Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2017) 47: 563-569

doi:10.3906/sag-1509-10

Repeated prevalence studies of nosocomial infections in one university hospital in Serbia

Milena ILIC[1,*], **Ljiljana MARKOVIC-DENIC**[2]
[1]Department of Epidemiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
[2]Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Received: 02.09.2015 • **Accepted/Published Online:** 22.09.2016 • **Final Version:** 18.04.2017

Background/aim: Nosocomial infections occur worldwide and affect both developed and resource-poor countries. The aim of this paper was to determine the prevalence and risk factors for nosocomial infections in one Serbian hospital.

Materials and methods: Three-point prevalence surveys were conducted in the Clinical Center of Kragujevac (1240 beds). The standard definitions for nosocomial infections of the Centers for Diseases Control and Prevention were used. The authors conducted surveys according to the same protocol.

Results: The prevalence of infected patients and the overall prevalence of nosocomial infections was 6.2% and 7.1% in 2003, 4.6% and 4.6% in 2005, and 7.6% and 8.7% in 2009, respectively. In all three studies, the risk factors for nosocomial infections were older age, intravascular catheters, urinary catheters, longer hospital stays, hospitalization in an intensive care unit, and surgeries. According to the multivariate regression analysis, a prolonged hospitalization and use of a urinary catheter were independent risk factors for nosocomial infections in the first and second study.

Conclusion: The overall healthcare-associated infection prevalence in our hospital increased from 2003 to 2009, and this was an incentive for a better definition of infection control priorities in high-risk departments.

Key words: Nosocomial infection, prevalence, repeated survey, university hospital, risk factors

1. Introduction

The incidence of nosocomial or healthcare-associated infections (HAIs) is a major public health problem worldwide (1–3). According to definitions provided by the Centers for Disease Control and Prevention (CDC) for the purposes of surveillance in acute care settings, an HAI is a localized or a systemic condition that appears as a result of an adverse reaction to the presence of an infectious agent or its toxin (4–6). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting.

A prevalence study is one possible method for surveillance of HAIs and has been accepted in many countries, including Serbia (7). Since the World Health Organization prevalence survey was conducted in 47 hospitals in 14 countries (8), many developed (9–13) and less-developed countries (14–17) have started to conduct their own prevalence studies. Although a large and prospective incidence study is a gold standard for HAI surveillance, it is expensive and time-consuming and requires a large staff. Prevalence studies offer advantages when a HAI surveillance system has not yet been developed, especially when financial support is also lacking (18). The results of repeated prevalence surveys can be compared over time and can also provide useful information regarding the evolution of HAI trends. Furthermore, repeated studies increase awareness among healthcare workers and can assist the infection control personnel in defining possible HAI problems in various departments (19,20).

The aim of this paper was to determine the prevalence of HAIs in a tertiary university hospital, compare the prevalence rate over time, and study the risk factors.

2. Materials and methods

2.1. Setting

The Clinical Center of Kragujevac is a 1240-bed tertiary-care university hospital in Kragujevac, Serbia. There are numerous medical departments in the center such as surgery, internal medicine, gynecology and obstetrics, orthopedics and traumatology, urology, ENT, ophthalmology, neurology, psychiatrics, pediatrics,

* Correspondence: drmilenailic@yahoo.com

infectious diseases, skin and venereal diseases, oncology, nuclear medicine, physical medicine and rehabilitation, clinical pharmacology, and an intensive care unit. Until 2000, the center did not have a ratified infection control program. However, guidelines for rational antibiotic use were recently suggested, as well as guidelines for prevention of surgical site infection and hand hygiene.

2.2. Study design

Three-point prevalence surveys were carried out in December 2003, May 2005, and June 2009. The same method was applied in all studies. All patients staying more than 48 h in the hospital at the time of the surveys were included in the studies. Every patient was registered only once. If a patient was visited twice on the same day at the time of the study, possibly due to a transfer between clinics, only the first treatment episode was registered. Every study was performed in a single day in one hospital ward, and the entire study was completed during 1 week, as recommended in previous research (HAI was defined according to CDC criteria (4) and subsequently translated into Serbian) (21). We used these definitions for all three studies. As a result, we were able to compare the results of the surveys. All infections were categorized into 13 major and specific infection sites. Asymptomatic bacteriuria was not considered as an infection. Only HAIs active on the day of the survey were taken into consideration.

