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Device-associated infection rates and bacterial resistance in six academic teaching hospitals of Iran: Findings from the International Nocosomial Infection Control Consortium (INICC)

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Summary: Device-associated health care-acquired infections (DA-HAIs) pose a threat to patient safety, particularly in the intensive care unit (ICU). However, few data regarding DA-HAI rates and their associated bacterial resistance in ICUs from Iran are available. A DA-HAI surveillance study was conducted in six adult and pediatric ICUs in academic teaching hospitals in Tehran using CDC/NHSN definitions. We collected prospective data regarding device use, DA-HAI rates, and lengths of stay from 2584 patients, 16,796 bed-days from one adult ICU, and bacterial profiles and bacterial resistance from six ICUs. Among the DA-HAIs, there were 5.84 central line-associated bloodstream infections (CLABs) per 1000 central line-days, 7.88 ventilator-associated pneumonias (VAPs) per 1000 mechanical ventilator-days and 8.99 catheter-associated urinary tract infections (CAUTIs) per 1000 urinary catheter-days. The device utilization ratios were 0.44 for central lines, 0.42 for mechanical ventilators and 1.0 for urinary catheters. The device utilization ratios of mechanical ventilators and urinary catheters were higher than those reported in the ICUs of the INICC and the CDC's NHSN reports, but central line use was lower. The DA-HAI rates in this study were higher than the CDC's NHSN report. However, compared with the INICC report, the VAP rate in our study was lower, while the CLAB rate was similar and the CAUTI rate was higher. Nearly 83% of the samples showed a mixed-type infection. The most frequent pathogens were *Acinetobacter baumannii*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*, followed by *Klebsiella pneumoniae* and *Enterococcus* spp. In the *S. aureus* isolates, 100% were resistant to oxacillin. Overall resistances of *A. baumannii* and *K. pneumonia* to imipenem were 70.5% and 76.7%, respectively. A multiple drug resistance phenotype was detected in 68.15% of the isolates. The DA-HAI rates in Iran were shown to be higher than the CDC-NHSN rates and similar to the INICC rates. Resistance to oxacillin and imipenem was higher as well. Comparing device use, DA-HAI rates, and bacterial resistance for the primary isolated bacteria indicated a direct association between urinary catheter use and the rates of CAUTI.

Background

Device-associated hospital-acquired infections (DA-HAI) are defined by the Centers for Disease Control and Prevention's (CDC's) National Healthcare Safety Network (NHSN) as infections acquired in a hospital by a patient who was admitted for a reason other than that infection [1,2]. DA-HAIs occur worldwide and affect both developed and resource-poor countries. In general, the rates of DA-HAIs in intensive care units (ICUs) are several times higher than other hospital wards. For DA-HAIs, the immune status of patients who are admitted to ICUs and usage of healthcare accessory devices are the main risk factors [3]. ICU staff and physicians could serve as vehicles that are involved in spreading resident pathogens from different wards of hospital to the ICUs [4]. Hospital environments can serve as major reservoirs of main bacterial pathogens, such as methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant Enterococci (VREs), carbapenem resistant *Klebsiella* spp., *Acinetobacter* spp. or *Pseudomonas* spp., and Gram positive or Gram negative bacteria that present with multidrug resistant (MDR) phenotypes. The emergence of MDR bacteria responsible for DA-HAIs is considered to be a major problem in most hospitals. Annually surveying the rates of DA-HAIs in hospitalized patients in ICUs is essential. A decrease in DA-HAIs could be achieved through the detection of the primary responsible pathogens and their resistance patterns for successful therapy.

In Asian countries, *Pseudomonas aeruginosa*, *Klebsiella* spp., *Escherichia coli*, Enterococci, and *S. aureus* are among the most frequent pathogenic bacteria in the ICUs. Imipenem resistant *P. aeruginosa*, third-generation-cephalosporin-resistant *K. pneumonia* and *Acinetobacter baumannii*, methicillin-resistant *S. aureus*, and quinolone-resistant *E. coli* are among the most common resistant strains that show a MDR resistance pattern in these countries [5]. In a previous study, hospitalized patients in the Middle East had a greater risk of contracting DA-HAIs (72.6%) compared with other countries [6]. The least active agents against the noted bacteria in these countries were reported to be ceftriaxone, ceftazidime and/or cefepime.

