A 5- Year Surveillance of Nosocomial Infections in a University Hospital: A Retrospective Analysis

Ilknur Erdem (✉ ilknurerdem@hotmail.com)

Namik Kemal University: Tekirdag Namik Kemal Universitesi

Ilker Yildirim

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Birol Safak

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Ritvan Karaali

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Berna Erdal

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Enes Ardic

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Mustafa Dogan

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

M Enes Kardan

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Caglar Kavak

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Kubra Sahin Karadil

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Emre Yildiz

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Birol Topcu

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Nuri Kiraz

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Cavidan Arar

Tekirdag Namik Kemal University: Tekirdag Namik Kemal Universitesi

Research

Keywords: Nosocomial infection, surveillance, antimicrobial resistance

Posted Date: April 16th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-415656/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

OBJECTIVE: ‘Nosocomial infections’ or ‘healthcare associated infections’ are a significant public health problem around the world. This study aimed to assess the rate of culture confirmed nosocomial infections (NIs), frequency of nosocomial pathogens and the antimicrobial resistance patterns of bacterial isolates in a University Hospital.

METHODS: A retrospective evaluation of NIs in a tertiary hospital, between the years 2015 and 2019 in Tekirdag, Turkey.

RESULTS : During the five years, the overall incidence rates (NI/100) and incidence densities (NI/1000 days of stay) of NIs were 2.04% (range 1.76-2.41/100) and 3.50/1000 patients-days (range 2.85-4.64/1000), respectively. 57.4 % of the infections were originated from the Intensive Care Units. The most common NIs according to the primary sites were bloodstream infections (55.3 %) and, pneumonia (20.4%). 67.5% of the isolated microorganisms as nosocomial agents were Gram negative bacteria, 24.9% of Gram positive bacteria and 7.6 % of candida. The most frequently isolated causative agents were *Escherichia coli* (16.7%) and *Pseudomonas aeruginosa* (15.7%). The rate of extended spectrum beta-lactamase production among *E. coli* isolates was 51.1%. Carbapenem resistance was 29.8% among isolates of *Pseudomonas aeruginosa*; 95.1% among isolates of *Acinetobacter baumannii*, 18.2% among isolates of *Klebsiella pneumoniae*. Colistin resistance was 2.4% among isolates of *Acinetobacter baumannii*. Vancomycin resistance was 5.3% among isolates of *Enterococci*.

CONCLUSION: Our study results demonstrates the microorganisms of isolated from Intensive Care Units demonstrates high level resistance to many antimicrobial agents. The rising in incidence of multidrug-resistant microorganisms indicate that more interventions are urgently needed to reduce NIs in our ICUs.

1. Introduction

Health care-related infections (HCAIs), previously referred to as nosocomial infections (NIs), are infections acquired by patients in health care settings. It usually occurs 48–72 hours after the patient's hospitalization, or within 10 days after discharge. Many studies have shown that the most common events that affect hospitalized patients are drug side effects, nosocomial infection, and surgical complications. The US Center for Disease Control and Prevention reported that approximately 1.7 million hospitalized patients annually acquire HCAI or NIs while being treated due to other health problems, and that more than 98 000 of these patients (approximately one in 17) die due to NIs. NIs are reported to be one of the 10 most important causes of death in the United States. However, the World Health Organization reports that NIs usually attract public attention when an outbreak occurs [1], [2], [3], [4], [5].

NIs have a dynamic process that varies in each center and over time. In many European multi-center studies, 4.6–9.3% of hospitalized patients have been reported to develop nosocomial infections. In another study, the frequency of NIs was 5.9% (country range: 2.9–10.0%). This rate was 7% in tertiary hospitals [2], [6], [7], [8]. NIs are most commonly associated with invasive medical devices or surgical

procedures. Intensive care unit (ICU) patients have a higher risk of developing nosocomial infections compared to other hospitalized patients.

