Abstract

Background: Surveillance of health care-associated infections (HCAIs) is an integral part of infection control programme, especially in Intensive-Care Units (ICUs).

Aims: Since device-associated infections (DAIs) are the major threat to patient safety, this study was conducted to measure DAIs rate in the ICUs.

Methods: Central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI) were assessed in the ICUs of 4 tertiary-care teaching hospitals in Tehran-Iran.

Results: The incidence rate of CLABSI, VAP, and CAUTI was 10.20, 21.08, and 7.42 per 1000 device-days, respectively. The utilization-ratio for central-line, ventilator, and urinary catheter was 0.62, 0.47, and 0.84, respectively. The most common organisms were Acinetobacter (33.5%) and Klebsiella (19.0%). About 60-80% of Enterobacteriaceae were extended spectrum beta-lactamases producing (ESBL+). About half of Pseudomonas aeruginosa isolates were resistant to piperacillin/tazobactam and carbapenem. Acinetobacter resistance rate to ampicillin/sulbactam and carbapenem was 70-80%. The prevalence of methicillin-resistant...
Staphylococcus aureus and vancomycin-resistant Enterococcus was 84.6% and 83.3%, respectively.

Conclusions: This study showed high incidence rate of DAIs and resistant organisms, and appropriate interventions are necessary to reduce these rates.

Keywords: device-associated infection, health care-associated infection, antibiotic resistance, ventilator-associated pneumonia, catheter-associated urinary tract infection, central line-associated bloodstream infection.

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Introduction

Health care-associated infections (HAIs) affect patients with indwelling devices in hospitals and other health-care facilities, and are the most common cause of increased morbidity, mortality, and cost to the hospitalized patients, especially in high-risk settings, such as intensive care units (ICUs) (1–4). Central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI), are three major device-associated infections (DAIs). These infections pose the greatest threat to patient safety, and the standard definitions have been provided by the Centers for Disease Control and Prevention (CDC) for these infections (5).

The rate of HAIs varies between countries, but in low- and middle-income countries, overall device-associated infections per 1000 device-days in adult ICUs are strikingly higher than proportions reported in high-income countries (6–8). In the ICUs of low- and middle-income countries, the CLABSI incidence per 1000 CL-days is 4.9–12.2 (0.9–3.5 in high-income
countries), the VAP incidence per 1000 ventilator-days is 16.8–23.9 (1.1–7.9 in high-income countries), and the CAUTI incidence per 1000 UC-days is 5.5–8.8 (1.3–4.1 in high-income countries) (1–4,6,7). In addition to the risk factors associated with HCAI in high-income countries, other risk factors have been identified in acute-care settings in low- and middle-income countries that are more broadly associated with poverty, such as a lack of basic hygiene and limited resources. These include malnutrition, age < 1 year, low birth weight, parenteral nutrition, or two or more underlying diseases (6). Although not demonstrated as independent risk factors, general barriers to optimal infection control practices in low- and middle-income countries are lack of financial support, inadequate numbers of trained personnel working in infection control, understaffed hospital units, and insufficient equipment and supplies. In resource-constrained settings, compliance with standard recommendations for infection prevention and control is generally not optimal, and the capacity of existing systems to respond to the increased demand associated with HCAI, such as length of stay, cost, effective antimicrobial therapy and advanced technology is also limited (8).

Surveillance of DAIs is an important part of any hospital’s infection control programme. It defines the extent of problem, which is the initial step toward planning the strategies to ensure the quality of health care and reducing threat of infection. In hospitals, information about the epidemiology of infections and antimicrobial resistance patterns of microorganisms is of utmost importance in the ICUs (1,2,8) and different incidences of DAIs state the importance of gathering and evaluating own hospital data for development of appropriate infection control programme. Since surveillance data on the epidemiology of device-associated infections and antimicrobial resistance patterns of related microorganisms are limited in the Islamic Republic of Iran, this study was conducted to determine the burden and antimicrobial resistance patterns of device-associated infections CLABSI, VAP (VAE), and CAUTI in 15 adult ICUs of 4 tertiary care teaching hospitals in Tehran, Islamic Republic of Iran.

