Catheter-associated urinary tract infections in intensive care units at a university hospital in Turkey

Derya Keten[1], Firdevs Aktas[2], Ozlem Guzel Tunccan[2], Murat Dizbay[2], Ayse Kalkanci[3], Gulsah Biter[4], Hamit Sirri Keten[5*]

[1]Clinic of Infectious Diseases and Clinical Microbiology, Kahramanmaras Necip Fazil City Hospital, Kahramanmaras, Turkey. [2]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Gazi University, Ankara, Turkey. [3]Department of Medical Microbiology, Faculty of Medicine, Gazi University, Ankara, Turkey. [4]Department of Medical Microbiology, Hakkari State Hospital, Hakkari, Turkey. [5]Onikisubat Community Health Center, Kahramanmaras, Turkey

Abstract

In this study, urinary catheter utilization rates, the causative agents for catheter-associated urinary tract infection (CAUTI) and their antimicrobial susceptibilities in intensive care units (ICUs) in 2009 were investigated at Gazi university hospital. We aimed to determine the causative agents and risk factors for CAUTIs, and antimicrobial susceptibilities of the pathogens; and also sensitivities of *Candida spp*. to antifungal agents with Microdilution and E-test. The most common etiological agents of CAUTIs were *Candida spp*. (34.7%). The most frequently isolated *Candida spp*. was *C.albicans* (52.4%). All *C. albicans spp*. were sensitive to fluconazole. Microdilution, used as a reference method to determine the sensitivity to antifungal agents, was compared with E test. E test was found to be sufficient to analyze sensitivity to amphotericin B, caspofungin, fluconazole and voriconazole, but inappropriate for itraconazole. *E.coli* and *Klebsiella spp.* were found to be causative agents for CAUTI in 20.6% and 9.9% of cases respectively. *Pseudomonas spp*. And *Acinetobacter spp.* were isolated in 14% and 8.2% of the cases, respectively. All *E.coli* and *Klebsiella* strains were found sensitive to carbapenems. Carbapenem sensitivity was found in 47.1% and 30% of the cases infected with *Pseudomonas* and *Acinetobacter* strains, respectively. According to our results, fluconazole therapy seems to be an appropriate choice for the treatment of CAUTIs caused by *C.albicans*. Third and fourth generation cephalosporins should not be used for empirical treatment because of the high prevalence of extended spectrum beta-lactamase production among *E.coli* and *Klebsiella* isolates.

KEY WORDS: antimicrobial, antifungal susceptibility, microdilution

Bosn J Basic Med Sci. 2014;14(4):227-233. © 2014 ABMSFBIH

INTRODUCTION

Urinary tract infections (UTIs) account for about 30%-40% of all hospital associated infections and are important since they increase mortality, morbidity, duration of hospital stay and health costs [1-3]. The most important risk factor for developing a UTI is urinary catheterization. It is estimated that 15%-25% of all the patients hospitalized in health centers undergo urinary catheterization at least once during their hospital stay and it is reported that the frequency of urinary catheterization has increased in the past 20 years. Patients admitted to intensive care units (ICU) are the most appropriate candidates for UTIs due to their more frequent necessity of urinary catheterization and longer duration of catheter use [1,3,4].

Apart from urinary catheterization, the other risk factors for developing a UTI are identified: Female gender, antibiotic use, *diabetes mellitus*, renal failure, malnutrition, omissions in urinary catheter care, contamination of drainage bags and periurethral colonization. Bacteriuria associated with duration of urinary catheter use is most commonly caused by a single pathogen, which is mostly a species of *Candida* or a gram negative enteric bacterium [1,2,4]. Before receiving the antibiotic susceptibility results, the antibiotics that should be considered are the ones that are thought to have the least resistance. After receiving culture results, the antibiotics that the pathogens are susceptible for should be used. The reason for not choosing.