Despite the early diagnosis of infections and improvements in hospital conditions, NIs continue to pose a significant risk of morbidity and mortality. In addition to increased morbidity and mortality, length of hospital stay, antibiotic use, the risk of developing multiple antibiotic resistance of pathogens and maintenance costs increase. Lower respiratory tract and bloodstream infections are the most fatal. Prevention of NIs is the responsibility of healthcare institutions and their employees. Everyone should work collaboratively to reduce the risk of infection for patients and staff. Surveillance of NIs is an important part of infection control and has been widely accepted worldwide as a primary step towards prevention. Local surveillance data are also important to guide empirical treatment and to ensure optimal therapy. Therefore, each center should determine its own distribution of NIs, causative agents and their antibiotic resistance status to guide in the development of infection control policies. In this study, we aimed to describe the incidence of NIs, distribution of infections, infectious agents and antibiotic resistance status of these agents in our hospital during the years 2015 and 2019.

2. Material-methods

2.1 Data collection

This study was a retrospective analysis of NIs of hospitalized patients at the Namik Kemal University Hospital, a tertiary care hospital with 430 beds, between the years 2015 and 2019. The intensive care units had 80 beds. Patient data were obtained by laboratory and patient-based active surveillance method. Follow-up, registration and examination of NIs were carried out by infection control team. The study included all patients hospitalized for more than 48 hours. The overall patient NI rate and the incidence density were determined. All NIs were culture-confirmed.

The bacterial identification was performed by the automatized VITEK 2 (bioMérieux, France) in addition to conventional microbiological methods. The antibiotic resistance patterns of isolated microorganisms were determined by the Kirby-Bauer disc diffusion method and automatized VITEK 2 system. Presence of ESBL positivity was detected using the double disk synergy test (DDST). Variations in the resistance rate during the 5-year period were analysed by the chi-square test for trends. *P*-value < 0.05 was considered significant.

2.2 Definition

NI was defined as a new infection that occurred more than 48 hours after hospital admission. The patients were assessed for NIs by using the clinical criteria of the Centers for Disease Control and Prevention [3],[4]. The incidence rates of NIs was calculated by dividing the total number of patients with NIs to total number of patients ($\times 100$) during the observed period. The incidence density of NIs was calculated by dividing the total number of NIs recorded in the observed period to total number of patient days ($\times 1000$).

Multidrug resistant (MDR) gram-negative bacteria were defined as gram-negative bacteria resistant to at least one agent in each of three or more categories of antimicrobial agents including β -lactam/ β -lactamase inhibitor combinations (piperacillin/ tazobactam), extended spectrum cephalosporins (ceftriaxone, ceftazidime, cefepime), carbapenems (imipenem / meropenem), monobactams, aminoglycosides (gentamicin, amikacin) and/or fluoroquinolones. In Gram-positive bacteria, vancomycin resistance for *Enterococcus faecium* and methicillin resistance for *Staphylococcus aureus* have been defined as MDR.

