Device-associated infection rates and bacterial resistance in the intensive care units of a Turkish referral hospital

Emin E. Tutuncu, MD, *Yunus Gurbuz,* MD, *Irfan Sencan,* MD, *Baris Ozturk,* MD, *Gonul C. Senturk,* MD, *Aysegul U. Kilic,* MD.

ABSTRACT

الأهداف: تقييم معدلات الالتهاب التي تسببها الأجهزة الطبية، بالإضافة إلى تحليل أشكال مقاومة الكائنات الدقيقة للمضادات الحيوية أثناء الإقامة في المستشفى.

الطريقة: أُجريت هذه الدراسة الاستطلاعية في 4 وحدات مختلفة للعناية المركزة وموزعة في مستشفى إس بي ديسكابي يلديريم بيازيت للتدريب والأبحاث، أنقرة، تركيا، وقد استمرت الدراسة خلال الفترة من يناير 2007م إلى مارس 2010م. لقد قمنا بمراقبة الالتهابات التي أصيب بها المرضى من جراء الأجهزة الطبية المختلفة وذلك من خلال جمع العزلات الجرثومية وتقييم مدى مقاومة هذه الكائنات الدقيقة للمضادات الحيوية.

النتائج: لقد تمت متابعة 6,005 مريضاً في قسم العناية المركزة وذلك لمدة يصل أقصاها إلى 46,355 يوماً، وقد كان مجموع عدد الالتهابات المرتبطة بالأجهزة الطبية 969. أشارت نتائج الدراسة إلى أن التهابات القناة البولية المرتبطة بالقسطرة كانت من أكثر هذه الالتهابات شيوعاً (55.3%، 11.9 حالة كل 1000 يوم)، وتلا ذلك الالتهاب الرئوي المرتبط بأجهزة التنفس الاصطناعي (38.9%، 21.2 حالة كل 1000 يوم)، بالإضافة إلى التهابات مجرى الدم المرتبطة بإدخال الخط المغذي المركزي (5.8%، 2.8 حالة كل 1000 يوم). ولقد كانت الجراثيم الراكدة (24.5%) من أكثر أنواع العزلات التي جُمعت من المرضى المصابين بالالتهاب الرئوي المرتبط بأجهزة التنفس الاصطناعي، فيما انتشرت الإشريكية القولونية (24.2%) بين المرضى المصابين بالتهابات القناة البولية المرتبطة بالقسطرة. وأظهرت النتائج بأن كلاً من المكورات العنقودية سالبة التخثر والفطريات المبيضة كانتا من أكثر الجراثيم المنتشرة بين المرضى المصابين بالتهابات مجرى الدم المرتبطة بالخط المغذي المركزي.

خاتمة: أثبتت الدراسة مدى ارتفاع معدلات الالتهابات المرتبطة بالأجهزة الطبية كأجهزة التنفس الاصطناعي، والقسطرة، والخط المغذي المركزي، وهذا يبرز في وحدات العناية المركزة عند مقارنة ما توصلنا إليه من النتائج مع شبكة سلامة الرعاية الطبية الوطنية. تشدد النتائج التي توصلنا إليها على أهمية تحسين كلاً من الممارسات المتعلقة بالتحكم بالعدوى، وكيفية التعامل مع الأجهزة الطبية والحول دون نقل العدوى إلى المرضى في المستشفى.

Objectives: To determine device-associated infection (DAI) rates, and the microbiological and antibiotic resistance profiles of infecting pathogens in our hospital.

Methods: Prospective surveillance of healthcare-associated infections was performed from January 2007 to March 2010 in 4 different intensive care units (ICUs) of SB Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey.