Data were collected using a standardized questionnaire based on the patients' medical and nursing records, microbiological and X-ray reports, and interviews with the patients and physicians. The following clinical characteristics were also recorded: demographic data, date of admission, disease type and comorbidities on admission, hospital ward and intensive care unit (ICU), interventions (the presence of an indwelling catheter at the time of the survey; a surgical procedure in the month preceding the survey, or the year preceding the survey in the case of a prosthesis implantation), their corresponding dates and duration of stay, and the use of antimicrobials. We calculated the length of hospitalization as the number of days from admission to the date of surveys. The same epidemiologist and infection control nurses conducted all surveys.

2.3. Data analysis

The prevalence of HAI was presented as the prevalence of infected patients (with at least one infection) and the prevalence of infection. Confidence intervals (CIs) of 95% were calculated. The differences between infected and noninfected patients were assessed using a chi-square or a Fisher exact test for categorical variables and a Student t-test for continuous variables. Univariate and multivariate logistic regression was used to examine variables potentially associated with HAIs. All statistical analyses were carried out using SPSS (SPSS Inc., Version 7.5, Chicago, IL, USA).

3. Results

A total of 764 patients were examined in the first study, 866 patients in the second, and 865 patients in the third. The prevalence of infected patients and the overall prevalence of HAI was 6.2% and 7.1% in 2003, 4.6% and 4.6% in 2005, and 7.6% and 8.7% in 2009, respectively (Table 1).

Table 2 shows the prevalence of infected patients with respect to different departments in the hospital. The highest prevalence rate was noted as occurring in urologic surgery, followed by orthopedic surgery and the ICU in the first and second surveys. In the third survey, the highest prevalence was observed in the ICU (53.8%), followed by urologic surgery (22.7%) and orthopedic surgery (19.1%).

The prevalence of HAIs according to the site of infections is shown in Table 3. Of all HAIs detected in all studies, the most frequent were surgical site infections (SSIs) in the first study and urinary tract infections (UTIs) in the second and third studies. SSI prevalence did not decrease significantly over time, while UTIs showed increased prevalence during the survey period.

Several risk factors associated with HAIs in the univariate logistic regression analysis are shown in Table 4. The mean age of the patients was 48.70 ± 23.95 years (range: 1–85) in the first study, 50.40 ± 24.63 (range: 1–91) in the second, and 50.62 ± 23.37 (range: 1–89) in the third. Older

Table 1. The three surveys of health care-associated infections (HAIs).

Variables	Survey I	Survey II	Survey III
Survey period	December 2003	May 2005	June 2009
Number of hospitalized patients	764	866	865
Patients with at least one HAI	47	40	66
Prevalence of infected patients (95% CI*)	6.2 (4.8–8.6)	4.6 (1.4–7.8)	7.6 (5.9–9.6)
Overall number of HAIs (%)	54	40	75
Prevalence of HAIs (%)	7.1	4.6	8.7

*95% CI: 95% confidence interval.

Table 2. Prevalence (%) of patients with health care-associated infection by unit/department.

Clinical department	Survey I (N = 764) Patients (%)	Survey II (N = 866) Patients (%)	Survey III (N = 865) Patients (%)
Medicine internal	16 (4.1)	12 (3.2)	36 (6.2)
Surgery	15 (9.3)	10 (4.1)	11 (6.5)
Urological	5 (21.0)	6 (25.0)	5 (22.7)
General	9 (9.0)	0 -	5 (4.2)
Other	1 (2.6)	4 (7.5)	1 (3.6)
Intensive care unit	2 (16.7)	11 (8.0)	7 (53.8)
Orthopedic	8 (20.0)	6 (12.0)	9 (19.1)
Obstetrics and gynecology	6 (2.2)	1 (3.1)	2 (3.4)
Total	47 (6.2)	40 (4.6)	6 (7.6)

Table 3. Prevalence of health care-associated infection (HAI) according to the site of infection.