The aim of this study was to determine the incidence of CAUTIs, risk factors, causative agents and their antimicrobial susceptibilities, and sensitivities of *Candida spp.* to

*Corresponding author: Dr. Hamit Sirri Keten, Onikisubat Community Health Center, Department of Family Medicine, TR-46050, Kahramanmaras,-Turkey, Tel: +90-553 5385501, Fax: +90-344 2212371
E-mail: hsketen@hotmail.com

Submitted: 15 September 2014 / Accepted: 24 October 2014

antifungals with Microdilution and E-test in ICUs at Gazi University Hospital.

MATERIALS AND METHODS

Gazi University Clinical Research Ethics Committee approved the study in accordance with Helsinki Declaration.

The setting of the study is a university hospital in which all types of patients are treated and followed. Furthermore, it has a capacity of 1081 beds. CAUTIs were diagnosed in 832 patients admitted to five different ICUs (Anesthesiology and Reanimation ICU, Neurosurgery ICU, Internal Medicine ICU, General Surgery ICU, Neurology ICU) at Gazi University Hospital between 1 January and 31 December 2009 according to the criteria issued by the Centre for disease control and prevention (CDC) in 2008 [5]. Out of 101 patients developing CAUTI, 49 (48.5%) were female and 52 (51.5%) were male.

The patients needing a supported respiration or the ones who will be in a need of long-term respiratory support are treated in Anesthesiology and Reanimation ICU. The patients whose vital signs are deteriorated after intracranial operation are treated in Neurosurgery ICU. In General Surgery ICU, the patients whose vital signs are deteriorated or unstable after operations are treated. The patients suffering from chronic diseases and the ones in poor general condition (for example; patients with *diabetes mellitus* (DM) or kidney failure and immune compromised patients, etc. are treated in Internal Medicine ICU; finally, the patients who had a cerebrovascular incident and the ones who have central nervous system diseases with unstable clinical findings are treated in Neurology ICU.

The information on patients was collected through daily (week days) visits of infection control nurses and was noted in the hospital infection charts. These specified charts contain data such as age and gender; underlying diseases, infection risk factors, the signs of infection, infection development period after hospitalization, the use of foreign objects (e.g.; urinary catheter), survival status, culture and antimicrobial susceptibility results, concomitant nosocomial infections (for example: bacteremia, ventilator-associated pneumonia, bloodstream infections, etc.), the antibiotics used and the treatments taken before the diagnosis of a CAUTI. In intensive care units, urine samples were taken from closed urine drainage systems. In order to prevent disruption of this closed system, urine samples were taken without opening the junction of the catheter collection tube. These samples were then sent to Microbiology or Infection Diseases laboratory. The microorganisms which had been isolated from the patients diagnosed with catheter-associated urinary tract infections were obtained from the Microbiology and Infectious diseases laboratories. The strains isolated from the patients were kept at Micro bank (Pro-Lab, Canada) at -80°C. Antimicrobial susceptibilities of obtained strains were evaluated.

Identification of causative agents

Fungal species were inoculated into Sabouraud Dextrose Agar. Following their inoculation at 37°C for 48 hours, germ tube formation in the resultant colonies was examined and *C. albicans* and other fungal species were identified. The species other than *C. albicans* were inoculated in Cornmeal Tween agar. Following their inoculation at 37°C for 48 hours, *C. Glabrata* was identified under direct microscopic examination. Other fungal species were identified with ID-32C kit (bioMerieux, France).

Bacteria were identified with BBL Crystal Enteric/Nonfermenter ID Kit and BBL Crystal Gram-Positive ID Kit (Becton Dickinson, USA) in addition to conventional methods.