Results: During the study period, 6,005 patients were followed-up in ICUs for a total of 46,355 patient-days. The total number of DAIs was 969. Catheter-associated urinary tract infection (CAUTI) was the most common DAI (55.3% of DAIs; 11.9 cases per 1000 catheter-days), followed by ventilator-associated pneumonia (VAP) (38.9% of DAIs; 21.2 cases per 1000 ventilator-days), and central line-associated blood stream infection (CLABSI) (5.8% of DAIs; 2.8 cases per 1000 central line-days). The most frequently isolated pathogens in patients with VAP were *Acinetobacter species* (24.5%) and *Escherichia coli* in CAUTI (24.2%). Coagulase negative *Staphylococci* and *Candida species* were the leading pathogens in patients with CLABSI.

Conclusion: We observed considerably high rates of VAP and CAUTI and a high rate of CLABSI in our ICUs when compared with the National Healthcare Safety Network data. These findings emphasize the need to improve infection control practices and management of invasive device use in our hospital.

Saudi Med J 2011; Vol. 32 (5): 489-494

From the Department of Infectious Diseases and Clinical Microbiology, SB Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey.

Received 10th November 2010. Accepted 21st February 2011.

Address correspondence and reprint request to: Dr. Emin E.Tutuncu, Department of Infectious Diseases and Clinical Microbiology, SB Diskapi Yildirim Beyazit Training and Research Hospital, PO Box 34 Asagi Ayranci, Ankara 06541, Turkey. Tel. +90 (532) 5115000. Fax. +90 (312) 3186690. E-mail: ediztutuncu@gmail.com

Healthcare-associated infections (HAIs) are a major global problem for patient safety, and are related to significantly increased morbidity, mortality, hospital stays, and costs. The HAIs account for an estimated 1.7 million infections and 99,000 deaths annually in the US.[1,2] Along with hand hygiene and isolation practices, surveillance is one of the most important steps in controlling HAIs. Surveillance provides data that allow the determination of endemic infection rates, early detection of epidemics, and assessment of the efficacy of interventions.[3] It was clearly demonstrated by Haley et al[4] that conducting organized surveillance and control programs can reduce HAI rates by more than 30%. Following recommendations from the Centers for Disease Control and Prevention's (CDC) National Nosocomial Infections Surveillance System (NNIS), a targeted surveillance by focusing on device-associated infections (DAIs) in intensive care units (ICUs) had been carried out in many hospitals, particularly in the US.[3,5] However, surveillance data regarding DAIs are limited in most developing countries. The aim of the present study was to evaluate DAI rates in different ICUs of a tertiary referral hospital in Turkey, to compare these rates with the international data, and to determine microbiological profiles and resistance patterns of infecting organisms.

Methods. This prospective surveillance study was conducted in the neurology ICU (N-ICU), neurosurgery ICU (NS-ICU), cardiovascular surgery ICU (CVS-ICU), and medical-surgical ICUs (MS-ICUs) of Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey. The MS-ICUs are located in 5 different wards with a total of 33 beds. The N-ICU has 7, NS-ICU has 6, and CVS-ICU has 6 beds. There are 4 isolation beds in the MS-ICUs. The total nurse-patient ratio in these ICUs was 1:2 during day shifts and it was 1:3 at other times. All patients admitted to ICUs during the study period from January 2007 to March 2010 with a length of stay of more than 48 hours were enrolled in the study. They were followed-up until 48 hours following ICU discharge. An infection control nurse, and an infection control practitioner visited all patients in ICUs on a daily basis. Demographic data including the age and gender, underlying diseases, admission date to hospital and the ICU, diagnosis at admission, risk factors for HAIs, physical examination findings, laboratory results, culture results, and susceptibility data, and antibiotics administered during the ICU follow-up were collected and recorded using standardized record cards. The number of patients in ICUs, patient-days and device-days for ventilators, urinary catheters, and central lines were recorded accordingly. The HAIs were defined

Table 1 - The total number of device-days, device-utilization ratios, ventilator-associated pneumonia, catheter-associated urinary tract infection, and central line-associated bloodstream infection rates per 100 patients and per 1000 device-days in 4 different ICUs in a Turkish referral hospital.