3. Results

During the study period, 1050 NI episodes were detected in 705 patients aged < 1-100 years old. 382 (54.2 %) of patients were male. The overall incidence rates (NI/100) and incidence densities (NI/1000 days of stay) of NIs were 2.04% (range 1.76–2.41) and 3.50/1,000 patient-day (range 2.85–4.64/1000), respectively. 603 (57.4 %) of the infections were originated from the Intensive Care Units. The distribution of infection rate and density by year was given in Table 1. NIs according to the primary sites were bloodstream infections (BSIs) (55.3%), pneumonia (20.4%), surgical site infections (SSIs) (13.7 %) and urinary tract infections (UTIs) (9.5%). BSIs were the most common hospital infections, followed by ventilator-associated pneumonia (VAP) in 2015, 2017, 2018 and 2019, and SSIs in 2016. 19.5% of BSIs are secondary BSIs. 732 (67.5%) of the isolated microorganisms as nosocomial agents were Gram negative bacteria, 271 (24.9%) of Gram positive bacteria and 82 (7.6%) of candida. 35.3% of the candida were *Candida albicans*. The most frequently isolated microorganisms were *Escherichia coli* (*E.coli*) (16.7%) followed by *Pseudomonas aeruginosa* (*Paeruginosa*) (15.7%), *Acinetobacter baumannii* (*A.baumannii*) (11.3%), *Klebsiella pneumoniae* (*K.pneumoniae*) (11.1%) and coagulase negative *Staphylococci* (CoNS) (10.0%). The most frequently isolated microorganisms were CoNS and *E. coli* in bloodstream infections; *E.coli* and *Paeruginosa* in urinary tract infections; *E.coli* in surgical site infections; *Paeruginosa* and *A. baumannii* in VAP respectively. The distribution of most commonly isolated microorganisms according to the type of infection was given in Table 2. The prevalence of extended spectrum beta-lactamase (ESBL)-producing *K.pneumoniae* was 60.3% and *E.coli* was found as 51.1%. In this study, all ESBL-producing *E.coli* isolates were sensitive (100%) to meropenem and *K. pneumoniae* showed 81.8% sensitive to meropenem. Carbapenem resistance was 29.8% among isolates of *Paeruginosa*; 95.1% among isolates of *A.baumannii*. Colistin resistance was 2.4% among isolates of *A.baumannii*; 1.2% among isolates of *Paeruginosa*, 1.7% among isolates of *K.pneumoniae*. Methicillin resistance was 31.7% and 83.4% among isolates of *Staphylococcus aureus* and CoNS respectively. No isolate was found to be resistant to vancomycin and linezolid among *Staphylococci*. Vancomycin resistance was 5.3% among isolates of *Enterococci*. The prevalence of nosocomial infections caused by MDR bacteria was 45.66 %. The distribution of the resistance profiles of nosocomial pathogens by year was given in Table 3. It is remarkable that NIs caused by colistin resistant *P. aeruginosa*, *A. baumannii*, *K. pneumoniae* have been detected in the last two years. In addition, the increasing rate of carbapenem resistant *K. pneumoniae* and vancomycin resistance *Enterococcus* (VRE) has also emerged. Carbapenem resistant *A.baumannii* isolates showed high resistance levels and the same change trends with time. *P*

aeruginosa resistance to carbapenem decreased slightly from 53–27% in the last two years, however this trend was not significant statistically ($p > 0.05$). There was no statistically significant difference between ESBL-producing *K.pneumoniae* numbers in comparisons of five years ($P > 0.05$). There was a statistically significant decrease in 2017 in EBSL- producing *E coli* ($P < 0.05$).

Table 1
The distribution of nosocomial infection rate and density by year

	2015	2016	2017	2018	2019	Total
NI rate	2.41	2.35	1.76	2.13	1.86	2.04
NI density	4.42	4.64	2.85	3.55	3.10	3.50
* Total number of nosocomial infections: 1050						
** Total number of inpatients: 51342						
*** total patient days: 299540						

Table 2
The distribution of the isolated microorganisms according to the type of infection

Organism type	BSI No (%)	VAP No (%)	SSI No (%)	UTI No (%)	Other No (%)	Total No (%)
Gram negative bacteria	349 32.2%	190 17.6 %	100 9.2%	83 7.6%	10 0.9%	732 67.5%
<i>E coli</i>	87 8.0%	20 1.8%	40 3.7%	33 3.0%	2 0.2%	182 16.7%
<i>Paeruginosa</i>	65 6.0%	66 6.1%	18 1.6%	19 1.7%	3 0.3%	171 15.7%
<i>Pseudomonas spp</i>	2 0.2%	1 0.1%	1 0.1%	--	--	4 0.4%
<i>A baumannii</i>	55 5.0%	51 4.7%	9 0.8%	5 0.5%	3 0.3%	123 11.3%
<i>K.pneumoniae</i>	70 6.5%	21 1.9%	11 1.0%	18 1.6%	1 0.1%	121 11.1%
<i>Enterobacter cloaceae</i>	14 1.3%	4 0.4%	8 0.7%	--	--	26 2.4%
<i>Enterobacter aerogenes</i>	5 0.5%	7 0.6%	1 0.1%	--	--	13 1.2%
<i>Enterobacter spp.</i>	3 0.3%	1 0.1%	1 0.1%	1 0.1%	--	6 0.6%
<i>Stenotrophomonas maltophilia</i>	15 1.4%	7 0.6%	2 0.2%	1 0.1%	--	25 2.3%
<i>Klebsiella oxytoca</i>	8 0.7%	-	--	-	--	8 0.7%
<i>Proteus mirabilis</i>	7 0.6%	2 0.2%	4 0.4%	4 0.4%	--	17 1.6%
<i>Serratia marcescens</i>	6 0.5%	4 0.4%	3 0.3%	1 0.1%	1 0.1%	15 1.4%
<i>Burkholderia cepacia</i>	2 0.2%	2 0.2%	1 0.1%	1 0.1%	--	6 0.6%
<i>Achromobacter denitrificans</i>	--	1 0.1%	--	--	--	1 0.1%
<i>Aeromonas sobria</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Chryseobacterium indologenes</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Citrobacter koseri</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Delftia acidovorans</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Moraxella catarrhalis</i>	--	1 0.1%	--	--	--	1 0.1%
<i>Morganella spp.</i>	1 0.1%	--	--	--	--	1 0.1%