Because of the high morbidity and mortality of DA-HAIs in Iran and the paucity of information regarding the types and resistance patterns of these pathogens, we report a summary of the data on DA-HAIs collected in 6 intensive care units (ICUs) in 6 Iranian hospitals from Tehran between August 2011 and October 2012.

This study aimed to analyze the occurrence of DA-HAIs in the ICUs of six different hospitals and compare them against the International Nosocomial Infection Control Consortium (INICC) [7] and the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) benchmark reports [8] to compare the rates of device use (DU), DA-HAI, and bacterial resistance for the primary isolated bacteria. The goal of this study was to identify the most important responsible bacterial pathogens and their resistance profiles in Tehran, Iran. Furthermore, this was the first study in Iran that sought to find any possible associations between the types of colonized bacteria in medical devices and those isolated from patients' clinical specimens.

Methods

Study setting and design

This prospective cohort surveillance study was conducted in 6 ICUs in 6 medium-sized academic hospitals from Tehran, Iran. Prospective surveillance was conducted on health care-acquired infections and related factors, including the following classified into specific module protocols: excess length of stay (LOS), crude excess length of stay, microbiological profile, bacterial resistance, and antimicrobial use. All DA-HAIs and surgical site infections (SSIs) were categorized using standard CDC-NHSN definitions that included laboratory tests, radiology tests, and clinical criteria [1]. Laboratory-confirmed bloodstream infections were recorded and reported [1].

Table 1 Device-associated infections and length of stay in ICU-I.

	August 2011—September 2012
Number of patients, *n*	2584
Number of bed days, *n*	16,796
Central line days, *n*	7364
LOS of patients without HAI	4.8 (4.6—4.9)
Mechanical ventilator days, *n*	6976
Urinary catheter days, *n*	16,796
Use of central line, rate (95% CI)	0.44 (0.43—0.45)
Use of mechanical ventilator, rate (95% CI)	0.42 (0.41—0.42)
Use of urinary catheter, rate (95% CI)	1.0 (1.0—1.0)
CLABSI, *n*	43
CLABSI per 1000 central line days (95% CI)	5.84 (4.2—7.9)
LOS of patients with CLABSI	28.3 (21.2—39.0)
VAP, *n*	55
VAP per 1000 mechanical ventilator days (95% CI)	7.88 (5.9—10.3)
LOS of patients with VAP	25.5 (18.6—34.7)
CAUTI, *n*	151
CAUTI per 1000 urinary catheter days	8.99 (7.6—10.5)
LOS of patients with CAUTI	12.9 (11.0—15.1)
Overall device-associated infections % (95% CI)	9.6% (8.5—10.3)
Overall device-associated infections by 1000 bed days (95% CI)	14.8 (13.0—17.0)

CI, confidence interval; CLABSI, central line-associated bloodstream infection; CAUTI, catheter-associated urinary tract infection; VAP, ventilator-associated pneumonia.
LOS, length of stay; DA-HAI, device-associated healthcare-acquired infection.

Data collection

Infection control professionals (ICPs) collected data on central line-associated bloodstream infections (CLABs), catheter-associated urinary tract infections (CAUTIs), ventilator-associated pneumonias (VAPs) and SSIs occurring in patients hospitalized in a specific patient-care location. The ICUs were stratified according to the type of patient as follows: adult, pediatric or neonatal.

The ICPs from the 6 participating hospitals had previous experience conducting DA-HAI surveillance and sent detailed and aggregated data to the INICC Headquarters in Buenos Aires, Argentina. The DA-HAI rates, device use and length of stay were analyzed in one of the six ICUs (ICU-I). The bacterial profile and bacterial resistance were analyzed in the six ICUs included in this study.