Methods
Setting

This observational, prospective study was conducted during a two-month period (February and March 2014) in 15 adult medical and surgical ICUs of four teaching hospitals in Tehran to assess the incidence of device-associated infections per 1000 device-days, targeted at three common DAIs: central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI) as defined by the CDC’s criteria (3,5,9). This study was approved by the local research and ethics committee, and the need for informed consent was waived in view of the observational nature of the study. The recorded data were coded for patient confidentiality, and only the infection control teams were informed.

In all four hospitals there is an infection control team including an infection control nurse (with at
least five years’ experience in infection control) and an infectious diseases specialist (Infection control physician with more than 10 years’ experience in infection control). The hospitals also have microbiology laboratories to provide in vitro susceptibility testing of clinical isolates using standardized methods.

**Surveillance**

In this study, DAI acquisition attributable to the ICU was measured. Each patient admitted to one of the 15 ICUs who received a device (central line, mechanical ventilation, urine catheter) was monitored prospectively for the development of device-associated infections on a daily basis. Infection control nurses collected data on CLABSI, VAP and CAUTI occurring in patients hospitalized in each ICU using CDC data sheet for surveillance of DAIs, and infection control physicians supervised the process. Patients who didn’t receive a device were excluded from the study. The demographic data of patients (name, gender, birth date, admission date, and ward), length of stay were recorded. Device-days and patient-days were collected as denominator data, and microbiological investigations were also recorded.

**Definitions of device-associated infections**

Device-associated infections (DAIs) were defined according to the CDC criteria published in January 2014 (5) (see Appendix).

**Culture techniques**

CLABSI: The central line was removed aseptically, and the distal 5 cm of the catheter (i.e., catheter tip) was cultured using a standardized semi-quantitative method. Concomitant blood cultures were drawn percutaneously.

VAP: In all cases, a deep tracheal aspirate from the endotracheal tube was cultured aerobically and a Gram stain was performed.

CAUTI: A urine sample was aseptically aspirated from the sampling port of the urinary catheter and cultured quantitatively.

To identify microorganisms, standard laboratory methods were used, and susceptibility tests were performed in all cases (10).
Device associated infection rate calculation

Device-associated incidence density was calculated by number of device-associated infection episodes \( \times 1000 \) / number of device-days. The incidence density rate of CLABSI (number of cases per 1,000 central line-days), VAP (number of cases per 1,000 mechanical ventilator-days), and CAUTI (number of cases per 1,000 urinary catheter days) were measured. The rates of CLABSI, VAP, and CAUTI per 1,000 device-days were calculated by dividing the total number of DAIs by the total number of specific device days and multiplying the result by 1,000.

Device utilization ratio was calculated by number of device-days divided by the number of patient-days. Device-days were calculated by the total number of days of exposure to the device (central line, ventilator, or urinary catheter) for all of the patients in the ICUs during the study time period, and patient-days were calculated by the total number of days that patients were in the ICUs during the study time period.

Statistical analysis

Variables including standard demographic information (name and identifier, gender, birth date, admission date, and ward), length of hospital stay, admission and discharge diagnoses, surgical/invasive procedures, device utility days (endotracheal tube, intravascular catheter, and urinary catheter), laboratory and pharmacy data were collected. Continuous variables were presented as means and standard deviations (SD) and categorical variables as numbers and percentages.

Results

Characteristics of 15 ICUs that participated in this study are shown in Table 1. For this surveillance study, device-associated infections (DAI) rate and device utilization (DU) ratio are summarized in Table 1. Out of 1545 patients, 169 episodes of device-associated infections were detected; 48 episodes of CLABSI, 74 episodes of VAP and 47 episodes of CAUTI.

The mean duration (±SD) between device insertion and symptom onset of infection was 18.8 (±16.4) days for CLABSI; 17.8 (±15.6) days for VAP; and 22.2 (±17.4) days for CAUTI. The mean age of patients suffered from DAIs was 55.3 (±21.9) years; the sex distribution was 58% male to 42% female; the mean length of hospital stay was 44.0 (±29.4) days (Table 2). Overall mortality was 50%; mortality rate for CLABSI, VAP and CAUTI was 45.5%, 50.7% and 27.5%.
respectively. Some patients who died experienced more than one infection.