Variable	MS-ICU	NS-ICU	N-ICU	CVS-ICU	Overall
Patient number	3,476	789	622	1,118	6,005
Patient days	29,257	5,910	7,990	3,198	46,355
Ventilator-associated pneumonia					
Device days for ventilators	12,926	1,802	1,851	1,201	17,780
Device utilization ratio	0.44	0.30	0.23	0.37	0.38
VAP (n)	276	42	43	16	377
Rate per 100 patients	7.9	5.3	6.9	1.4	6.3
Rate per 1000 device days	21.4	23.3	23.2	13.3	21.2
(95% CI)	(18.9-23.9)	(16.3-30.3)	(16.3-30.1)	(6.8-19.8)	(19.1-23.3)
Catheter-associated UTI					
Device days for urinary catheters	28,381	5,587	7,901	3,031	44,900
Device utilization ratio	0.97	0.95	0.99	0.95	0.97
CAUTI (n)	346	59	123	8	536
Rate per 100 patients	10.0	7.5	19.8	0.7	8.9
Rate per 1000 device days	12.2	10.6	15.6	2.6	11.9
(95% CI)	(10.9-13.5)	(7.9-13.3)	(12.9-18.3)	(0.8-4.4)	(10.9-12.9)
Central line-associated BSI					
Device days for central lines	12,980	2,167	1,625	3,167	19,939
Device utilization ratio	0.44	0.36	0.20	0.99	0.43
CLABSI (n)	38	11	4	3	56
Rate per 100 patients	1.1	1.4	0.6	0.3	0.9
Rate per 1000 device days	2.9	5.1	2.5	0.9	2.8
(95% CI)	(2-3.8)	(2.1-8.1)	(0.1-4.9)	(0.1-1.9)	(2.1-3.5)

MS-ICU - medical-surgical intensive care unit, NS-ICU - neurosurgery intensive care unit, N-ICU - neurology intensive care unit, CVS-ICU - cardiovascular surgery intensive care unit, VAP - ventilator-associated pneumonia, UTI - urinary tract infection, CAUTI - catheter-associated urinary tract infection, CLABSI - central line-associated bloodstream infection, BSI - blood stream infection, CI - confidence interval

Table 2 - Overall distribution of isolated microorganisms according to infection site.

Microorganisms	VAP	CAUTI	CLABSI	Total
		n (%)		
Acinetobacter species	103 (24.5)	35 (5.9)	5 (7.4)	**143 (13.2)**
Pseudomonas species	98 (23.3)	72 (12.1)	3 (4.4)	**173 (16)**
Escherichia coli	23 (5.4)	144 (24.2)	2 (2.9)	**169(15.6)**
Klebsiella species	31 (7.4)	84 (14.1)	2 (2.9)	**117 (10.8)**
Proteus species	25 (5.9)	24 (4)	-	**49 (4.5)**
Serratia species	12 (2.9)	3 (0.5)	-	**15 (1.4)**
Enterobacter species	11 (2.6)	7 (1.2)	2 (2.9)	**20 (1.8)**
Stenotrophomonas maltophilia	11 (2.6)	2 (0.3)	2 (2.9)	**15(1.4)**
Other gram negatives	3 (0.7)	5 (0.8)	2 (2.9)	**10(0.9)**
Coagulase-negative *staphylococci*	47 (11.2)	15 (2.5)	20 (29.4)	**82 (7.6)**
Staphylococcus aureus	46 (10.9)	5 (0.8)	6 (8.8)	**57(5.3)**
Enterococcus species	5 (1.2)	55 (9.3)	4 (5.9)	**64(5.9)**
Other gram positives	1 (0.2)	1 (0.1)	-	**2(0.2)**
Candida species	5 (1.2)	142 (23.9)	20 (29.4)	**167 (15.4)**
Total	**421 (100)**	**594 (100)**	**68 (100)**	**1,083 (100)**

VAP - ventilator-associated pneumonia, CAUTI - catheter-associated urinary tract infection, CLABSI - central line-associated bloodstream infection

Table 3 - Antibiotic resistance patterns of the most frequently isolated pathogens.