Major site of infection	Survey I HAI (%)	Survey II HAI (%)	Survey III HAI (%)	P
Urinary tract	10 (1.3)	18(2.1)	25 (2.9)	0.021
Bloodstream	3 (0.4)	1 (0.1)	3 (0.3)	0.783
Pneumonia	6 (0.8)	5 (0.6)	19 (2.2)	0.069
Surgical site	18 (2.4)	7 (0.8)	13 (1.5)	0.068
Skin and soft tissue	11 (1.4)	6 (0.7)	9 (1.0)	0.345
Other	6 (0.7)	3 (0.3)	6 (0.7)	0.779
Total	54 (7.1)	40 (4.6)	75 (8.7)	0.003

Table 4. Intrinsic and extrinsic risk factors for health care-associated infection: univariate logistic regression analysis.

Variables	2003		2005		2009	
	Infected patients N (%)	OR[*] (95% CI)[†]	Infected patients N (%)	OR (95% CI)	Infected patients N (%)	OR (95% CI)
Age ≥65 years	23 (9.2)	2.20 (1.20–4.05)	21 (6.4)	1.89 (0.99–3.55)	33 (11.6)	2.23 (1.37–3.63)
Sex (Male)	22 (6.6)	0.80 (0.44–1.44)	21 (5.4)	0.73 (0.39–1.39)	37 (9.2)	0.78 (0.48–1.26)
Hospital unit		2.23 (1.23–4.04)		0.98 (0.51–1.87)		1.58 (0.97–2.57)
Internal medicine	21 (4.4)		24 (4.7)		36 (6.5)	
Surgery	26 (9.2)		16 (4.6)		30 (9.5)	
Hospitalization in an ICU[‡]	7 (21.9)	3.71 (1.69–8.17)	11 (8.0)	2.09 (1.02–4.29)	18 (27.3)	1.51 (1.02–2.24)
Hospital stay (days): ≥8	35 (10.8)	3.49 (1.84–6.64)	31 (7.7)	4.24 (1.99–9.01)	53 (12.8)	4.94 (2.71–9.00)
Surgical interventions[§]	19 (14.8)	3.43 (1.84–6.38)	12 (7.2)	1.86 (0.92–3.73)	23 (15.6)	2.99 (1.77–5.05)
Intravascular devices	35 (10,0)	3.74 (1.91–7.33)	25 (8.1)	3.21 (1.67–6.19)	47 (10.6)	2.35 (1.39–3.99)
Urinary catheter	19 (18.8)	5.30 (2.82–9.96)	17 (10.6)	2.41 (1.47–3.96)	32 (18.9)	5.29 (3.18–8.79)
Antibiotic use	44 (11.3)	15.80 (4.86–51.33)	39 (14.6)	101.67 (13.89–744.27)	55 (16.6)	10.32 (5.34–19.42)

[*]OR: odds ratio, value according to univariate logistic regression analysis; [†]95% CI: 95% confidence interval; [‡]ICU: intensive care unit; [§]underwent previous surgical procedure (in the 30 days before onset of infection or the 30 days before the survey day).

age, intravascular catheters, urinary catheters, longer hospital stay from admission to the date of the surveys, hospitalization in an ICU, and surgical interventions and antibiotic use were associated with HAIs in all three studies.

According to multivariate regression analysis, a hospitalization equal to or longer than 8 days from admission to the date of the surveys and the use of urinary catheters were independent risk factors for HAI in the first and the second study. In addition to these factors, older age was an independent risk factor in the third study (Table 5).

In total, microbiological examination was conducted in 71.4% cases of HAI, 87.0% (47/54) in the first study, 62.5% (25/40) in the second, and 73.3% (55/75) in the third. The most frequently isolated bacteria are shown in the Figure. The increase of gram-negative rods is noted. The number of patients receiving treatment with at least one antibiotic agent on the day of the study was 330 (45.8% of the total) in the first study, 268 (30.9% of the total) in the second, and 324 (37.5% of the total) in the third.

4. Discussion

Prevalence surveys of HAIs have been widely used both in national and local settings. Over time, more comprehensive data have been obtained from repeated prevalence surveys. However, when prevalence surveys are conducted, they should be performed with standardized methodology (18). Despite the long period that elapsed between our studies, we assume that the prevalence rates can be clearly compared because the same infection control staff conducted all studies using the same definitions of HAI, and the tests were carried out in the same laboratory for microbiological confirmation of infections.