Tests for sensitivity to antifungal agents

Microdilution and E-test were used to investigate sensitivity to fluconazole, voriconazole and amphotericin B and in both methods, *C.parapsilosis* ATCC 22019 and *C.krusei* ATCC 6258 species were used as controls.

a. Microdilution: The sensitivity of *Candida* species to antifungal agents was investigated as recommended in M27-A3 guidelines by Clinical and Laboratory Standards Institute (CLSI). RPMI 1640 liquid agar with L-glutamine, without sodium bicarbonate was used for inoculation. Since its pH should be 7.0, the agar was tamponated with molar morpholinepropanesulfonic acid (MOPS), the pH of which was 0.165. Fluconazole was diluted in the range of 0.12-64 µ/mL and other drugs were diluted in the range of 0.03-16 µ/mL. Before the test, stock solutions of the drugs were two-fold diluted. Fluconazole and caspofungin solutions were prepared with test agars, and solutions of amphotericin B were prepared with the solvent dimethyl sulphoxide (DMSO); finally, the solutions of other antifungal agents were prepared with water. Exposure of amphotericin B solution to light was prevented. U-shaped polypropylene ninety-well microplaques were used for preparation of the solutions. After 24-hour incubation, the value from the well which looked clear first in absence of growth was considered as minimal concentration value (MCV) for amphotericin B and caspofungin. The value from the well where growth decreased considerably and which became clearer first at least by 50% was considered as MCV for azoles.

b. E-test: E test was performed in RPMI agar with 2% glucose by a commercially available product by AB Biodisk (Solna, Sweden). As in disk diffusion method, the amount of inoculum was prepared as it was equal to 0.5 McFarland turbidity

standards and contained 10^6 inoculum densities CFU/mL. The inoculum was spread on the plaques and inoculated for 48 hours. The first contact on the strip on which inhibition ellipsis appeared was considered as MCV and microcolonies in the zone were disregarded as in disk diffusion test.

c. Comparing microdilution with E-test: Since MICs obtained with E-test could be compared with those with microdilution easily, when a strain was found to be resistant or sensitive with one method and sensitive with the other method depending on the dose, it was considered a small mistake; when a strain was found to be resistant with E -test but sensitive with microdilution, it was considered to be a big mistake; and, finally, when a strain was found to be sensitive with E -test but resistant with microdilution, it was considered a very big mistake [6].

Tests for sensitivity to antibacterial agents

Sensitivity to antimicrobial agents was tested with Kirby-Bauer disk diffusion in accordance with CLSI standards and Mueller Hinton Agar was used. Antimicrobial agents to be used in sensitivity analyses of microorganisms were selected in accordance with recommendations of CLSI [7,8]. Oxoid disks were used for tigecycline, and Bioanalyse disks fulfilling CLSI standards were used for the others. The cut-off value for sensitivity to antimicrobial agents was based on CLSI, the cut-off value for sensitivity to tigecycline was based on European Committee for Antimicrobial Susceptibility Testing (EUCAST) and the cut-off value for the sensitivity to cefoperazone-sulbactam was set as found in the literature [8-11]. *S. aureus* ATCC 25923, *E. coli* ATCC 35218 and *P. aeruginosa* ATCC 27853 were used as standard strains to check the standardization of the disks.

Statistical analyses

Statistical Package Program for Social Sciences 15.0 was used for statistical analyses. Descriptive statistics were used to determine patient characteristics; the relation between features of microorganisms and patient characteristics were analyzed using Yates corrected Pearson correlation and Fisher's Chi-square tests. $p<0.005$ was considered statistically significant.

RESULTS

The study population included 832 patients hospitalized in five different ICUs at Gazi university hospital. A hundred and one patients developing 126 attacks of catheter associated urinary tract infections (CAUTI) were included in the study sample. Of 101 patients, 85% suffered at least one attack of CAUTI, 7% suffered two attacks of CAUTI and 6% suffered three or more attacks of CAUTI.

Out of 101 patients developing a CAUTI, 49 (48.5%) were female and 52 (51.5%) were male. These 101 patients developed a total of 126 attacks of CAUTI. They were aged between 18 years and 89 years (±16.9) with a mean age of 64.9 years. Fifty-four point five percent of the patients were aged 65 years or older. Sixty-two patients (61.4%) were found to have signs of systemic inflammatory response syndrome (SIRS).

Forty-three patients (42.6%) recovered; however, 58 of them (57.4%) died. The rates of ventilator use ($p<0.001$), vascular interventions ($p=0.001$), endoscopic interventions ($p=0.01$), ventilator associated pneumonia ($p=0.007$), primary blood circulation infections ($p=0.03$) and SIRS ($p=0.04$) signs were significantly higher in patients who died.