Microorganisms	Resistance pattern	Resistant isolates %
Acinetobacter species	Carbapenem resistance	(79.7)
Pseudomonas species	Carbapenem resistance	(39.3)
Escherichia coli	ESBL production	(37.9)
Klebsiella species	ESBL production	(48.7)
Staphylococcus aureus	Methicillin resistance	(73.7)
Coagulase-negative *staphylococci*	Methicillin resistance	(87.8)
Enterococcus species	Vancomycin resistance	(4.7)

ESBL - extended-spectrum beta-lactamases

according to the standard definitions of the CDC.[6] Patients with signs and symptoms of infection in the first 48 hours of the ICU stay were not considered as having ICU-acquired HAIs and excluded from the study. If a urinary tract infection (UTI), pneumonia or blood stream infection (BSI) was associated with the use of a catheter, ventilator, or a central line, the diagnosis of a DAI was established. Although all ICU-acquired infections were recorded, only results of DAIs are presented in this study. The isolates were identified by conventional methods and antibiotic susceptibility tests were performed according to standard guidelines.[7] Device utilization ratios were calculated by dividing the total number of device-days by the total number of patient-days. The DAI rates for pneumonia, UTI, and BSI were calculated by dividing the total number of DAIs by the total number of device-days and multiplying the result by 1000.[8]

Results. During the surveillance period, 6005 patients were followed up in ICUs, resulting in a total of 46,355 patient-days. The mean length of stay in ICUs was 7.7 days. The total number of DAIs during the surveillance period was 969. The mean overall DAI rate was 16.1% or 20.9 infections per 1000 patient-days. Catheter-associated urinary tract infection (CAUTI) was the most frequently diagnosed DAI (55.3%). Ventilator-associated pneumonia (VAP) accounted for 38.9% of all DAIs, followed by central line-associated blood stream infection (CLABSI) (5.8%).

The mean overall DAI rates were 21.2 for VAP, 11.9 for CAUTI, and 2.8 for CLABSI infections per 1000 device-days. The total number of device-days, device-utilization ratios, VAP, CAUTI, and CLABSI rates per 100 patients and per 1000 device-days from 4 different ICUs are shown in **Table 1**. The overall device use ratios were 0.97 for urinary catheters, 0.43 for central lines, and 0.38 for ventilators. Device-utilization ratios for ventilators and urinary catheters were similar in all 4 ICUs. The central line utilization ratio was considerably higher in the CVS-ICU compared to other ICUs. During the study period, a total number of 1,083 microorganisms were recovered from patients. Isolated microorganisms according to infection site are presented in **Table 2**. Of the isolated pathogens, 711 (65.7%) were gram negatives, 205 (18.9%) were gram positives, and 167 (15.4%) were fungi. The results of antibiotic susceptibilities of selected microorganisms are presented in **Table 3**.

Discussion. The ICU type-specific, device-associated, device-day infection rates and device utilization ratios appear to represent the best available healthcare associated infection rates for meaningful intrahospital and interhospital comparisons.[9] Although the National Healthcare Safety Network (NHSN) reports DAI rates for the US hospitals annually, most other countries do not have a similar system to follow these infections. The International Nosocomial Infection Control Consortium (INICC) is an international, multi-center HAI control program with a surveillance system based on that of the US NHSN, collecting surveillance data from developing countries.[10,11] The overall DAI rates per 100 patients and per 1000 ICU-days were 16.1 and 20.9 in this study, which closely resembled the mean values of 14.7% and 22.5 infections per 1000 ICU days in the INICC study.[11] Data reported from Turkey generally yielded higher rates of DAIs. Inan et al[9] reported 29.1 infections per 100 patients and the mean overall infection rate per 1000 patient-days was 34.2. In another study, overall DAI rates were reported to be 38.3% and 33.9 infections per 1000 ICU days, which were considerably higher than our results.[12]