The overall prevalence rates of HAI in our study were 7.1%, 4.6%, and 8.7% in the first, second, and third study, respectively. These rates were lower than the rates of studies carried out in university hospitals in neighboring countries (15,22) and in other developing countries (14,23) but higher than the rates in most developed countries. Studies conducted in western European countries showed that the prevalence of HAI in hospitals was between 3.5% and 8.5% (9–13,24). Ten annual prevalence surveys were conducted in a 900-bed tertiary-care hospital in the USA; however, the prevalence of patients with HAIs showed no significant increase during the 10-year period, although the rate of bloodstream infection significantly increased (25).

Although surgical interventions are still an important risk factor for HAI (26), our study shows that the prevalence of SSIs nonsignificantly decreased over time, while the prevalence of UTIs significantly increased. The national recommendation for prevention of SSI, which includes antibiotic prophylaxis, published at the beginning of 2005, probably influenced this decreasing trend. Similar results were also obtained for the whole of Serbia. Specifically, SSIs were the most common type in the first national study conducted in 1999, making up 34% of all HAIs, but came in second position in the second and third national studies (accounting for 24% and 23% of all HAIs, respectively) after UTIs (17). SSIs are the most frequent type of infection in hospitals in developing countries (27), while UTIs are the most frequent in developed European countries and in the United States (28).

It is well known that improvements in the timing of initial antibiotic administration, appropriate choice of antibiotic agents, and short durations of antibiotic administration are inversely related to the risk of SSI (29). Therefore, there is an urgent need to organize the infection control measures for UTI and pneumonia. Specific guidelines for these infections, which are crucial at the national level and

Table 5. Risk factors for health care-associated infection: multivariate logistic regression analysis.

	Survey I (N = 764)	Survey II (N = 866)	Survey III (N = 865)
Variable		P*	
Age ≥65 years	NS	NS	≤0.05
Hospital stay (days): ≥8	≤0.001	≤0.05	≤0.001
Surgical interventions†	≤0.05	NS	NS
Urinary catheter	≤0.01	NS	≤0.05
Antibiotic use	≤0.01	≤0.001	≤0.001

P: probability value according to multivariate logistic regression analysis (NS: not significant; P ≤ 0.05; P ≤ 0.01; P ≤ 0.001);
†underwent previous surgical procedure (in the 30 days before onset of infection or the 30 days before the survey day).