Data analysis

Device-days consisted of the total number of central line (CL)-days, urinary catheter (UC)-days, or ventilator days.

Crude excess LOS of DA-HAI equaled the crude LOS of ICU patients with DA-HAI minus the crude LOS of patients without DA-HAI.

EpiInfo® version 6.04b (CDC, Atlanta, GA) and SPSS 16.0 (SPSS Inc. an IBM company, Chicago, Illinois) were used to conduct data analysis. Relative risk (RR) ratios, 95% confidence intervals (CIs) and *P*-values were determined for the primary and secondary outcomes.

Results

The ICUs from Iran belonged to six different public academic teaching hospitals. The length of participation of the hospitals in this study was one year. We calculated the DA-HAI rates, DU ratios and LOS in one of the ICUs (ICU-I) and compared them with the INICC global results and the CDC-NHSN. The bacterial profile and bacterial resistance were calculated in the six participant ICUs and were also compared with INICC and CDC-NHSN.

Table 1 shows the DA-HAI rates, LOS and DU ratios according to the infection types (CLABSI, CAUTI, and VAP); the Outcome Surveillance component was fully implemented. The UC had an extremely high DU rate (1.0). CAUTI was also the most common DA-HAI, with a rate of 8.99 per 1000 UC-days. Of the UTIs, 82.9% (151 out of 182) were related to UCs, 78.5% (55 out of 70) of the pneumonias were related to mechanical ventilators, and 93.4% (43 out of 46)

Table 2 Comparison of the ICU-I results with the device-associated infection rates in the INICC and CDC-NHSN reports.

	This study (August 2011–September 2012)	INICC 2007–2012 report	This study vs. INICC RR (95% CI), *P* value	CDC-NHSN 2012 report	This study vs. NHSN RR (95% CI), *P* value
Central line use	0.44	0.54	1.24 (1.21–1.27), 0.001	0.35	0.79 (0.78–0.81), 0.001
Mechanical ventilator use	0.42	0.36	0.86 (0.85–0.89), 0.001	0.24	0.57 (0.56–0.59), 0.001
Urinary catheter use	1.0	0.62	0.62 (0.61–0.63), 0.001	0.64	0.53 (0.53–0.54), 0.001
CLAB rate per 1000 CL days	5.84	4.9	1.19 (0.88–1.60), 0.267	0.9	6.25 (4.61–8.47), 0.001
VAP rate per 1000 MV days	7.88	16.5	0.48 (0.37–0.62), 0.001	1.1	7.22 (5.45–9.57), 0.001
CAUTI rate per 1000 UC days	8.99	5.3	1.69 (1.43–1.98), 0.001	1.2	7.25 (6.15–8.54), 0.001

CLABSI, central line-associated bloodstream infection; CAUTI, catheter-associated urinary tract infection; VAP, ventilator-associated pneumonia; RR, relative risk; CI, confidence interval; INICC, International Nosocomial Infection Control Consortium; CDC-NHSN, Centers for Disease Control and Prevention's National Healthcare Safety Network.

Table 3 Frequency of the bacterial pathogens responsible for the single and mixed type infections in HAIs from the six participating ICUs.

Bacterial pathogens	No. of isolated pathogens	Urinary tract infection	Bloodstream infection	Surgical site infection	Pneumonia	Mixed type infection rates N[a] (%)
Staphylococcus aureus	33	0/0	1/1	1/6	26/26	28 (12.2)
Enterococcus spp.	20	8/8	4/4	1/5	0/3	13 (5.6)
Pseudomonas aeruginosa	33	5/5	2/2	5/7	19/19	31 (13.5)
Acinetobacter baumannii	76	2/3	3/4	4/9	54/60	63 (27.5)
Staphylococcus epidermidis	6	1/2	1/2	0/0	2/2	4 (1.7)
Bacillus spp.	5	1/1	0/0	0/0	4/4	5 (2.2)
E. coli	7	1/1	0/0	0/3	3/3	4 (1.7)
Citrobacter spp.	1	0/0	0/0	0/0	1/1	1 (0.4)
Enterobacter spp.	2	0/0	0/0	0/1	1/1	1 (0.4)
Klebsiella pneumoniae	25	3/3	1/1	6/6	15/15	25 (11)
Proteus spp.	5	1/1	0/0	1/1	3/3	5 (2.2)
Streptococcus spp.	1	0/0	0/0	0/0	0/1	0 (0)
Burkholderia spp.	1	0/0	0/0	0/0	0/1	0 (0)
Total						180/215 (83.7)