Ventilator utilization ratios in the N-ICU and CVS-ICU were similar to that of the NHSN, whereas the same ratio in the MS-ICU exceeded the seventy-fifth percentile. Most strikingly, utilization ratios for urinary catheters in all ICUs were greater than the ninetieth percentiles reported by the similar ICUs in the NHSN system. Although the central line use in the CVS-ICU was almost 100%, this ratio in other ICUs was around the twenty-fifth percentile.[8]

Device associated infection rates. The CAUTI and VAP rates in MS-ICUs were found to be 4 to sevenfold higher than the pooled mean rates reported by the NHSN, and the CLABSI rate was also slightly higher.[8] When compared with the INICC data,[10] we found a similar VAP rate (21.4 versus 19.8); higher CAUTI and lower CLABSI rates (12.2 versus 6.6; 2.9 versus 8.9). Previous reports from Turkey usually demonstrated similar results. The largest multicenter study from Turkey by Leblebicioglu et al[12] gathered data from 13 MS-ICUs. Mean overall DAI rates for VAP, CAUTI, and CLABSI were found to be 26.5, 8.3 and 17.6 in this study. In addition, VAP, CAUTI, and CLABSI rates were 20.7, 13.6 and 9.7 in the study by Inan et al.[9] Our DAI rates in MS-ICUs were comparable to those previously reported from Turkey and developing countries.

Although limited, previous reports from different hospitals usually yielded higher DAI rates in N-ICUs. Depressed consciousness and impaired protective oropharyngeal reflexes pose a major risk for the development of VAP in neurologic patients.[13] The VAP rates for patients followed in N-ICUs were reported to be 20.4 and 27.4 in 2 different studies from Germany.[13,14] The VAP incidence in our hospital's N-ICU was in line with these findings. Among neurologic ICUs reported to the NHSN,[8] rates were 6.7 for VAP, 7.4 for CAUTI, and 1.4 for CLABSI. Our results were 2 to fourfold higher than these reported data.

In addition to the risk factors for patients followed in the N-ICU, NS-ICU patients may suffer from additional risk factors such as trauma and operation. Published data revealed VAP rates between 10.3-19.9, CAUTI rates between 4.5-8.5, and CLABSI rates between 0.9-13.1 per 1000 device-days in neurosurgical ICUs.[10,15-17] The VAP, CAUTI and CLABSI rates in the NS-ICU were found to be 23.3, 10.6 and 5.1 in our study. Compared with DAI rates reported by the NHSN,[8] these rates were found to be 2 to fourfold higher. However, these rates were similar to the data from the INICC report.[10] The pooled mean VAP, CAUTI and CLABSI rates of cardiothoracic surgery ICUs reported to the NHSN were 3.9, 3.6 and 1.4.[8] These rates were reported to be 18.8, 1.3 and 1.6 in the INICC report.[10] The DAI rates in our CVS-ICU were 13.3, 2.6 and 0.9. Lower CAUTI and CLABSI rates in the CVS-ICU when compared to other ICUs may be explained by the location of this ICU; it is adjacent to the CVS operation room. Hence, all urinary and intravascular catheterizations in this ICU are performed in the operation room with strict barrier precautions. The Turkish National Healthcare Associated Infections Surveillance Report, data summary for 2006-2007 was issued in December 2009.[18] When compared with this report, VAP rates in all ICUs were greater than the fiftieth percentile, except in the NS-ICU that was between the twenty-fifth - fiftieth percentiles. The CAUTI rates of all ICUs were around the seventy-fifth percentile and CLABSI rates were at the fiftieth percentile or lower.