The causative agents for various types of device-associated infections are shown in Table 3. Since more than one organism may cause an infection, 179 isolates were responsible for 169 episodes of infections, and Gram negative organisms were the predominant isolates [147 (82.1%)]. 29 (16.2%) Gram positive organisms and 3 (1.7%) fungi were also isolated. A total of 52 pathogens were isolated from blood cultures as CLABSI agents; Acinetobacter [12 (23.1%)] and Klebsiella [10 (19.2%)] were the most common isolates. The same organisms, Acinetobacter [38 (48.1%)] and Klebsiella [14 (17.7%)], were more commonly implicated in VAP. In CAUTI, among the 48 detected organisms, Escherichia coli (E.coli) [15 (31.3%)] was the most prevalent isolate detected.

The antimicrobial resistance pattern of the isolates is shown in Table 4. With the exception of colistin, more than 65% of Acinetobacter strains were resistant to various antimicrobial agents: more than 90% were resistant to ceftazidime and fluoroquinolones, about 70-80% resistant to aminoglycosides and ampicillin/sulbactam, and 66.7% to carbapenem. Half of Pseudomonas aeruginosa isolates were resistant to ceftazidime, piperacillin/tazobactam, and carbapenem, 47.4% to aminoglycosides, and 37.9% to fluoroquinolones. Among Enterobacteriaceae isolates, 80% of E.coli isolates and 70% of Klebsiella isolates were extended spectrum beta-lactamases producing (ESBL); resistance to fluoroquinolone was 40-70% in this group. Methicillin resistant Staphylococcus aureus (MRSA) and vancomycin resistant Enterococcus (VRE) was more than 80% among isolates.

VAE definition of CDC: All cases of VAP in this study were categorized as probable VAP, within the VAE algorithm.

INIS software

This software is a national freeware for the surveillance of health care-associated infections. As a part of the study, the data collected about patients with or without DAIs as confirmed by physicians, were compared with the output of INIS software. The software identified all DAIs cases with no false-positive or false-negative results. The feedback of infection control practitioners showed that INIS software is user-friendly (http://inis.health.gov.ir).

Discussion

Health care-associated infections, particularly device-associated infections, are a serious cause of concern for hospitals (1–8). Surveillance of device-associated infections can inform on the strategies for the prevention and control of these infections. However, in low- and middle-income countries, due to poor infection control programmes and lack of an appropriate surveillance, the rate of health care associated infections is higher than in high-income
countries (2,3,6). Due to difficulty of conducting prospective surveillance studies, there has been only sparse information available on DAIs rate in the literature particularly from the Islamic Republic Iran.

In the Islamic Republic of Iran the infection prevention and control (IPC) team primarily consists of an IPC-nurse (supervisor) and a physician. The wards’ head-nurses cooperate in implementing the IPC programme. The IPC program includes technical guidelines, training courses, surveillance of HAI, and etc. Although the IPC-programme is available scientifically, implementing it usually encounters many challenges.

In the present study, a prospective surveillance was carried out for three main DAIs (CLABSI, VAP, and CAUTI) in ICUs of four teaching tertiary hospitals in the country. The incidence density for CLABSI, VAP, and CAUTI per 1000 device-days was found to be 10.20, 21.08, and 7.42 respectively.

According to WHO report, the incidence density for CLABSI, VAP, and CAUTI per 1000 device-days in developed countries is 3.5, 7.9, and 4.1 respectively; and in developing countries is 12.2, 23.9, and 8.8 (2). In the present study, the rate of DAIs in the ICUs was two to three times higher than high-income countries, but less than the mean rate in low- and middle-income countries. According to International Nosocomial Infection Control Consortium (INICC) report for DAIs in 503 Intensive Care Units (ICUs) in low- and middle-income countries, presented by Rosenthal et al., the incidence density for CLABSI, VAP, and CAUTI per 1000 device-days was 4.78, 14.7, and 5.30 respectively (3); these infections were higher in the present study. On the National Health care Safety Network (NHSN) annual report for 2012 by Dudeck et al., even in the high-risk ICUs in the United States of America, the rate for CLABSI, VAP, and CAUTI per 1000 device-days was only 3.4, 4.4, and 5.0 respectively (4). Unfortunately, these rates were much higher in Iranian ICUs. There were some possible reasons, including relative low compliance of hand hygiene, lack of proper training and deficiency in continuous supervision, no strict control on antibiotic therapies (stewardship), some limitations for isolation (e.g., absence of private room in most ICUs), insufficient number of nurses to implement proper cohorting of staff and patients.