[a] *N* indicates the number of each isolated bacterial genus among samples from 228 patients with suspected HAIs. The number of mixed type infection/total number of infections caused by the same pathogen in HAIs are represented separately.

of the bloodstream infections were related to central lines. The data presented also include the crude LOS of patients hospitalized in the same ICU during the surveillance period with and without DA-HAI and the crude excess length of stay of patients with CLABSI, CAUTI, and VAP. The VAP presented with the highest LOS (30 days).

Table 2 compares the rates and DU of this ICU from Iran with the INICC international report for the period from 2007 to 2012 and the 2012 CDC-NHSN report [2].

Table 3 provides data on the frequency of bacterial pathogens in the six ICUs from the Iranian hospitals stratified by types of the infections. The most frequent pathogens were *S. aureus* and *P. aeruginosa*, followed by *Klebsiella pneumoniae* and *Enterococcus* spp.

Table 4 provides data on the bacterial sensitivity patterns in the six ICUs stratified by the types of the infections. We found a high overall resistance to oxacillin, amoxicillin-clavulanate, and cefotaxime. The lowest resistance was found for vancomycin, which was identified as the most effective drug among the 15 tested antibiotics against these bacteria at laboratory conditions.

Table 5 presents the frequency of antimicrobial resistance rates to the most commonly prescribed antibiotics for DA-HAIs in the six ICUs studied. We found that the resistance to oxacillin was 100% in both the strains of *S. aureus* related to pneumonia and overall. The overall resistance of *A. baumannii* and *K. pneumoniae* to imipenem was 70.5% and 76.7%, respectively. The MDR phenotype was detected in 68.15% of the isolated bacteria from the clinical samples. The MDR phenotype was most common in *A. baumannii* (67 out of 67; 100%), followed by *S. aureus* (14 out of 17; 82%), *Klebsiella* spp. (13 out of 16, 81%), *Enterococcus* spp. (18 out of 22, 82%), *E. coli* (3 out of 6, 50%), and *P. aeruginosa* (12 out of 26; 46%).

Finally, Table 6 compares the resistance rates in pathogens associated with urinary tract infections in the six ICUs of this study with CDC-NHSN [3] and INICC rates [7]. We found that oxacillin resistance to *S. aureus* was higher in this study than in the INICC and CDC reports. Similarly, the resistance of *A. baumannii* to imipenem was higher than in these reports.

Discussion

Several studies have shown that the DA-HAIs are an important issue in Iran. Afhami et al. found that VAP was the most common infection in ICUs, and the rate per 1000 MV days was 9.96, which is similar to our 7.88 rate [4]. However, in this study, CAUTI was the most common DA-HAI. A study by Askarian et al. showed that the highest LOS was associated with bloodstream infections (9.2 days) [5]. In our study, the highest LOS was associated with VAP (25 days) and the overall length of stay of patients with DA-HAI was higher (ranging between 13 and 25 days). In a study conducted in one

Table 4 Percentages of antibiotic resistance of the pathogenic bacteria among the acquired hospital infections in the six studied intensive care units.