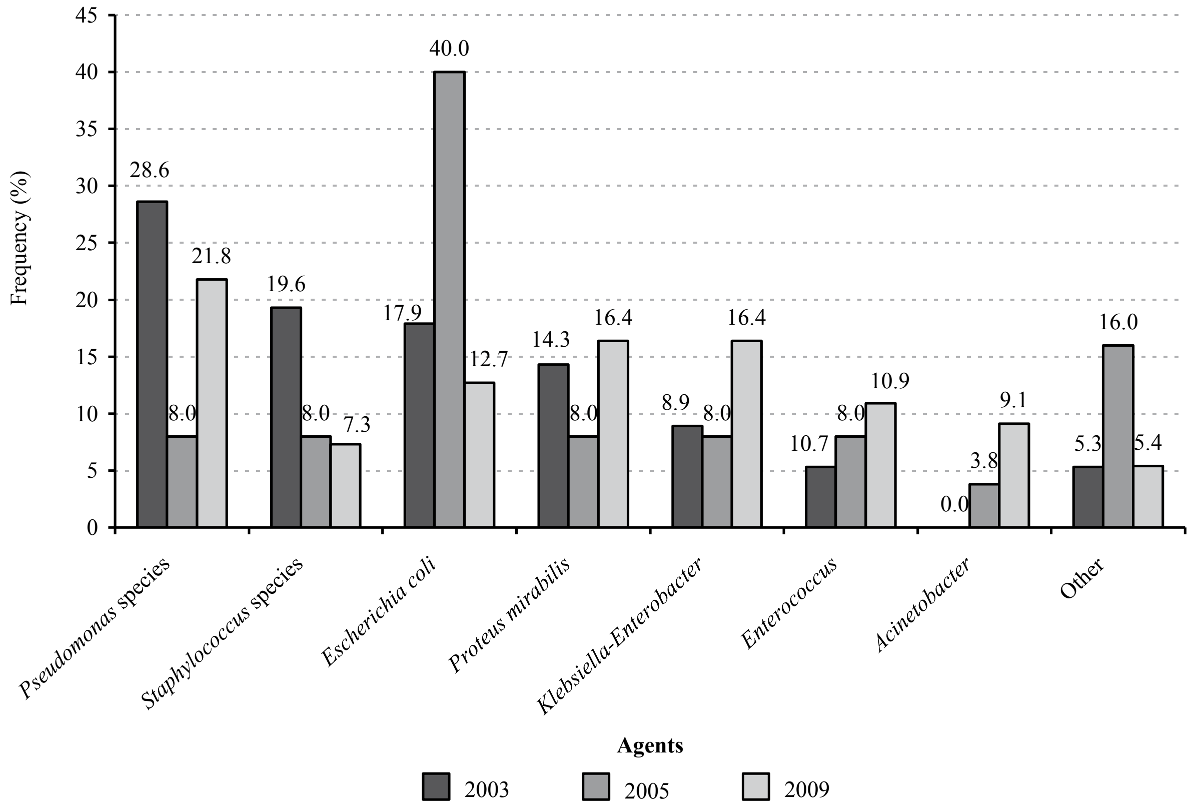

Figure. Three surveys of nosocomial infections prevalence at the Clinical Center in Kragujevac: frequency of the isolated microbial agents.

in accordance with international guidelines, should also be adapted in our hospital. The higher prevalence of SSIs, noted in our study more than in some other studies (9–13,24,25), was frequently linked to peripheral intravenous catheters. Namely, the majority of all intravascular devices, which were primary risk factors for HAI, were peripheral vascular catheters. Although the inoculum amount was small, when infusate was administered for a long period the bacteria could proliferate and cause infections (30). In addition, a urinary catheter was the main risk factor for HAI in all three surveys and, according to the multivariate logistic regression, the presence of a catheter was an independent risk factor in the first and third surveys. Urinary catheters are the most important risk factors for hospital UTI. Urinary catheterization for a period longer than 6 days increased the risk of acquiring catheter-related UTI and, by 30 days of indwelling, infection was almost universal (31). Accordingly, the most important preventive strategies were restricted exposure, short residence time, intermittent catheterization, and the use of aseptic techniques and infection control measures during catheter interventions.

The prevalence of HAIs in our studies was higher in the ICU than in other wards, especially in 2009. A stay in an ICU as one of the factors contributing to infection during hospitalization was confirmed in many studies (12–15,22,23). HAI prevalence in an ICU was 5 to 10 times higher than in other hospital units. This might be due to the characteristics of patients hospitalized in ICUs and the high exposure rates of ICU patients to invasive procedures. The Extended Prevalence of Infection in Intensive Care (EPIC II) study, conducted in 2007 at 1265 ICUs in 75 countries, showed that 51% of all patients hospitalized were infected on the day of the study (32). A significant relationship between the time spent in the ICU prior to the study day and the development of infection was noted. According to our results, patients who had been in the hospital longer than 8 days at the time of the survey had an increased risk of nosocomial infection. It is well known that a prolonged hospital stay can expose patients to hospital bacteria and increase the risk of infection. However, the HAI itself prolonged the duration of hospitalization.

Antibiotic use is more the consequence of HAI treatment than a risk factor for their development. Antibiotic use in all of our three studies was higher than in a study conducted in four European countries in which about one-third of patients were being treated with antimicrobials at the time of the study (11). Moreover, only a few patients with HAIs were without antibiotherapy. As a result, the confidence interval for antibiotic use was substantial, especially in the second survey. It has already been determined that Serbia is ranked fifth out of 12 newly independent countries and southeastern European countries in terms of overall use of antibiotics, after Turkey, Montenegro, Tajikistan, and Kosovo (33). We believe that further analyses of antibiotic use and its effect on the development of resistant strains are needed in our hospital.