Of all CAUTIs, 71 (58.7%) were due to gram-negative bacteria, 42 (34.7%) were due to *Candida spp.* and 8 (6.6%) were due to gram-positive bacteria. The most frequently isolated causative agent was *Candida spp*. (34.7%), followed by *E.coli* (20.6%), *Pseudomonas spp*. (14%), *Klebsiella spp*. (9.9%) and *Acinetobacter spp*. (8.2%).

Out of 126 attacks of CAUTI, 42 (34.7%) were caused by *Candida spp*. and 84 (65.3%) were caused by bacteria. Differences between the patients in whom *Candida* was isolated and those in whom bacteria were isolated were investigated. When survival and mortality rates were compared, it became evident that mortality rates were significantly higher in patients in whom *Candida spp.* were identified ($p=0.008$). As for the underlying diseases, the rate of infection with *Candida spp*. was significantly higher in patients with *diabetes mellitus* (DM), but the rate of infection with bacteria was significantly higher in patients without DM ($p=0.04$), furthermore the rate of infection with *Candida spp.* was significantly higher in patients requiring ventilation ($p=0.01$). In addition, the rates of intubation, mechanical ventilation and vascular interventions were significantly higher in patients infected with *Candida* ($p=0.02$, $p=0.01$, $p=0.007$). The rate of SIRS was significantly higher in patients infected with bacteria ($p=0.04$).

Table 1 shows MIC values of *Candida spp.* for amphotericin B and caspofungin and MIC_{50} and MIC_{90} values of *C.albicans*. Sensitivity to amphotericin B and caspofungin was found to be similar with proximate MIC values shown by both microdilution and E-test.

Table 2 shows MIC values of *Candida spp.* for itrakonazol, fluconazole and voriconazole as shown by both microdilution and E-test. There were differences in MIC values between these three antifungal agents.

Table 3 shows data from comparisons of ±2 dilution conversions to evaluate consistency between E-test and microdilution.

There was no error in determining the sensitivity to caspofungin and amphotericin B with both E-test and microdilution

TABLE 1. Sensitivity of *Candida spp.* isolated from CAUTIs to caspofungin and amphotericin B.

	Caspofungin						Amphotericin B					
	Microdilution			E-test			Microdilution			E-test		
	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}
C. albicans (n=22)	0.03-0.25	0.05	0.25	0.03-0.5	0.003	0.125	0.03-0.25	0.06	0.25	0.03-0.125	0.003	0047
C. glabrata (n=6)	0.03-0.125	-	-	0.047-0.25	-	-	0.03-0.125	-	-	0.003-0.125	-	-
C. kefyr (n=3)	0.03-0.03	-	-	0.06-0.032	-	-	0.03-0.125	-	-	0.003-0.032	-	-
C.parasilosis (n=4)	0.125-0.25	-	-	0.032-0.75	-	-	0.03-0.125	-	-	0.003-0.047	-	-
C.tropicalis (n=7)	0.03-0.25	-	-	0.03-0.047	-	-	0.03-0.125	-	-	0.03-0.094	-	-

methods. However, there were different rates of errors in determining the sensitivity to fluconazole, voriconazole and itraconazole (Table 2). Categorical agreement (CA) between 2 tests was above 80%, for fluconazole and voriconazole, while it was below 64.3% for itraconazole.

E.coli and *Klebsiella spp.*, which were found to be the second and the third most frequent causative agents respectively, were not resistant to carbapenems, but they were resistant to piperacillin and tazobactam in 28% and 66.7% of the infections, cefoperazone and sulbactam in 32% and 66.7% of the infections and ceftazidime in 72% and 100% of the infections respectively. *E.coli* and *Klebsiella spp*. were found to produce large spectrum betalactamase in 64% and 91.6% of the infections respectively. *Pseudomonas* and *Acinetobacter spp.* were resistant to carbapenem in 52.9% and 70% of the infections respectively, but they were not resistant to colistin.