HAI type	IMP	VAN	OXA	CLIN	AMO	GEN	NOR	OFX	LEVO	CTX	TET	PIP	FEP	TMS-SX
Urinary tract infection	66.6	50	–	80	100	75	33.3	33.3	33.3	100	100	33.3	66.7	66.7
Surgical site infection	73	33.3	100	–	90	73.3	57.1	57.1	64.3	66.7	65.2	64.3	66.7	64.7
Bloodstream infection	66.6	–	–	–	–	50	0	0	66.7	100	16.7	66.7	66.7	100
Pneumonia	81.7	10	93.3	100	100	68	50	43.8	64.8	98.2	63.5	85.9	68	78.9
Total	71.4	18.2	96.6	90	98.2	68.5	46.4	42.9	63.8	94.4	63	79.8	78.9	77

HAI, healthcare-associated infection; IMP: imipenem; VAN: vancomycin; OXA: oxacillin; CLIN: clindamycin; AMO: amoxi-clav; GEN: gentamicin; NOR: norfloxacin; OFX: ofloxacin; LEVO: levofloxacin; CTX: cefotaxim; TET: tetracycline; PIP: piperacillin; FEP: cefepime; TMP-SMX: trimethoprim/sulfamethoxazole.

hospital in Iran, Mohammadtaheri et al. found a high rate of bacterial resistance (96.2%), particularly oxacillin/methicillin resistance to *S. aureus* [6]. In our study, 100% of the isolates were resistant to oxacillin. In a recent study by Tao et al. in 2012 in China, the three main pathogens *A. baumannii* (29%), *P. aeruginosa* (16%), and *S. aureus* (18%) were reported to be the main isolated microorganisms in VAP [9]. A study by Leblebicioglu et al. in 2007 in Turkey showed that 54.5% of VAP cases were caused by *Acinetobacter* spp., 14.9% by *Pseudomonas* spp., 11.9% by *S. aureus* and 7.9% by *Enterobacteriaceae* [10]. The results of our study also showed the same bacteria as the most frequent pathogens isolated from patients with pneumonia and a history of ventilation (*Acinetobacter* spp. [60%], *P. aeruginosa* [19%], and *S. aureus* [26%]). *Acinetobacter* spp., *P. aeruginosa* and *S. aureus* were similarly considered to be the most prevalent pathogens causing SSI. However, in a report by Hidron et al. on 7025 SSI samples, *Coagulase-negative Staphylococci* and *S. aureus* were identified to be the most prevalent pathogens in SSI [8]. Vancomycin-resistant *Enterococci* (VRE) showed a prevalence rate of 24.5%, which was lower than that reported by Hidron et al. (54.5%) [8]. The resistance rates of *P. aeruginosa* to piperacillin were near to those reported by the INICC in 2006—2007 (15.9—33.8%) but higher than those reported by NHSN in 2009—2010 (16.6%) [7,8]. Our results showed higher resistance rates for *E. coli*, *Acinetobacter* spp. and *K. pneumonia* compared with studies performed in Taiwan and Pakistan [11,12]. Among the studied bacteria, *A. baumannii* exhibited the highest level of bacterial resistance to all of the tested agents. As this bacterium presented frequently in mixed type infections, this increased level of resistance could be explained by the acquisition of resistance genes from other bacteria. Finally, the international benchmarks of bacterial resistance rates in pathogens related to CAUTI in the six ICUs of this study showed that the patterns of resistance of oxacillin to *S. aureus* and of *A. baumannii* to imipenem were higher in this study than both the INICC [7] and CDC rates [3].

The most significant finding in our study was that the rates of DU, DA-HAI, and bacterial resistance for the primary isolated bacteria indicated a direct association between urinary catheter use and the rates of CAUTI. This finding revealed that DA-UTI, particularly CAUTI, in the ICUs of Tehran poses a greater threat to patients' safety. However, colonization of the most common bacteria in these devices was not associated with the rates of bacterial resistance because the resistance rates of strains of *P. aeruginosa* and *Enterococcus* spp.

Table 5 Frequency of the antimicrobial resistance rates to their most frequently associated prescribed antibiotics for their infections in the six intensive care units of the studied hospitals.