According to the definitions of HAI, bacteriological confirmation is needed for many types of infections. However, some HAIs, such as SSIs and pneumonia, can be diagnosed according to their clinical symptoms and signs. For this reason, the number of bacteriologically confirmed HAIs is always less than the total number of infections. The episodes of HAIs documented by microbiological results were similar to those published in other European surveys (9,13,15). The most common isolated organisms in our surveys were gram-negative rods, similar to those in published results in developing countries (15,22,23).

The main limitation of our investigation is the type of study design as a point prevalence survey. In a prevalence study, a cross-sectional approach is used, and it is more likely to locate and record HAIs of longer duration and patients with more comorbidities. In addition, the quality of data depends on the availability of information in patient records, nursing records, and prescription records. The availability of bacteriological results also influences the quality and accuracy of HAI diagnosis. However, well-documented protocol, trained data collectors, and validation of the collected data could decrease potential bias. In our study, one trained infection control doctor (MI) and the same infection control nurses conducted all three studies, which was a major advantage of our investigation. In addition, in all studies, the same methodology and the same definition of HAI were used.

In conclusion, the considerable burden of HAIs in our university hospital was described. Repeated prevalence surveys of HAIs, compared over a period of time, can lead to the implementation of specific infection control policies.

Acknowledgment

This study was conducted as part of project No. 175046, funded by the Ministry of Education, Science, and Technological Development, Republic of Serbia, 2011–2014.

References

1. World Health Organization. Report on the Burden of Endemic Health Care-Associated Infection Worldwide. Geneva, Switzerland: WHO; 2011.
2. Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, Donaldson L, Pittet D. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet 2011; 377: 228-241.
3. Marchetti A, Rossiter R. Economic burden of healthcare-associated infection in US acute care hospitals: societal perspective. J Med Econ 2013; 16: 1399-1404.
4. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988; 16: 128-140.
5. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008; 36: 309-332.
6. Centers for Disease Prevention and Control. CDC/NHSN Surveillance for Specific Types of Infections. Atlanta, GA, USA: CDC; 2016.
7. Ministry of Health, Republic of Serbia. Rulebook on Prevention, Early Detection and Suppression of Hospital Infections. Official Gazette No. 101/13. Belgrade, Serbia: Ministry of Health, Republic of Serbia; 2013.
8. Mayon-White RT, Ducel G, Kereselidze T, Tikomirov E. An international survey of the prevalence of hospital-acquired infection. J Hosp Infect 1988; 11 (Suppl. A): 43-48.
9. Eriksen HM, Iversen BG, Aavitsland P. Prevalence of nosocomial infections in hospitals in Norway, 2002 and 2003. Hosp Infect 2005; 60: 40-45.
10. Gordts B, Vrijens F, Hulstaert F, Devriese S, Van de Sande S. The 2007 Belgian national prevalence survey for hospital-acquired infections. J Hosp Infect 2010; 75: 163-167.
11. Sax H, Uçkay I, Balmelli C, Bernasconi E, Boubaker K, Mühlemann K, Ruef C, Troillet N, Widmer A, Zanetti G et al. Overall burden of healthcare-associated infections among surgical patients. Results of a national study. Ann Surg 2011; 253: 365-370.
12. Smyth ET, McIlvenny G, Enstone JE, Emmerson AM, Humphreys H, Fitzpatrick F, Davies E, Newcombe RG, Spencer RC; Hospital Infection Society Prevalence Survey Steering Group. Four country healthcare associated infection prevalence survey 2006: overview of the results. J Hosp Infect 2008; 69: 230-248.
13. Lyytikäinen O, Kanerva M, Agthe N, Möttönen T, Ruutu P; Finnish Prevalence Survey Study Group. Healthcare-associated infections in Finnish acute care hospitals: a national prevalence survey, 2005. J Hosp Infect 2008; 69: 288-294.
14. Ider BE, Clements A, Adams J, Whitby M, Muugolog T. Prevalence of hospital-acquired infections and antibiotic use in two tertiary Mongolian hospitals. J Hosp Infect 2010; 75: 214-219.