Abbreviation: BSI, bloodstream infection; VAP, ventilator- associated pneumonia; SSI, surgical site infection; UTI, urinary tract infection.

Organism type	BSI No (%)	VAP No (%)	SSI No (%)	UTI No (%)	Other No (%)	Total No (%)
<i>Ochrobactrum anthropi</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Proteus vulgaris</i>	--	--	1 0.1%	--	--	1 0.1%
<i>Ralstonia pickettii</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Raoultella planticola</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Sfingomonas paucimobilus</i>	--	1 0.1%	--	--	--	1 0.1%
Nonfermentative gram negative bacilli	2 0.2%	2 0.2%	--	--	--	4 0.4%
Gram positive bacteria	184 16.9%	29 2.7%	48 4.4%	8 0.8%	2 0.2%	271 24.9%
Coagulase negative staphylococci	97 8.9%	--	12 1.1%	--	--	109 10.0%
<i>S.aureus</i>	23 2.1%	23 2.1%	16 1.5%	--	1 0.1%	63 5.8%
<i>E.faecalis</i>	31 2.9%	--	9 0.8%	1 0.1%	--	41 3.8%
<i>E faecium</i>	29 2.6%	1 0.1%	4 0.4%	1 0.1%	1 0.1%	36 3.3%
<i>E gallinorum</i>	1 0.1%	--	--	--	--	1 0.1%
<i>Enterococcus spp</i>	3 0.3%	1 0.1%	6 0.6%	6 0.6%	--	16 1.5%
<i>Streptococcus pneumoniae</i>	--	3 0.3%	--	--	--	3 0.3%
<i>Corynebacterium spp.</i>	--	1 0.1%	--	--	--	1 0.1%
<i>Actinomyces</i>	--	--	1 0.1%	--	--	1 0.1%
Yeast	67 6.2%	2 0.2 %	--	13 1.2%	--	82 7.6%
<i>Candida</i>						

Abbreviation: BSI, bloodstream infection; VAP, ventilator- associated pneumonia; SSI, surgical site infection; UTI, urinary tract infection.

Organism type	BSI No (%)	VAP No (%)	SSI No (%)	UTI No (%)	Other No (%)	Total No (%)
<i>C.albicans</i>	25 2.3%	--	--	4 0.4%	--	29 2.7%
<i>C parapsilosis</i>	24 2.2%	--	--	1 0.1%	--	25 2.3%
<i>C glabrata</i>	5 0.5%	1 0.1%	--	--	--	6 0.6%
<i>C guillemondii</i>	2 0.2%	--	--	--	--	2 0.2%
<i>C krusei</i>	3 0.3%	--	--	--	--	3 0.3%
<i>C tropicalis</i>	1 0.1%	1 0.1%	--	2 0.2%	--	4 0.4%
Nonalbicans <i>candida spp</i>	7 0.6%	--	--	6 0.5%	--	13 1.2%
Total	600 55.3%	221 20.4%	148 13.7%	104 9.5%	12 1.1%	1085 100%
Abbreviation: BSI, bloodstream infection; VAP, ventilator- associated pneumonia; SSI, surgical site infection; UTI, urinary tract infection.						