DISCUSSION

In this study, 48.5% of the patients were female, the mean age of the patients was 64.9 years and 54.5% of the patients were 65 years old or older. Sixty-two patients (61.4%) had signs of SIRS during attacks of UTI. As for other risk factors, of all the patients, 48.5% were had immunosuppression, 18.8% suffered from a malignant disease or trauma, and 17.8% of patients suffered from DM. In Clec'h's, Erben's and Talaat's studies, age over 65 years, female gender, presence of DM, mechanical ventilation, central venous catheterization and unconsciousness were reported to be risk factors [3,12,13]. The results of our study were consistent with the results of other studies in terms of risk factors.

In the present study, the crude mortality rate in patients developing CAUTI was 57.4%. According to data from International Nosocomial Infection Control Consortium, the crude mortality rate is 35.8% and the attributed mortality rate is 20.5 [14]. We could not estimate the mortality rate attributable to CAUTIs since our study did not have a control group.

Catheter-related UTI rate in studies involving European countries was 62.2%. Short-term catheterization (under 30 days) rate was 90.8%. The duration of catheterization was 1-7 days for 44.8% of the cases; 8-30 days for 46% of the cases [15]. In our study, more than 50% of the most common CAUTIs were developed within the first 30 days after the beginning of the hospitalization.

In a study from Turkey by Inan *et al*., the most frequently isolated causative agents were *Candida spp*. in 37.1% of the UTIs, *E.coli* in 21.1% of the UTIs and *Pseudomonas spp*. in 16.5% of the UTIs [16]. Five out of seven studies on causative agents of CAUTIs revealed that the most frequent agent was *Candida spp*. and out of the remaining two, one by Gikas *et al*. revealed that the most frequent agent was *P. aeruginosa* (30.6%) and the other study by Ko *et al*. indicated that the most frequent agent was *E.coli* (23.4%) [3,4,13,16,17-19]. As highlighted above, the most frequently isolated agent was *Candida spp*., consistent with the findings of our study.

Standard sensitivity of *Candida* species to antifungal agents is determined by microdilution. Although routine use of E-test is not recommended, in the present study, both E-test and microdilution indicated that *Candida spp.* had similar MIC values for amphotericin B and caspofungin. However, in this study, these tests revealed different MIC values for azoles; i.e. itraconazole, fluconazole and voriconazole. In the literature, it has been reported that the rate of consistency between these two tests for *Candida spp*. was 78%-96% [20-25]. The rate of consistency was reported to be 89.3% for fluconazole by Yücesoy *et al*. and 80.4% for fluconazole, 95.6% for voriconazole, 93.4% for caspofungin and 84.7% for amphotericin B by Özcan *et al*. [26, 27]. As a result, we found a higher rate of consistency for amphotericin B and caspofungin than it was reported in the literature and a similar rate of consistency for fluconazole and voriconazole then was reported in the literature; also, we found a lower rate of consistency for itraconazole.

In the present study, *Klebsiella spp*. was found to be the fourth most frequent causative agent that was not resistant to carbapenem, but resistant to piperacillin-tazobactam and cefoperazone-sulbactam in 66.7% of the infections and ceftazidime in 100% of the infections. In a study by NHSN, *Klebsiella spp.* was reported to be resistant to carbapenem in 10.1% of the infections and to ceftazidime in 21.2% of the infections in 2006-2007 [28,29]. In this study, *Klebsiella spp.* was found to have a high rate of resistance for ceftazidime.