Several factors may have contributed to these high DAI rates. Our hospital is a tertiary reference hospital with more than 800 beds. It was shown that large-sized medical centers and teaching hospitals tend to have higher healthcare-associated infection rates.[9,19] Understaffing and a low nurse-patient ratio are frequently reported problems in developing countries.[9,11] The total nurse-patient ratio in our ICUs was lower than has been recommended.[20] Inadequate infrastructure (for example insufficient bed area) and inadequacies in appropriate medical supplies (for example sterile closed drainage systems for urinary catheters and endotracheal tubes with a subglottic secretion drainage lumen) especially during the first 2 years of the study period may have increased our DAI rates. The lack of available beds in long-term care facilities in Turkey may extensively prolong the ICU follow-up in some instances and leads to longer lengths of stay, which in turn increase the likelihood of the development of recurrent HAIs. Particularly, urinary catheter utilization was higher than the ninetieth percentiles of the similar ICUs reported by the NHSN. This may be one of the reasons for our considerably higher CAUTI rates. Finally, infection control shortcomings may also be related with higher DAI rates in our hospital.

Better implementation of infection control measures, reducing the utilization of invasive devices by using alternative methods, continuous education of healthcare workers, improving compliance with published guidelines, and implementing protocols for the correct use of ventilators, urinary catheters, and central lines can help to improve our DAI rates.

Microbiological findings. A recent international prevalence study by Vincent et al[21] showed that 62% of the isolates recovered from the patients in ICUs were gram-negative organisms, most commonly *Pseudomonas species* and *Escherichia coli (E. coli)*. Similar to this finding, we have found that *Pseudomonas* species and *E. coli* were the most frequently recovered pathogens from patients with DAIs in our hospital. In patients with VAP, *Acinetobacter* species and *Pseudomonas* species were the most frequently isolated. This finding is in accordance with previous reports from Turkey[9] and other countries, such as Greece.[22] Although *Staphylococcus aureus* (*S. aureus)* was the leading cause of VAP according to the NHSN data,[23] this microorganism was isolated from only 11% of our VAP cases. The *E. coli* and *Candida* species accounted for almost half (48%) of all CAUTIs. Similarly, these 2 pathogens are the most frequently reported isolates in the NHSN report.[23] It is assumed that the high frequency of *Candida* species in patients with urinary tract infections may be related to the long duration of catheterization.[12] Coagulase negative *Staphylococci* are reported to be the leading cause of CLABSI.[24] We have found that coagulase negative *Staphylococci* and *Candida* species were the leading pathogens in patients with CLABSIs with the same frequency (29.4%). Even though the frequency of *Candida* species in our patients with CLABSIs was higher than that reported by the NHSN, it has been noticed that there may be significant variabilities in the relative frequency of candidemia in different regions even within a given country.[25]

Resistance findings. The HAIs due to antimicrobial resistant pathogens became a major problem in the last decade. Describing the magnitude of the problem with respect to antimicrobial-resistant pathogens is challenging, because the levels of antimicrobial resistance vary for different geographic areas.[23,26] Hence, surveillance of local antimicrobial resistance is essential to understand trends in resistance and to facilitate treatment decisions. The rates of ESBL expression among nosocomial *E.coli* and *Klebsiella* species have risen substantially in several countries.[27] European Antimicrobial Resistance Surveillance System data shows that Greece has the highest rate of ESBL production in Europe, whereas the northern European countries have lower rates.[27,28] The results of surveillance of microbial resistance in European ICUs revealed that third generation cephalosporin resistance rates of *E.coli* and *Klebsiella* species isolates from Turkey were 42% and 52%.[29] The results of our study (38% and 49%) were consistent with this finding.