Table 3

The distribution of resistance profiles of most commonly isolated microorganisms by year (%)

	2015 N (%)	2016 N (%)	2017 N (%)	2018 N (%)	2019 N (%)	Total N (%)
Extended-spectrum beta lactamase positive <i>E.coli</i>	10 50.0	17 55.0	18 30.0	30 70.0	18 64.0	93 51.1
Extended-spectrum beta lactamase positive <i>K. pneumoniae</i>	9 60.0	8 50.0	14 50.0	20 67.0	22 69.0	73 60.3
Carbapenem resistant <i>A.baumannii</i>	9 82.0	23 82.0	24 92.0	33 94.0	28 93.0	117 95.1
Colistin resistant <i>A.baumannii</i>	0 0.0	0 0.0	0 0.0	2 5.7	1 3.2	3 2.4
Carbapenem resistant <i>Paeruginosa</i>	10 53.0	8 42.0	9 32.0	13 23.0	11 27.0	51 29.8
Colistin resistant <i>Paeruginosa</i>	0 0.0	0 0.0	0 0.0	1 1.8	1 2.5	2 1.2
Carbapenem resistant <i>K.pneumoniae</i>	0 0.0	1 6.2	8 29.0	7 23.0	6 20.0	22 18.2
Colistin resistant <i>K.pneumoniae</i>	0 0.0	0 0.0	0 0.0	1 2.8	1 4.0	2 1.7
Methicillin resistant <i>S.aureus</i>	1 25.0	1 20.0	7 37.0	7 24.0	4 40.0	20 31.7
Vancomycin resistant <i>Enterococcus</i>	0 0.0	0 0.0	1 5.9	2 12.5	2 9.5	5 5.3

4. Discussion

NI prevalence in the European Union / European Economic Area was 5.9% (country range: 2.9–10.0%) [7]. The rate of NIs in our country is reported to be between 1.3–16.6% in the various studies [9]. According to the data of our hospital, culture confirmed NI rate was found to be 2.04%. NI density in our hospital was 3.50 / 1000 patient days. There are also studies with same values to our study results. In a study, NI rate was 1.6, NI density was 3.6 [10]. This rate is lower than the reported many studies in the world. The possible cause of this situation can be explained by the fact that the NIs in our hospital are predominantly originated by ICUs.

Wenzel et al. [11] reported that although 5–10% of hospitalized patients were followed in the ICU, 25% of NIs were seen in this unit. In our study, 57.4% of NIs were originated by Intensive Care Units. 18.6% of the beds in our hospital are intensive care beds. The rate of NIs was higher than other services in our hospital too. Because patients in ICUs are with a worse general condition who remain in the hospital for a long time period; and with a more frequent invasive procedures, more resistant bacterial infections and more frequent use of antibiotics.

The most common NIs are urinary tract infections (UTIs), pneumonia, bloodstream infections (BSIs) and surgical site infections (SSIs) [12]. In some studies was reported that respiratory tract infections were the most common type [13, [14], [15]. There are also some studies indicate that SSIs are more common [10]. In our hospital, 53.5 % of NIs were BSIs. While 34% were catheter-related BSIs, 19.5% were secondary BSIs. 20.4% of ventilator-associated pneumonia (VAP) were accompanied by BSIs, 13.7% were SSIs, 9.5% were UTIs. These results indicate that catheter care should be revised in our hospital.

Gram-negative bacteria have been reported as causative agents in approximately half of all NIs. These bacteria predominate in most cases of ventilator-associated pneumonia and urinary tract infections. *Acinetobacter* is the only gram-negative bacillus that increased significantly in incidence as a cause of ventilator-associated pneumonia compared to previous years. In the SENTRY study, *Acinetobacter* species were accounted for 7% of ICU infections in the USA and European countries [16], [17], [18], [19]. Infections caused by non-fermentative Gram negative bacteria have increased compared to previous years in our study.

Microorganisms that cause NIs are often resistant to antimicrobial agents. Unfortunately, the dramatic increase in multidrug-resistant (MDR) microorganisms including *Paeruginosa*, *A.baumannii*, and ESBL-producing or carbapenemase-producing *Enterobacteriaceae*, are being reported as agents of nosocomial infections in recent decades. For example, 50–60% of more than 2 million NIs in the USA are caused by antibiotic-resistant pathogens. The incidence of MDR gram negative bacteria in the ICU is higher compared with other hospital units. Antibiotic use has been identified as an important risk factor in the emergence of antibiotic resistance [20]. In this study, The prevalence of nosocomial infections caused by MDR bacteria was 45.66 %.