Published surveillance data from other low- and middle-income countries have shown a wide range of results that make the comparison and discussion difficult; some studies such as ones conducted in Argentina (CABS1 30.3, VAP 46.3, CAUTI 18.5 per 1000 device-days) or India (VAP 30.67) showed the incidence density higher than present study (11,12). But some others like those done by Mesiano et al. in Brazil (CLABS1 6.4) or Memish et al. in Saudi Arabia (VAP 16.8) showed lower incidence density than the present study (13,14). In a recent published
research from India by Datta et al. the incidence density for CLABSI, VAP, and CAUTI was 13.50, 6.15, and 10.75 respectively that compared with the present study, showed higher incidence of CLABSI and CAUTI, and lower VAP rate (15). However, another study from India by Singh et al. showed higher VAP rate (21.92 per 1000 device days) but very lower CLABSI (0.48 per 1000 device days) and CAUTI (0.6 per 1000 device days) rate (16).

In most surveillance studies conducted in the Islamic Republic of Iran, variables such as device utilization ratio, device-days, patient-days and incidence density have not been calculated. Instead, only the percent of infected patients has been reported. That makes the comparison inapplicable. However, among few studies which reported incidence density, two studies conducted by Afhami et al. on CLABSI and VAP showed the rate of 1.98 per 1000 catheter-days for CLABSI, and 9.96 per 1000 ventilator-days for VAP (17,18). In the present study, the incidence of CLABSI and VAP was higher. Different incidences of DAIs may depend on the definition, type of hospital or ICU, type of patients admitted, infection control programs of the institute, and antibiotic prescription policy.

In the present study, the utilization ratio for central line, ventilator, and urinary catheter was 0.62, 0.47, and 0.84 respectively. According to International Nosocomial Infection Control Consortium (INICC) report by Rosenthal et al., the utilization ratio for central line, ventilator, and urinary catheter was 0.53, 0.38, and 0.62 respectively (3). In the report of National Health care Safety Network (NHSN) by Dudeck et al., the utilization ratio for central line, ventilator, and urinary catheter was 0.57, 0.37, and 0.70 respectively (4). In comparison with these data, the overall device utilization ratio was 10–20% higher in Iranian ICUs. A reason might be the type of the patients admitted in these ICUs because the hospitals in this study were tertiary-level referral hospitals and most patients had serious co-morbidities, and more device utilization was needed to care for such patients.

In the present study, the mean age of patients suffered from DAIs was around 55 years, males more than females, mean length of stay was more than one month, and half of patients died finally. In the report of INICC by Rosenthal et al., the mean length of stay was about 20 days (CLABSI: 19.47 days, VAP: 19.66 days, CAUTI: 20.99 days) and the mortality was about 21% (CLABSI: 24.9%, VAP: 23.4%, CAUTI: 13.3%) (3). These data indicate that length of stay (LOS) and mortality of infected patients is high in Iranian ICUs, comparatively. In other reports about LOS or mortality, especially in low- and middle-income countries, the rate was similar to ours or even higher (2,14–19).

The organisms isolated in the present study were commonly gram-negative Enterobacteriaceae; similar finding were observed by other investigators (1-4,6,15,16,18).
According to WHO report, the most common organisms in ICU-acquired infections are Enterobacteriaceae (20%), S. aureus (20%), Pseudomonas (17%), Enterococcus (10%), and Acinetobacter (5%) (2); the researchers found similar types of organisms but with lower rate of S. aureus and higher rate of Acinetobacter. In a review of microbiologic pattern of HAIs in low-and middle-income countries, the most common pathogens for BSI were S. aureus, Acinetobacter and Enterobacteriaceae; the most common pathogens for VAP were Pseudomonas, Acinetobacter and Enterobacteriaceae; the most common pathogens for UTI were Enterobacteriaceae, Pseudomonas, and Acinetobacter; and the rate of MRSA was 54.5%.6 In the present study, the same organisms detected but with a higher rate of MRSA (84.6%). In the Islamic Republic of Iran, studies about UTI agents and VAP agents showed the same pattern with predominance of gram-negative bacteria (15, 20).