TABLE 2. Sensitivities of *Candida spp.* isolated from CAUTIs to itraconazole, voriconazole and fluconazole

	İtrakonazol						Fluconazole						Voriconazole					
	Microdilution			E-test			Microdilution			E-test			Microdilution			E-test		
	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}	MIC	MIC_{50}	MIC_{90}
C. albicans (n:22)	0.03-8	0.125	8	0.003-0.19	0.008	0.19	0.125-128	0.5	2	0.003-0.125	0.003	0.006	0.003-16	0.06	0.5	0.003-0.064	0.006	0.064
C. glabrata (n:6)	0.03-2	-	-	0.003-128	-	-	0.06-2	-	-	0.03-128	-	-	0.03-0.06	-	-	0.003-16	-	-
C. kefyr (n:3)	0.06-0.06	-	-	0.003-0.064	-	-	0.125-0.5	-	-	0.003-0.008	-	-	0.06-0.032	-	-	0.003-0.008	-	-
C. parasilosis (n:4)	0.03-0.5	-	-	0.003-0.5	-	-	0.125-128	-	-	0.003-128	-	-	0.06-2	-	-	0.003-0.38	-	-
C. tropicalis (n:7)	0.06-4	-	-	0.003-0.032	-	-	0.125-128	-	-	0.006-0.064	-	-	0.06-8	-	-	0.006-0.064	-	-

TABLE 3. Categorical agreement (CA) between 2 methods: MIC Values of *Candida spp.* obtained with E-test and those obtained with microdilution (n=42).

	Minor error* n (%)	Major error** n (%)	Very major error*** n (%)	Total CA n (%)
Fluconazole	-	1 (2.4)	4 (9.5)	37 (%88.1)
Itraconazole	7 (16.6)	1 (2.4)	7 (16.6)	27 (%64.3)
Voriconazole	1 (2.4)	1 (2.4)	4 (9.5)	36 (%85.7)

*Minor error: Finding a species resistant or sensitive to an agent with one method and sensitive depending on a given dose with the other method, ** Major error: Finding a species resistant with E-test and sensitive with microdilution, *** Very major error: Finding a species sensitive to an agent with E-test and resistant with microdilution.

We found *E.coli and Klebsiella spp.* produced large spectrum beta-lactamase in 64% and 91.6% of the infections respectively. In a study by Talaat, *E.coli* and *Klebsiella spp.* were reported to produce large spectrum beta-lactamase in 78.6% and 56% of the infections respectively [13]. The rate of beta-lactamase producing *E.coli spp.* in this study were lower than it was reported in the literature but the rate of beta-lactamase producing *Klebsiella spp.* were higher than reported in the literature.

Among other pathogens we isolated in this study, *Pseudomonas* and *Acinetobacter* were found to be resistant to carbapenems in 52.9% and 70% of the infections respectively; neither of these pathogens was found to be resistant to colistin. In a study by Gikas, *P. aeruginosa* was reported to be resistant to carbapenem in 29.8% of the infections, but *A. baumannii* was reported not resistant to carbapenem [18]. INICC showed that *Pseudomonas* and *Acinetobacter*, which were found to be pathogens responsible for CAUTIs, were reported resistant to carbapenem in 34.7% and 38.9% of the infections respectively in 2003-2008 and 36.5% and 52.2% of the infections respectively in 2004-2009 [30,31]. Colistin seems to be the first option for the empirical treatment of infections due to *Pseudomonas* and *Acinetobacter spp.* in hospitals where the resistance rates of these species to carbapenem is high. The second most appropriate alternative for the treatment of the infections caused by *Pseudomonas spp.* could be amikacin and ceftazidime. However, there is no alternative to colistin for the treatment of the infections due to *Acinetobacter spp*.

In patients with sepsis early initiation of appropriate antibiotic therapy is lifesaving. Ceftazidime and amikacin as the first option is the probability of microorganisms to be resistant.

CONCLUSIONS

According to our results, fluconazole therapy seems an appropriate choice for the treatment of CAUTIs caused by *C.albicans*. Third and fourth generation cephalosporins

should not be used for empirical treatment because of the high prevalence of extended spectrum beta-lactamase production among *E.coli* and *Klebsiella* isolates. Colistin seems to be the most appropriate choice for the treatment of CAUTI caused by *Pseudomonas* and *Acinetobacter spp*.

DECLARATION OF INTERESTS

The authors declare no conflict of interests.