MDR microorganism is a serious public health problem in the world. The treatment is difficult, morbidity and mortality are high. Antibiotics used in treatment are limited, patients have longer hospital stay and increased treatment costs. In a European study, one out of every 20 inpatients reported that health-related infections developed and the causative microorganisms (*Klebsiella pneumoniae* and *Acinetobacter* spp.) were generally multiple resistant [6],[8],[21]. In a systematic review of Southeast Asian countries (Brunei, Myanmar, Cambodia, East Timor, Indonesia, Laos, Malaysia, Philippines, Singapore, Thailand and Vietnam), the prevalence of NI was 9.1% and the common microorganisms *Paeruginosa*, *Klebsiella* spp. and *A.baumannii* [22]. The most common causative agent of NIs were Gram negative bacteria in our hospital. The most resistant microorganism in our study was *Acinetobacter* spp. The rate of ESBL-producing *E. coli* and *K. pneumoniae* was high. About 51.1% of *E.coli* and 60.3 % of *K.pneumoniae* isolates were identified as ESBL producers. It is interesting that the susceptibility of *P. aeruginosa* to carbapenems remains high. Carbapenem resistance was 29.8%, 95.1%, 18.2% in *Paeruginosa*, *A.baumannii* and *Klebsiella pneumoniae* isolates, respectively. Especially in *A. baumannii* isolates antibiotic resistance was higher than other isolates. Microorganisms isolated from ICUs showed high resistance to many antimicrobial agents. There was an increase in infections caused by colistin resistant *P. aeruginosa*, *A. baumannii*, *K. pneumoniae* and carbapenem resistant *K. pneumoniae* in the last two years. In addition, the increasing rate of vancomycin resistance *Enterococcus* (VRE) has emerged. Unnecessary antibiotic administration and prolonged intensive care hospitalization may increase the spread of multidrug resistant pathogens. Monitoring of antimicrobial susceptibility, and appropriate antimicrobial use might be effective to prevent in the emergence of antimicrobial resistance in ICUs.

5. Conclusion

In conclusion, this study demonstrates a high rate of antimicrobial resistance to commonly prescribed antibiotics among the microorganisms isolated from the patients with NIs hospitalized in ICUs. Infection control and antibiotic management strategies should be reconsidered in our ICUs. It is clear that if effective measures are not taken in the time, antibiotic resistance will be become alarming and will be a major challenge for years to come.

Declarations

Conflicts of interest:

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Financial Disclosure:

The authors declared that this study has received no financial support.

Ethical approval:

This study was approved by the Ethical Committee of Namik Kemal University, Faculty of Medicine (approval number **2021.86.04.10**).

Authors' contributions

IE, IY made contributions to the study design and lead data acquisition as well as analysis and interpretation of data. IE,IY,BS, BE,MD,CK,CA designed the study and made substantial contributions to analysis and interpretation of data. IE, RK, EA,IY,MEK,EY,KSK took part in data acquisition. All authors read and approved the final manuscript.

