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Attitudes Toward Nosocomial Infections Associated Mortality at Intensive Care Units, and Evaluation of the Risk Factors

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Abstract

Background: Nosocomial infections (NIs) are an important public health problem worldwide, particularity in the intensive care units (ICUs).
Objectives: The current study aimed to detect and highlight NIs as the critical factor in increasing mortality and morbidity to clarify the current health priorities and challenges in Iran.
Patients and Methods: It was a retrospective study on 376 selected patients admitted in ICU at a public hospital in Tehran, Iran, from 2012 to 2014. The major studied NIs included: ventilator associated pneumonia (VAP), central venous catheter related primary bloodstream infections (CRBSIs or BSI), surgical site infections (SSIs) and catheter associated urinary tract infections (CAUTI or UTI). NIs were defined based on the centers for disease control and prevention (CDC) definitions. Site specific NIs rates, mortality rate and the length of hospital stay and other demographic or clinical variables were extracted.
Results: Three hundred-four patients were examined for NIs. NIs rate was 19.7% and mortality rates were 44.4% and 21.72% in infected and uninfected patients, respectively. The most frequent NIs was VAP and the highest observed rates of mortality were BSI in males (P = 0.050) and UTI in females (P = 0.05). The mortality rate in the infected patients was twice the other patients [2.187 (CI: %95: 1.154.13), P = 0.010]. The results showed that patients with cardiovascular respiratory dysfunction were exposed to higher risk of death. Infection rate increased in patients with diabetes and endocrine disease.
Conclusions: To manage ICU patients, risk factors and causative procedures contributing to incidence and development of Nis should be considered. The most considerable points are accurate disinfection and more strict infection control procedure especially for prevent of VAP and BSI, which associated with the increasing of patient's mortality. This issue is more crucial in the cases of the cardiovascular respiratory and diabetic patients.

Keywords: Nosocomial Infections, Death, Mortality Rate, Cardiovascular-Respiratory Dysfunction, Diabetes, Immune Dysfunction

1. Background

Iran health system, established in 1980, includes family planning, vaccination, maternal and prenatal care, children health, growth monitoring, hospital infection control and programs to prevent epidemiological disasters. However, the national nosocomial infection surveillance program was established in Iran in 2007 based on national nosocomial infection surveillance (NNIS) system definitions classified for four major groups including pulmonary, urinary tract, blood stream and surgical site infections (1). Nowadays, mortality has significantly decreased due to infectious disease control. Despite, the healthcare proceedings, and appearance of new antibiotics, the prevalence of nosocomial infections (Nis) is not significantly eradicated and it is an important part of health surveillance, which is rarely studied at hospitals in Iran (2-5). The NIs rate was estimated about 10% to 15% by national health system in Iran. Out of six million hospitalized patients, about six-hundred-thousand patients are infected with NIs in Iran (3).

Intensive care units (ICUs) are unfortunately the center of nosocomial infections. Since the 1980s, infectious disease specialists have recognized that ICU patients acquire NIs 5 to 10 times more than the patients in the other wards

of hospitals due to the use of invasive therapeutic devices (6). This rate varies by the type of infections and ICU, site of infections and the prevalence of specific pathogens (7, 8). Bacterial colonization is strongly associated with hospital stay and is especially common in the critically ill patients hospitalized for various reasons, including impaired host defenses, the frequent use of invasive devices, and the repeated or long-term administration of antibiotics. The main predisposing factors are associated with either an increased risk of colonization and increased immunity in the host (5).

NIs are associated with considerable morbidity, extra cost, and are responsible for more mortality (9-13). On the basis of data from death certificates, these infections are the 10th leading cause of death in the United States (5, 14). Importantly, bloodstream infections (BSIs) are major causes of morbidity and mortality (10, 13, 15).

The current study used the definitions of nosocomial infections provided by the standard centers for disease control and prevention (CDC) and national nosocomial infections surveillance (NNIS) (16), which investigated the rate of mortality in patients with any types of NIs at ICUs.

2. Objectives

The most evident attempt was to estimate annually NIs associated mortality restricted to ICU wards in Iranian national health care system. The current study focused on NIs associated mortality estimation limited to the hospitalized patients at ICU of university hospital, since the patients are potentially susceptible to infections (17). The current study aimed to highlight the necessity for efficient policy making aimed to increase the survival rate of critical ICU's patients at university hospitals. One of the most significant results of the current attempt was to summarize and highlight the major findings of the epidemiology of NIs and evaluate annually NIs related mortality rate for ICU patients in Iran.