In Table 5 the resistance pattern of organisms isolated in the present study is compared with those reported by INICC and NHSN (3,4). The organisms isolated in the present study were more antibiotic resistant than INICC’s study, except for fluoroquinolone resistance of Pseudomonas and carbapenem resistance of Acinetobacter and Ecoli. One limitation of this study was that the researchers collected only DAIIs in ICUs but no other HCAIs (for example, surgical site infections) and not in other wards. Also, the hospitals in the present study were in teaching tertiary-care setting; therefore, the patients with severe underlying diseases managed in these hospitals required more invasive procedures and more intensive care, so the infection rate in the present study may be higher than the overall country rate.

**Conclusion**

This study documents a high incidence rate of device-associated infections and high frequency of resistant organisms in the ICUs. Effective strategies to control resistant bacteria should be implemented and rational use of antibiotics as prophylaxes and adherence to infection control practices are necessary to reduce these infections.

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Competing interests: None declared.
References


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Appendix

A. Definitions of device-associated infections according to the CDC criteria 2014:

A.1) CLABSI definition. Central line was in place for >2 calendar days (the central line was in place on the date of bloodstream infection or the day before); and patient has a recognized pathogen cultured from one or more blood cultures and organism cultured from blood is not related to an infection at another site; OR patient has at least one of these signs or symptoms (fever >38oC, chills, or hypotension) not related to an infection at another site and the same common commensal is cultured from two or more blood cultures drawn on separate occasions.

A.2) VAP definition. Pneumonia (PNEU) was identified by using a combination of radiologic, clinical and laboratory criteria: the presence of a new or progressive and persistent infiltrate, consolidation, or cavitation on chest X-ray after mechanical ventilation, and at least two of the
following: temperature higher than 38°C or less than 36°C; leukocytosis: leukocyte count > 11000/mm³, or leukopenia < 4000/mm³; purulent endotracheal secretions; isolation of pathogenic bacteria from endotracheal aspiration / blood / pleural fluid; and increasing oxygen requirements.

Ventilator-associated PNEU (VAP) was defined as a pneumonia where the patient was on mechanical ventilation for >2 calendar days on the date of event, with day of ventilator placement being Day 1, and the ventilator was in place on the date of event or the day before [Date of event (infection date): For VAP the date of event was the date when the last element used to meet the Pneumonia (PNEU) criteria occurred].

Ventilator-Associated Events (VAE) definition: There are three definition tiers within the VAE algorithm: 1) Ventilator-Associated Condition (VAC); 2) Infection-related Ventilator-Associated Complication (IVAC); and 3) Possible and Probable VAP. VAC: Patient who had at least 2 days of stability on the ventilator, began worsening oxygenation (increase in FiO2 of ≥ 0.20 (20 points) or PEEP of ≥ 3 cmH2O) that sustained for ≥ 2 days; IVAC: VAC and Temperature >38°C or <36°C, OR white blood cell count ≥ 12,000 cells/mm³ or ≤ 4,000 cells/mm³; and a new antimicrobial agent is started and continued for ≥ 4 calendar days; Possible/Probable-VAP: IVAC and purulent respiratory secretions and/or positive culture (of sputum, endotracheal aspirate, bronchoalveolar lavage, lung tissue, protected specimen brushing, or pleural fluid); OR positive lung histopathology, positive diagnostic test for Legionella spp., or positive diagnostic test on respiratory secretions for specific respiratory viruses.

A.3) CAUTI definition. Patient had an indwelling urinary catheter in place for >2 days (catheter was in place on the date of urinary infection or the day before); and at least one of these signs or symptoms (fever>38°C; urgency; frequency; dysuria; suprapubic tenderness; costovertebral angle pain or tenderness) and a positive urine culture of ≥ 105 colony-forming units (CFU)/ml with no more than 2 species of microorganisms. OR above signs or symptoms and at least one of these findings (positive dipstick for leukocyte esterase and/or nitrite; pyuria; microorganisms seen on Gram’s stain of unspun urine) and a positive urine culture of ≥ 103 and <105 CFU/ml with no more than 2 species of microorganisms. OR without any urinary signs or symptoms but the urine culture and blood culture both were positive with the same uropathogen.

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