References

- [1]. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. *Am J Infect Control*. 1988; 16(3): 128-40.
- [2]. Haque M, Sartelli M, McKimm J, Bakar MA. Health care-associated infections—an overview. *Infect Drug Resist*. 2018;11; 2321–33.
- [3]. Horan T, Andrus M, Dudeck M. 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(5): 309–32.
- [4]. Johnson NB, Hayes LD, Brown K, Hoo EC, Ethier KA. Centers for Disease Control and Prevention (CDC). CDC National Health Report: leading causes of morbidity and mortality and associated behavioral risk and protective factors-United States, 2005-2013. *MMWR Suppl*. 2014;63(4):3–27.
- [5]. World Alliance for Patient Safety [webpage on the Internet]. The Global Patient Safety Challenge 2005–2006 “Clean Care is- Safer Care.” Geneva: WHO Available from: <http://www.who.int/gpsc/en/>. Accessed April 4, 2018.
- [6]. Eriksen HM, Iversen BG, Aavitsland P. Prevalence of nosocomial infections in hospitals in Norway, 2002 and 2003. The French Prevalence Survey Study Group. *J Hosp Infect*. 2005;60(1):40–5.
- [7]. Suentens C, Latour K, Kärki T, et al. the Healthcare-Associated Infections Prevalence Study Group. Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys, 2016 to 2017. *Euro Surveill* 2018; 23(46): doi: 10.2807/1560-7917.ES. 2018.23.46. 1800516.
- [8]. The French Prevalence Survey Study Group. Prevalence of nosocomial infections in France: results of the nation-wide survey in 1996. *J Hosp Infect*. 2000; 46(3):186–93.
- [9]. Vancelik S, Ozden K, Ozkurt Z, Altoparlak U, Aktas E, Savci AB. Hospital Infections in Ataturk University Medical Faculty Hospitals: results of year 2005. *TAF Preventive Medicine Bulletin* 2006; 5(3): 159-65.

- [10]. Scherbaum M, Kösters K, Mürbeth RE, Ngoa UA, Kremsner PG, Lell B, Alabi A. Incidence, pathogens and resistance patterns of nosocomial infections at a rural hospital in Gabon. *BMC Infect Dis* 2014;14:124.
- [11]. Wenzel RP, Thompson RL, Landry SM et al. Hospital-acquired infections in intensive care unit patients: an overview with emphasis on epidemics. *Infect Control* 1983; 4:371-5.
- [12]. Khan HA, Baig FK, Mehboob R. Nosocomial infections: Epidemiology, prevention, control and surveillance. *Asian Pac J Trop Biomed* 2017;7(5): 478–82.
- [13]. Magill SS, Edwards JR, Bamberg W, et al; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014;370:1198-208.
- [14]. Saleem Z, Godman B, Hassali MA, Hashmi FK, Azhar F, Rahman IU. Point prevalence surveys of health-care associated infections: a systematic review. *Pathog Glob Health* 2019;113(4): 191-205.
- [15]. Zhang Y, Zhang J, Wei D, Yang Z, Wang Y, Yao Z. Annual surveys for point-prevalence of healthcare-associated infection in a tertiary hospital in Beijing, China, 2012-2014. *BMC Infect Dis* 2016;16: 161.
- [16]. Mancini A, Verdini D, La Vigna G, Recanatini C, Lombardi FE, Barocchi S. Retrospective analysis of nosocomial infections in an Italian tertiary care hospital. *New Microbiol* 2016;39(3): 197-205.
- [17]. Sader HS, Farrell DJ, Flamm RK, Jones RN. Antimicrobial susceptibility of Gram negative organisms isolated from patients hospitalized in intensive care units in United States and European hospitals (2009-2011). *Diagn Microbiol Infect Dis* 2014; 78:443-8.
- [18]. Tabatabaei SM, Pour FB, Osmani S. Epidemiology of hospital-acquired infections and related antimicrobial resistance patterns in a tertiary care teaching hospital in Zahedan, Southeast Iran. *Int J Infection* 2015; 2(4): e29079.
- [19]. Bhandari P, Thapa G, Pokhrel BM, Bhatta DR, Devkota U. Nosocomial isolates and their drug resistant pattern in ICU patients at National Institute of Neurological and Allied Sciences, Nepal. *Int J Microbiol* 2015; 2015:572163.
- [20]. Bereket W, Hemalatha K, Getenet B, Wondwossen T, Solomon A, Zeynudin A, Kannan S. Update on bacterial nosocomial infections. *Eur Rev Med Pharmacol Sci* 2012; 16:1039-44.
- [21]. Cassini A, Plachouras D, Eckmanns T, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. *PLoS Med* 2016; 13(10):e1002150.
- [22]. Ling ML, Apisarnthanarak A, Madriaga G. The Burden of Healthcare-Associated Infections in Southeast Asia: A Systematic Literature Review and Meta-analysis. *Clin Infect Dis* 2015; 60 (11):1690–9.