3. Patients and Methods

3.1. Study Population

This cross-sectional retrospective surveillance study was performed on the patients admitted at medical-surgical ICU (MS-ICU) ward of Taleghani hospital, Tehran, Iran, from 2012 to 2014. It is a no-referral state general hospital affiliated to Shahid Beheshti University of Medical Sciences. Since other studies showed the mortality rate of at least twice, compared to non-nosocomial infections, with 95% of confidence and 80% of power, it was calculated that the study needed about 70 subjects in each group (nosocomial and non-nosocomial infections). All patients hospitalized at ICU in the period of the study were investigated and included in this research. Out of 376 patients, 304 ones were included in the study according to the inclusion criteria. Those patients hospitalized at ICU with less than 48 hours of stay, and patients stayed in ICU due to non-hospital-acquired infections and neonatal patients (under 15 years) were excluded from the study. The written consent was received from all of the patients or their first relatives.

3.2. Measurement of Hospital-Acquired-Infections Associated Mortality

All relevant data were collected from the patients' medical records and available flowcharts. Samples for microbiological diagnostic tests were routinely taken, if infection was clinically suspected. Demographic information, severity of underlying medical disease, previous ward before ICU admission and Glasgow coma scale (GCS) scores (18) were studied. In addition, detailed information about durations of invasive procedures -such as mechanical ventilation (MV) usage, central venous catheterization, urinary catheterization, nasogastric tube, digestive and respiratory tract, surgical intervention, dialysis, recent surgery and blood transfusion- and hospital stay were also recorded. Rate of infection was calculated based on national healthcare safety network (NHSN) definitions (16). NIs associated mortality was evaluated and its related annual rate was estimated. The study was approved by the ethics committee and conducted in accordance with its guidelines (number 90/125, date: 03.06.2012). The patients' names and personal information were kept confidential.

3.3. Data Analysis

Epidemiology of NIs and mortality rate were evaluated in the studied patients. Results were analyzed by comparison of NIs and mortality risk factors in the patients. Differences were analyzed by Chi-square and t-test. Odds ratios (OR) and the confidence intervals (95% CI) of the ORs were calculated by logistic regression analysis. The normality of numeric variables was checked by Kolmogorov-Smirnov test. All of the statistical analyses were two sided, and $P < 0.050$ was considered significant.

4. Results

Of the 376 patients, 304 ones were recruited in the study, including163 males and 141 females subjects admitted in the ICU ward; 19.2% of them were the patients infected with HAIs.

There were 60 (19.7%) patients with NIs and 244 (80.3%) patients were uninfected. Male was the dominant gender in both infected and uninfected patients. The investigated criteria are separately illustrated in Table 1 for both groups. The mean age of patients was 59.47 ± 3.03 in the infected and 50.07 ± 1.15 in the uninfected groups. The mean of hospitalization stay was studied in the patients, and it was observed that the hospitalization stay increased in the infected group ($P < 0.001$). The results showed differences in GCS between the infected and uninfected groups, and, GCS mean of infected patients were less than those of the other patients ($P < 0.001$). Also, blood transfusion (BT) unit was used more by the infected patients compared to the un-infected ones ($P < 0.001$).

Table 1. Profile of the Studied Population[a]

Variable	Patients With Infection (n = 60)	Patients Without Infection (n = 244)
Gender		
Male	33 (55)	130 (53.3)
Female	27 (45)	114 (46.7)
Age range, y	15 - 91	19 - 86
Age, mean ± SD	59.47 ± 3.03	50.07 ± 1.15
Hospitalization, mean ± SD	12.98 ± 1.44	7.27 ± 0.92
GCS, mean ± SD	10.98 ±0.33	12.62 ± 0.13
Blood unit, mean ± SD	11 ± 1.5	6.21 ± 0.8

Abbreviation: GCS, Glasgow coma scale.
[a]Values are expressed as No. (%) unless otherwise indicated.

On the other hand, the relationship between NIs and mortality rate in ICU patients were studied. Table 2 depicted the details of this relationship in males and females separately. However, the confounding effects of age and gender were omitted by logistic regression analysis. NIs increased in dead patients in both genders. These results showed that NIs increased the mortality rate especially in males ($P = 0.040$). Long term hospitalization (15 days and longer) was significantly more in dead patients than other patients for male gender ($P = 0.010$). Also, the results indicated that GCS in dead patients decreased compared to other patients in both genders ($P < 0.001$, $P < 0.001$). Although mortality rate was not influenced by BT ($P = 0.110$, $P = 0.730$), one of the questions on the study was: "What is the relationship between MV, NIs and mortality"? Logistic regression indicated that MV was commonly used in dead patients. Besides, it is noteworthy that NIs also associated with MV usage, and MV usage increased in the infected patients ($P < 0.001$).