REFERENCES

[1] Healthcare Infection Control Practices Advisory Committee (HICPAC) [Internet]. Guideline for prevention of catheter-associated urinary tract infections 2009 [cited 2014 feb 15]. Available from http://www.cdc.gov/hicpac/pdf/CAUTI/CAUTIguideline2009final.pdf.

[2] Falkiner FR. The insertion and management of indwelling urethral catheters--minimizing the risk of infection. J Hosp Infect 1993;25(2):79-90. http://dx.doi.org/10.1016/0195-6701(93)90098-K.

[3] Clec'h C, Schwebel C, Francais A, Toledano D, Fosse JP, Garrouste-Orgeas M, et al. Does catheter-associated urinary tract infection increase mortality in critically ill patients? Infect Control Hosp Epidemiol 2007;28(12):1367-73. http://dx.doi.org/10.1086/523279.

[4] Laupland KB, Bagshaw SM, Gregson DB, Kirkpatrick AW, Ross T, Church DL. Intensive care unit-acquired urinary tract infections in a regional critical care system. Crit Care 2005;9(2):R60-5. http://dx.doi.org/10.1186/cc3023.

[5] CDC [Internet]. Centers for Disease Control and Prevention. National Healthcare Safety Network Manual: Patient Safety Component Protocol [cited 2014 feb 15]. Available from www.cdc.gov/ncidod/dhqp/pdf/nhsn/nhsn September 2008.

[6] Quaiyumi S. Macro and microdilution methods. In: Schwalbe R, Steele-Moore L, Goodwin AC (eds), Antimicrobial Susceptibility Testing Protocols. New York: CRS Press 2007; 75-79; 2007. http://dx.doi.org/10.1201/9781420014495.ch4.

[7] Clinical and Laboratory Standards Institute 2009 [Internet]. Performance standards for antimicrobial susceptibility testing; 19th informational supplement [cited 2014 feb 15]. Available from http://www.microbiolab-bg.com/CLSI.pdf.

[8] CLSI [Internet]. Performance Standards for Antimicrobial Susceptibility Testing;15th Informational Supplement M-S, Vol 30: No 1. CLSI; 2010 [cited 2014 feb 15]. Available from http://www.microbiolab-bg.com/CLSI.pdf.

[9] Jones RN, Ferraro MJ, Reller LB, Schreckenberger PC, Swenson JM, Sader HS. Multicenter studies of tigecycline disk diffusion susceptibility results for Acinetobacter spp. J Clin Microbiol 2007;45(1):227-30. http://dx.doi.org/10.1128/JCM.01588-06.

[10] Bradford PA, Sanders CC. Use of a predictor panel for development of a new disk for diffusion tests with cefoperazone-sulbactam. Antimicrob Agents Chemother 1992;36(2):394-400. http://dx.doi.org/10.1128/AAC.36.2.394.

[11] European Committee on Antimicrobial Susceptibility Testing (EUCAST) [Internet]. Breakpoint tables for interpretation of MICs and zone diameters Version 1.3 J, 2011 [cited 2014 feb 15]. Available from: http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Breakpoint_table_v_4.0.pdf.

[12] Erben N, Alpat SN, Kartal ED, Ozgunes I, Usluer G. [Analysis of the risk factors in nosocomial urinary tract infections and effect of urinary catheter use on distribution of the causative agents]. Mikrobiyol Bul 2009;43(1):77-82.

[13] Talaat M, Hafez S, Saied T, Elfeky R, El-Shoubary W, Pimentel G. Surveillance of catheter-associated urinary tract infection in 4 intensive care units at Alexandria university hospitals in Egypt. Am J Infect Control 2010;38(3):222-8. http://dx.doi.org/10.1016/j.ajic.2009.06.011.

[14] 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(9):627-37. http://dx.doi.org/10.1016/j.ajic.2008.03.003.

[15] Bouza E, San Juan R, Munoz P, Voss A, Kluytmans J. A European perspective on nosocomial urinary tract infections I. Report on the microbiology workload, etiology and antimicrobial susceptibility (ESGNI-003 study). European Study Group on Nosocomial Infections. Clin Microbiol Infect 2001;7(10):523-31. http://dx.doi.org/10.1046/j.1198-743x.2001.00326.x.