Although methicillin resistance in *S. aureus* was found to be higher than that reported by the NHSN[23] (56% versus 74%), this rate was lower than that reported by Hanberger et al.[29] Vancomycin resistance in *Enterococci* remains a problem with an overall lower and inconsistent impact in Europe in contrast to the US.[26] Vancomycin resistant *Enterococci* do not seem to constitute a major problem for our hospital. Only <5% of *Enterococci* isolates were found to be resistant to vancomycin, whereas it was reported as being as high as 33% by the NHSN.[23] Antibiotic resistance is even more serious among *P. aeruginosa* and *A. baumannii*.[26] The *P. aeruginosa* resistance rates to carbapenems appear to be rather high all over Europe. The highest rates were reported by Greece and Italy, 49 and 33%.[28] Thirty percent of *P. aeruginosa* isolates from Turkey were found to be resistant to carbapenems in the same report and even higher resistance rates were reported by others.[29]

Concerning *Acinetobacter* species, the most recent data revealed that carbapenem resistance rates were as high as 33% in the US[23] and 38% in Turkey.[29] We have found that 39% of *P. aeruginosa* isolates were resistant to carbapenems in our hospital. Although this rate was in line with the literature, we observed considerably higher carbapenem resistance rates among *Acinetobacter* species than those from other studies. Even though we have found high resistance rates for certain microorganisms, most of our susceptibility data were consistent with the data from Europe. Among all organisms recovered from patients with DAIs, above-mentioned resistant pathogens accounted for 39% in our hospital. Antibiotic resistance profiles of these commonly encountered organisms demonstrate the need and importance of local epidemiologic data for better management of patients with HAIs. Limiting and improving the use of antimicrobial agents, following published guidelines to prevent DAIs and more consistent application of infection control measures and isolation practices will be required to control antibiotic resistance.

The major limitation of this study was that presented data comes from a single center and represents neither Turkish hospitals' DAI rates nor antibiotic susceptibilities of selected microorganisms.

In conclusion, we observed considerably high rates of VAP and CAUTI and a high rate of CLABSI in our ICUs when compared with the NHSN data. In addition, we noted high rates of resistance among pathogens frequently encountered in DAIs. These findings emphasize the need to improve infection control practices and management of invasive device use in our hospital. In this setting, ongoing surveillance programs could contribute to reducing HAIs.

Acknowledgment. *The authors would like to thank the following infection control nurses for their cooperation and support in this surveillance study: F. Callak Oku, E. Sendag, G. Sevinc, and A. Tekin.*