The current study showed that distribution of NIs was not equal in ICU patients (Table 3). Whereas, VAP was the dominant infection in ICU patients and also the most mortality rate belonged to the patients with VAP, no significant difference was observed in dead and alive patients ($P = 0.800$, Table 4). However, logistic regression analysis along with the omitting confounding factors indicated that patients with BSI and UTI were more susceptible to morbidity and mortality in the ICU ward ($P = 0.030$, $P = 0.040$). Table 4 illustrated NIs epidemiology in alive and dead patients separately for both males and females. Patients with cardiovascular–respiratory and diabetic diseases were more exposed the NIs. Mortality rate significantly increased in patients with cardiovascular-respiratory diseases (OR: 3.3, (95% CI: 1.6 - 6.8), $P < 0.001$) (Table 5). Although neoplasm and cancers are among the major risk factors for death in Iran, there was no significant difference in infected and uninfected patients in the current study.

5. Discussion

The United States, estimated that NIs was 11% in medical ICU (19) but, in the current study NIs was 19.7%. Similar to the present study, most of the studies found VAP as the most frequent NIs (4, 7, 12, 13, 20) and other studies reported analogous rates of NIs in Argentina and Latin American countries (5, 7). Although some studies detected that UTI was the most prevalent NIs (11, 21), it is considerable that researches distinguished higher prevalence of NIs in university hospitals (20, 22). UTI prevalence in the current study was the third most common type of infection similar to large surveillance program reports across Europe (23). ICU patients commonly require careful monitoring of intake and outtake and urinary catheter was used for them and consequently UTI was prevalent in ICU.

In the present study, the total rate of mortality was estimated 26%. However, some studies reported higher rates of mortality (24, 25), versus several others which observed lower rates (1) than the current study. The current study showed that risk of death is almost twice for patients with NIs. Along with the significant relationship between NIs and mortality, the maximal risk of NIs belonged to patients with BSI and UTI in the present study. Although it is reported that VAP had the highest rate of mortality (21, 22), some authors reported lower mortality rates for BSI and UTI patients (22, 26). These various reported observations may be due to different sampling, classification and diagnosis of the associated underlying data, calculation methods, inclusion and exclusion criteria, studied population and race, geographic regions, lifestyle, and dietary habits. Nevertheless, VAP was the most frequent NIs in ICU patients, followed by BSI and UTI, in the current study. It is

Table 2. Investigated Criteria Associated With Mortality in Males and Females

Variable	Male				Female			
	Dead Group[a]	Alive Group[a]	Adjusted OR (95% CI)[b]	P Value	Dead Group[a]	Alive Group[a]	Adjusteda OR (95% CI)[b]	P Value
Nosocomial infections								
Without NIs	26 (65)	104 (84.6)	1.00 (reference)	NA	27 (69.2)	87 (85.3)	1.00 (reference)	NA
With NIs	14 (35)	19 (15.4)	2.42 (1 - 5.8)	0.004	12 (30.8)	15 (14.7)	2 (0.78 - 5.09)	0.140
Hospitalization, day								
1 - 5	15 (37.5)	78 (63.4)	1.00 (reference)	NA	20 (51.3)	59 (57.8)	1.00 (reference)	NA
6 - 10	15 (37.5)	32 (26)	2.07 (0.87 - 4.92)	0.009	13 (33.3)	22 (21.6)	1.7 (0.67 - 4.2)	0.250
11 - 15	2 (5)	5 (4.1)	2.23 (0.38 - 12.89)	0.360	1 (2.6)	7 (6.9)	0.5 (0.05 - 4.45)	0.530
> 15	8 (20)	8 (6.5)	4.56 (1.44 - 14.43)	0.010	5 (12.8)	14 (13.7)	0.92 (0.26 - 3.18)	0.900
GCS								
10.01 - 15	23 (57.5)	113 (91.9)	1.00 (reference)	NA	18 (46.2)	94 (92.2)	1.00 (reference)	NA
5.01 - 10	17 (42.5)	10 (8.1)	11.44 (4.16 - 31.45)	< 0.001	21 (53.8)	8 (7.8)	31.5 (9.64 - 102.88)	< 0.001
Blood transfusion								
Without BT	10 (25)	49 (39.8)	1.00 (reference)	NA	15 (38.5)	43 (42.2)	1.00 (reference)	NA
With BT	30 (75)	74 (60.2)	1.93 (0.85 - 4.39)	0.110	24 (61.5)	59 (57.8)	1.14 (0.51 - 2.56)	0.730
Mechanical ventilation								
Without MV	9 (22.5)	83 (67.5)	1.00 (reference)	NA	5 (12.8)	66 (64.7)	1.00 (reference)	NA
With MV	31 (77.5)	40 (32.5)	8.6 (3.49 - 21.29)	< 0.001	34 (87.2)	36 (35.3)	31 (6.69 - 144)	< 0.001

