dis* 2008;**47**:760—7.
17. Tao L, Hu B, Rosenthal VD, Gao X, He L. Device-associated infection rates in 398 intensive care units in Shanghai, China: International Nosocomial Infection Control Consortium (INICC) findings. *Int J Infect Dis* 2011;**15**:e774—80.
18. Brusselaers N, Vogelaers D, Blot S. The rising problem of antimicrobial resistance in the intensive care unit. *Ann Intensive Care* 2011;**1**:47.
19. Geffers C, Gastmeier P. Nosocomial infections and multidrug-resistant organisms in Germany: epidemiological data from KISS (the Hospital Infection Surveillance System). *Dtsch Arztebl Int* 2011;**108**:87—93.
20. Jean SS, Hsueh PR, Lee WS, Chang HT, Chou MY, Chen IS, et al. Nationwide surveillance of antimicrobial resistance among non-fermentative Gram-negative bacteria in Intensive Care Units in Taiwan: SMART programme data 2005. *Int J Antimicrob Agents* 2009;**33**:266—71.
21. Lamoth F, Wenger A, Prod'hom G, Vallet Y, Plüss-Suard C, Bille J, et al. Comparison of hospital-wide and unit-specific cumulative antibiograms in hospital- and community-acquired infection. *Infection* 2010;**38**:249—53.
22. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2007. Oslo. 2007. Available at: http://www.whocc.no/atcddd/.
23. Baughman RP. The use of carbapenems in the treatment of serious infections. *J Intensive Care Med* 2009;**24**:230—41.
24. Liu KS, Wang YT, Lai YC, Yu SF, Huang SJ, Huang HJ, et al. Antimicrobial resistance of bacterial isolates from respiratory care wards in Taiwan: a horizontal surveillance study comparison of the characteristics of nosocomial infection and antimicrobial-resistant bacteria in adult intensive care units and two respiratory care facilities for mechanically ventilated patients at a tertiary care centre in Taiwan. *Int J Antimicrob Agents* 2011;**37**:10—5.
25. Weist K, Pollege K, Schulz I, Rüden H, Gastmeier P. How many nosocomial infections are associated with cross-transmission? A prospective cohort study in a surgical intensive care unit. *Infect Control Hosp Epidemiol* 2002;**23**:127—32.