[16] 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(4):343-8. http://dx.doi.org/10.1086/503344.

[17] Ko MC, Liu CK, Woung LC, Lee WK, Jeng HS, Lu SH, et al. Species and antimicrobial resistance of uropathogens isolated from patients with urinary catheter. Tohoku J Exp Med 2008;214(4):311-9. http://dx.doi.org/10.1620/tjem.214.311.

[18] Gikas A, Roumbelaki M, Bagatzouni-Pieridou D, Alexandrou M, Zinieri V, Dimitriadis I, et al. Device-associated infections in the intensive care units of Cyprus: results of the first national incidence study. Infection 2010;38(3):165-71. http://dx.doi.org/10.1007/s15010-010-0007-2.

[19] 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(11):e774-80. http://dx.doi.org/10.1016/j.ijid.2011.06.009.

[20] Dannaoui E, Colin S, Pichot J, Piens MA. Evaluation of the E test for fluconazole susceptibility testing of Candida albicans isolates from oropharyngeal candidiasis. Eur J Clin Microbiol Infect Dis 1997;16(3):228-32. http://dx.doi.org/10.1007/BF01709586.

[21] Koc AN, Gokahmetoglu S, Oguzkaya M. Comparison of Etest with the broth microdilution method in susceptibility testing of yeast isolates against four antifungals. Mycoses 2000;43(7-8):293-7. http://dx.doi.org/10.1046/j.1439-0507.2000.00574.x.

[22] Pfaller MA, Messer SA, Karlsson A, Bolmstrom A. Evaluation of the Etest method for determining fluconazole susceptibilities of 402 clinical yeast isolates by using three different agar media. J Clin Microbiol 1998;36(9):2586-9.

[23] Simor AE, Goswell G, Louie L, Lee M, Louie M. Antifungal susceptibility testing of yeast isolates from blood cultures by microbroth dilution and the E test. Eur J Clin Microbiol Infect Dis 1997;16(9):693-7. http://dx.doi.org/10.1007/BF01708563.

[24] van Eldere J, Joosten L, Verhaeghe V, Surmont I. Fluconazole and amphotericin B antifungal susceptibility testing by National Committee for Clinical Laboratory Standards broth macrodilution method compared with E-test and semiautomated broth microdilution test. J Clin Microbiol 1996;34(4):842-7.

[25] Sewell DL, Pfaller MA, Barry AL. Comparison of broth macrodilution, broth microdilution, and E test antifungal susceptibility tests for fluconazole. J Clin Microbiol 1994;32(9):2099-102.

[26] Yucesoy M. Mutlu E, Yuluğ N. Evaluation of the E test method for antifungal susceptibility testing. ANKEM 2001;15 (4):670-7.

[27] Ozcan SK, Mutlu B, Dundar D, Willke A. [Comparison of broth microdilution and E-test methods for the antifungal susceptibility testing of Candida spp. strains isolated from blood cultures]. Mikrobiyol Bul 2010;44(2):263-71.

[28] 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(11):996-1011. http://dx.doi.org/10.1086/591861.

[29] Inan D, Saba R, Keskin S, Öngüt G, Öğünç D, Günseren F, et al. Hospital infection surveillance in intensive care units of Akdeniz University Hospital: Device utilization and device-associated infection rates. Hastane infeksiyonları dergisi 2004;8(1):50-6.

[30] Rosenthal VD, Bijie H, Maki DG, Mehta Y, Apisarnthanarak A, Medeiros EA, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. Am J Infect Control 2012;40(5):396-407. http://dx.doi.org/10.1016/j.ajic.2011.05.020.

[31] Rosenthal VD, Maki DG, Jamulitrat S, Medeiros EA, Todi SK, Gomez DY, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary for 2003-2008, issued June 2009. Am J Infect Control 2010;38(2):95-104 e2. http://dx.doi.org/10.1016/j.ajic.2009.12.004.