References

1. Lynch P, Pittet D, Borg MA, Mehtar S. Infection control in countries with limited resources. ***J Hosp Infect*** 2007; 65: 148-150.
2. Klevens RM, Edwards JR, Richards CL Jr, Horan TC, Gaynes RP, Pollock DA, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. ***Public Health Rep*** 2007; 122: 160-166.
3. Weber DJ, Sickbert-Bennett EE, Brown V, Rutala WA. Comparison of hospitalwide surveillance and targeted intensive care unit surveillance of healthcare-associated infections. ***Infect Control Hosp Epidemiol*** 2007; 28: 1361-1366.
4. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. ***Am J Epidemiol*** 1985; 121: 182-205.
5. Burke JP. Infection control - a problem for patient safety. ***N Engl J Med*** 2003; 348: 651-656.
6. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. ***Am J Infect Control*** 1988; 16: 128-140.
7. Cockerill FR, editor. Performance standards for antimicrobial susceptibility testing: Nineteenth Informational Supplement. 1st ed. Wayne (PA): Clinical and Laboratory Standards Institute; 2009.
8. Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, et al. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. ***Am J Infect Control*** 2009; 37: 783-805.
9. Inan D, Saba R, Yalcin AN, Yilmaz M, Ongut G, Ramazanoglu A, et al. Device-associated nosocomial infection rates in Turkish medical-surgical intensive care units. ***Infect Control Hosp Epidemiol*** 2006; 27: 343-348.
10. Rosenthal VD, Maki DG, Mehta A, Alvarez-Moreno C, Leblebicioglu H, Higuera F, et al. International Nosocomial Infection Control Consortium report, data summary for 2002-2007, issued January 2008. ***Am J Infect Control*** 2008; 36: 627-637.
11. Rosenthal VD, Maki DG, Salomao R, Moreno CA, Mehta Y, Higuera F, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. ***Ann Intern Med*** 2006; 145: 582-591.
12. Leblebicioglu H, Rosenthal VD, Arikan OA, Ozgültekin A, Yalcin AN, Koksal I, et al. Device-associated hospital-acquired infection rates in Turkish intensive care units. Findings of the International Nosocomial Infection Control Consortium (INICC). ***J Hosp Infect*** 2007; 65: 251-257.
13. Zolldann D, Spitzer C, Häfner H, Waitschies B, Klein W, Sohr D, et al. Surveillance of nosocomial infections in a neurologic intensive care unit. ***Infect Control Hosp Epidemiol*** 2005; 26: 726-731.
14. Dettenkofer M, Ebner W, Els T, Babikir R, Lucking C, Pelz K, et al. Surveillance of nosocomial infections in a neurology intensive care unit. ***J Neurol*** 2001; 248: 959-964.
15. Orsi GB, Scorzolini L, Franchi C, Mondillo V, Rosa G, Venditti M. Hospital-acquired infection surveillance in a neurosurgical intensive care unit. ***J Hosp Infect*** 2006; 64: 23-29.
16. Dettenkofer M, Ebner W, Hans FJ, Forster D, Babikir R, Zentner J, et al. Nosocomial infections in a neurosurgery intensive care unit. ***Acta Neurochir (Wien)*** 1999; 141: 1303-1308.
17. Zolldann D, Thiex R, Häfner H, Waitschies B, Lütticken R, Lemmen SW. Periodic surveillance of nosocomial infections in a neurosurgery intensive care unit. ***Infection*** 2005; 33: 115-121.
18. Refik Saydam National Hygiene Center of Turkey. Turkish National Healthcare Associated Infections Surveillance Report, data summary for 2006-2007. ***Turkish Journal of Hospital Infections*** 2009; 13: 215-269.
19. Durando P, Icardi G, Ansaldi F, Crimi P, Sticchi C, Compagnino F, et al. Surveillance of hospital-acquired infections in Liguria, Italy: results from a regional prevalence study in adult and paediatric acute-care hospitals. ***J Hosp Infect*** 2009; 71: 81-87.
20. Ferdinande P. Recommendations on minimal requirements for Intensive Care Departments. Members of the Task Force of the European Society of Intensive Care Medicine. ***Intensive Care Med*** 1997; 23: 226-232.
21. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. ***JAMA*** 2009; 302: 2323-2329.
22. Dima S, Kritsotakis EI, Roumbelaki M, Metalidis S, Karabinis A, Maguina N, et al. Device-associated nosocomial infection rates in intensive care units in Greece. ***Infect Control Hosp Epidemiol*** 2007; 28: 602-605.
23. 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.
24. Raad I, Hanna H, Maki D. Intravascular catheter-related infections: advances in diagnosis, prevention, and management. ***Lancet Infect Dis*** 2007; 7: 645-657.
25. Falagas ME, Roussos N, Vardakas KZ. Relative frequency of albicans and the various non-albicans Candida spp among candidemia isolates from inpatients in various parts of the world: a systematic review. ***Int J Infect Dis*** 2010; 14: e954-e966.
26. Rossolini GM, Mantengoli E. Antimicrobial resistance in Europe and its potential impact on empirical therapy. ***Clin Microbiol Infect*** 2008; 14; 2-8.
27. Falagas ME, Karageorgopoulos DE. Extended-spectrum beta-lactamase-producing organisms. ***J Hosp Infect*** 2009; 73: 345-354.
28. European Antimicrobial Resistance Surveillance System. EARSS Annual Report 2008. [updated 2011 March 8; Accessed 2010 September 8] Available at: http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Documents/2008_EARSS_Annual_Report.pdf
29. Hanberger H, Arman D, Gill H, Jindrák V, Kalenic S, Kurcz A, et al. Surveillance of microbial resistance in European Intensive Care Units: a first report from the Care-ICU programme for improved infection control. ***Intensive Care Med*** 2009; 35: 91-100.