15. Faria S, Sodano L, Gjata A, Dauri M, Sabato AF, Bilaj A, Mertiraj O, Llazo E, Kodra Y, Schinaia N et al. The first prevalence survey of nosocomial infections in the University Hospital Centre 'Mother Teresa' of Tirana, Albania. J Hosp Infect 2007; 65: 244-250.

16. Ćosić G, Đekić J, Petrović M, Krtinić G, Karać T, Jandrić-Kočić J, Marković-Denić L. The most frequent hospital-acquired infections related to medical interventions in hospitals in Vojvodina province. Arch Bio Sci 2014; 66: 523-535.

17. Ministry of Health of the Republic of Serbia. Third National Prevalence Study of Hospital Infections. Belgrade, Serbia: Ministry of Health of the Republic of Serbia; 2012.

18. Humphreys H, Smyth ET. Prevalence surveys of healthcare-associated infections: what do they tell us, if anything? Clin Microbiol Infect 2006; 12: 2-4.

19. Zhang Y, Zhang J, Wei D, Yang Z, Wang Y, Yao Z. Annual surveys for point-prevalence of healthcare-associated infections in a tertiary hospital in Beijing, China. BMC Infect Dis 2016; 16: 161.

20. Hajdu A, Eriksen H, Sorknes N, Hauge S, Loewer H, Iversen H, Aavitsland P. Evaluation of the national surveillance system for point-prevalence of healthcare-associated infections in hospitals and in long-term care facilities for elderly in Norway, 2002-2008. BMC Public Health 2011; 11: 923.

21. Drndarević D, Janković S. Hospital infections. Definitions. Textbook 1. 1st ed. Belgrade, Serbia: Srboštampa, 1998.

22. Metintas S, Akgun Y, Durmaz G, Kalyoncu C. Prevalence and characteristics of nosocomial infections in a Turkish university hospital. Am J Infect Control 2004; 32: 409-413.

23. Kallel H, Bahoul M, Ksibi H, Dammak H, Chelly H, Hamida CB, Chaari A, Rekik N, Bouaziz M. Prevalence of hospital-acquired infection in a Tunisian hospital. J Hosp Infect 2005; 59: 343-347.

24. Klavs I, Bufon Luznik T, Skerl M, Grgic-Vitek M, Lejko Zupanc T, Dolinsek M, Prodan V, Vegnuti M, Kraigher A, Arnez Z et al. Prevalence of and risk factors for hospital-acquired infections in Slovenia-results of the first national survey, 2001. J Hosp Infect 2003; 54: 149-157.

25. Weinstein JW, Mazon D, Pantelick E, Reagan-Cirincione P, Dembry LM, Hierholzer WJ Jr. A decade of prevalence surveys in a tertiary-care center: trends in nosocomial infection rates, device utilization, and patient acuity. Infect Control Hosp Epidemiol 1999; 20: 543-548.

26. Mihaljević L, Bedenić B, Mihaljević S, Majerović M, Petrović P, Vasilj I. Microbiological surveillance of the surgical intensive care unit in Zagreb--a pivot for guideline-based therapy of severe sepsis. Coll Antropol 2007; 31: 1093-1097.

27. Allegranzi B, Nejad SB, Combescure C, Graafmans W, Homa Attar H, Donaldson L, Pittet D. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet 2011; 377: 228-241.

28. World Health Organization. Report of the Burden of Endemic Health-Care Associated Infections Worldwide. A Systematic Review of the Literature. Geneva, Switzerland: WHO; 2011.

29. Nichols RL. Preventing surgical site infections: a surgeon's perspective. Emerg Infect Dis 2001; 7: 220-224.

30. Lee L, Liao F, Lee C, Huang H, Fang T. Soft tissue infections related to peripheral intravenous catheters in hospitalised patients: a case-control study. J Hosp Infect 2010; 76: 124-129.

31. Maki DG, Tambyah PA. Engineering out the risk for infection with urinary catheters. Emerg Infect Dis 2001; 7: 342-347.

32. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA-J Am Med Assoc 2009; 302: 2323-2329.

33. Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, Korinteli I, Raka L, Kambaralieva B, Cizmovic L et al. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis 2014; 14: 381-387.