Abbreviations: 95% CI, 95% confidence interval; GCS, Glasgow coma scale; OR, odds ratio.
[a]Values are expressed as No. (%).
[b]Adjusted for age.

Table 3. Epidemiology of Nosocomial Infections in Alive and Dead Patients

Variable	Alive Group[a]	Dead Group[a]	Adjusted OR (95% CI)[b]	P Value
Type of nosocomial infections				
Without any NIs	191 (84.9)	53 (67.1)	reference = 1	
BSI	6 (2.7)	6 (7.6)	3.67 (1.12 - 12.04)	0.030
UTI	5 (2.2)	5 (6.3)	4.08 (1.06 - 15.65)	0.040
SSI	1 (0.4)	1 (1.3)	2.45 (0.12 - 47.49)	0.550
VAP	20 (8.9)	9 (11.4)	1.12 (0.44 - 2.8)	0.800
More than one infections	2 (0.9)	5 (6.3)	3.8 (0.62 - 23.89)	0.140

Abbreviations: BSI, bloodstream infections; OR, odds ratio; UTI, urinary tract infection; SSI, surgical site infections; VAP, ventilator associated pneumonia ventilator associated pneumonia.
[a]Values are expressed as No. (%).
[b]Adjusted for age.

true that blood transfusion units increased in the patients with NIs, but it was not statistically associated with death.

Patients with cardiovascular-respiratory dysfunction and also patients with diabetes are more exposed to the infection. Hyperglycemic environment is in favor of immune dysfunction and increases the risk of NIs in patients with diabetes.

Overall, the current study found that NIs increased the

Table 4. Epidemiology of Nosocomial Infections in Alive and Dead Patients for Both Male and Female Gender

Variable	Male				Female			
	Alive Group[a]	Dead Group[a]	Adjusted OR (95% CI)[b]	P Value	Alive Group[a]	Dead Group[a]	Adjusted OR (95% CI)[b]	P Value
Without any infection	104 (84.6)	26 (65)	reference	NA	87 (85.3)	27 (69.2)	reference	NA
BSI	2 (1.6)	3 (7.5)	6 (0.95 - 37.78)	0.050	4 (3.9)	3 (7.7)	2.4 (0.5 - 11.47)	0.260
UTI	4 (3.3)	2 (5)	2 (0.34 - 11.52)	0.400	1 (1)	3 (7.7)	9.6 (0.96 - 96.8)	0.050
SSI	0	1 (2.5)	NA	NA	1 (1)	0	NA	NA
VAP	11 (8.9)	5 (12.5)	1.8 (0.58 - 5.69)	1.800	9 (8.8)	4 (10.3)	1.43 (0.4 - 5)	0.570
More than one infection	2 (1.6)	3 (7.5)	6 (0.95 - 37.78)	0.050	0	2 (5.1)	NA	NA

Abbreviations: BSI, bloodstream infections; OR, odds ratio; UTI, urinary tract infection; SSI, surgical site infections; VAP, ventilator associated pneumonia ventilator associated pneumonia.
[a] Values are expressed as No. (%).
[b] Adjusted for age.

Table 5. Diseases, Risk of Death and Infection

Disease Categorical	Death				Nosocomial Infections			
	Dead Group (Case)	Alive Group (Control)	Adjusted OR (95% CI)[a]	P Value	Infected Group	Uninfected Group	Adjusted OR (95% CI)[a]	P Value
Neoplasm	36.7	27.5	1.5 (0.8 - 2.8)	0.200	30	29.2	1.6 (0.76 - 3.5)	0.200
Cardiovascular and respiratory disease	24.1	8.4	3.3 (1.6 - 6.8)	< 0.001	31.7	7.8	5.8 (2.7 - 12.3)	< 0.001
Digestive disease	41.8	50.7	0.64 (0.35 - 1.17)	0.140	48.8	46.7	1.2 (0.6 - 2.47)	0.570
Diabetes and endocrine disease	22.8	13.8	1.68 (0.82 - 3.45)	0.150	13.5	26.7	2.5 (1.13 - 5.5)	0.020
Other disease	15.2	20.4	0.8 (0.35 - 1.9)	0.650	18	23.3	2.8 (1.13 - 7.3)	0.020

[a] Adjusted for age; OR, odds ratio.

risk of mortality twice in the patients hospitalized in ICU ward. It is means that reducing the occurrence of NIs may greatly decrease the risk of mortality for critically Iranian patients stayed in the ICU.