Pathogen/antimicrobial	Resistance (%)				
	Pneumonia	Surgical site infection	Bloodstream infection	Urinary tract infection	Total
E. coli		—	—	—	—
Imipenem	100	0	—	66.7	41.7
Pseudomonas aeruginosa		—	—	—	—
Cefepime	33.3	57.1	0	53.3	36
Piperacillin	33.3	28.6	0	33.3	23.8
Imipenem	33.3	57.1	46.7	0	34.3
Klebsiella pneumoniae		—	—	—	—
Imipenem	100	80	0	50	76.7
Enterococcus spp.		—	—	—	—
Vancomycin	50	33.3	—	10	23.2
Staphylococcus aureus		—	—	—	—
Oxacillin	100	100	—	—	100
Acinetobacter baumannii		—	—	—	—
Imipenem	—	85.7	100	96.4	70.5

that are frequently isolated from the urine and catheters of patients with CAUTI were lower than other clinical samples. This association appears to be related to their ability to form a biofilm in these devices.

Our study has a number of limitations, including incompletely reported data by the hospital infection control departments in some of the participating hospitals during the study period. The second limitation was the lack of data regarding antibiotic prescriptions in each ICU to assess any association between the antibiotic consumption and the HAIs caused by the MDR bacteria colonizing the medical devices.

In conclusion, the data presented in this report support that DA-HAIs in Iran pose a grave and frequently concealed risk to patient safety compared with the developed world. More research needs to be conducted to show the association between the incidence of invasive DU in these ICUs and its role in DA-HAIs. Our main goal should be to enhance infection control practices by facilitating elemental, feasible and inexpensive tools and resources to tackle this problem effectively and systematically. These practices would lead to greater and stricter adherence to infection control programs and guidelines with correlated reductions in DA-HAI and its adverse effects.

Table 6 Comparison with the International Nosocomial Infection Control Consortium and Centers for Disease Control and Prevention's National Healthcare Safety Network reports for the resistance rates of pathogenic bacteria related to urinary tract infections.

Pathogen/antimicrobial	Resistance (%)		
	This study	INICC 2007—2012	NHSN CDC 2009—2010
E. coli			
Imipenem	66.7	5.1	2.3
Pseudomonas aeruginosa			
Piperacillin	33.3	37	16.6
Imipenem	0.0	33.5	21.3
Klebsiella pneumoniae			
Imipenem	50.0	13.9	12.5
Staphylococcus aureus			
Oxacillin	100.0	36.4	58.7
Acinetobacter baumannii			
Imipenem	96.4	67.7	74.2

INICC, International Nosocomial Infection Control Consortium; CDC-NHSN, Centers for Disease Control and Prevention's National Healthcare Safety Network.

Conflict of interest

All of the authors report no conflicts of interest related to this article. Every hospital's Institutional Review Board agreed to the study protocol, and patient confidentiality was protected by codifying the recorded information, making it only identifiable to the infection control team.

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Author's contributions

Masoud Alebouyeh and Mohammad Reza Zali conceptualised and designed the study. Department of Health Assistance, Shahid Beheshti University of Medical Sciences provided the data using WHONET software. Somayeh Jahani-Sherafat, Maryam Razaghi, Elahe Tajeddin, Simasadat Seyedjavadi, Marjan Rashidan, Maryam Rostampour, Arezo Haghi, Masoumeh Sayarbayat, Somayeh Farazmandian, Tahere Yarmohammadi, Fardokht Keshavarzi Arshadi, Nahid Mansouri, Mohammad Reza Sarbazi, and Mariano Vilar collected or provided and assembled the data. Somayeh Jahani-Sherafat, Mariano Vilar, Victor D. Rosenthal, and Masoud Alebouyeh analyzed and interpreted the data. Mariano Vilar, Victor D. Rosenthal, and Masoud Alebouyeh conducted the epidemiological analysis. Victor D. Rosenthal, Mariano Vilar, Masoud Alebouyeh, and Somayeh Jahani-Sherafat performed the statistical analysis. Administrative, technical, and logistic support was provided by Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of medical Sciences, Tehran, Iran and Department of Health Assistance, Shahid Beheshti University of medical Sciences, Tehran, Iran. Somayeh Jahani-Sherafat, Mariano Vilar, Victor D. Rosenthal, and Masoud Alebouyeh drafted the article. All the authors collected the data, provided study patients, critically revised the article for important intellectual content and gave final approval of the article.

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