Mortality in intensive care unit is commonly much higher than other wards and one of the goals of patients care in this unit is to save them from mortality. Causes of death in these patients are very different. Discovering the causes of mortality and finally trying them to resolve it, is the most important objective and the critical point in this unit of the hospital. It seems that nosocomial infections are associated with high mortality and increasing the length of stay at ICU. Although multiple studies highlighted the importance of regular hand washing by the staff in reducing NIs, NIs is not reduced to zero. Several reasons can cause the NI appearance and improvement. Since the ICU patients are critically ill, their immune system cannot response against the infections and they are easily infected by various nosocomial pathogens.

VAP is the most frequent infection, followed by catheter-related bloodstream infections. However, the highest rate of mortality was observed in UTI and BSI patients. Since the mortality rate is associated with increased infections especially for patients with UTI and BSI, it can be reduced in patients in intensive care unit by reducing the risk of infections. It suggests that ICU patients were completely isolated and NIs risk factors such as invasive instruments and devices should be used with caution if necessary for ICU patients.

Infections enhanced the cardiovascular-respiratory

dysfunction at ICU hospitalized patients. It can be said that dysfunctional cardiovascular-respiratory and diabetes mutually enhance the risk of infections. They are synergic factors that can improve the morbidity and mortality risk in ICU hospitalized patients.

There were rare studies associated with hospital related infectious diseases in Iran; therefore, the current study is beneficial to study hospital related infectious diseases and investigate their control and reduction.

The present study was conducted in one hospital. If other studies are conducted in all of the hospitals in Tehran province and the associated results are merged with those of the present study, more beneficial results could be achieved.

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Footnotes

Authors' Contribution: Maryam Karkhane and Mohamad Amin Pourhoseingholi: study concept and design; Maryam Karkhane, Mohamad Amin Pourhoseingholi, Zahra Kimiia, Seyed Mehdi Mortazavi, Mohammad Reza Akbariyan Torkabad and Seyed Karim Hossieni Aghdam: acquisition of data; Maryam Karkhane and Mohamad Amin Pourhoseingholi: analysis and interpretation of data; Maryam Karkhane and Mohamad Amin Pourhoseingholi: drafting of the manuscript; Mohamad Amin Pourhoseingholi and Abdolrazagh Marzban: critical revision of the manuscript for important intellectual content; Mohamad Amin Pourhoseingholi: statistical analysis; Mohammad Reza Zali: study supervision.

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References

1. 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**(21):2323–9. doi: 10.1001/jama.2009.1754. [PubMed: 19952319].
2. Forouzanfar MH, Sepanlou SG, Shahraz S, Dicker D, Naghavi P, Pourmalek F, et al. Evaluating causes of death and morbidity in Iran, global burden of diseases, injuries, and risk factors study 2010. *Arch Iran Med.* 2014;**17**(5):304–20. [PubMed: 24784860].
3. Chen YY, Wang FD, Liu CY, Chou P. Incidence rate and variable cost of nosocomial infections in different types of intensive care units. *Infect Control Hosp Epidemiol.* 2009;**30**(1):39–46. doi: 10.1086/592984. [PubMed: 19046058].
4. Lee JH, Kim SW, Yoon BI, Ha US, Sohn DW, Cho YH. Factors that affect nosocomial catheter-associated urinary tract infection in intensive care units: 2-year experience at a single center. *Korean J Urol.* 2013;**54**(1):59–65. doi: 10.4111/kju.2013.54.1.59. [PubMed: 23362450].
5. Vincent JL. Nosocomial infections in adult intensive-care units. *Lancet.* 2003;**361**(9374):2068–77. doi: 10.1016/s0140-6736(03)13644-6.
6. Benet T, Haesebaert J, Hernu R, Piriou V, Guerin C, Aubrun F, et al. Characterization of patients exposed to multiple devices but free of hospital-acquired infection at intensive care unit discharge. *Am J Infect Control.* 2015;**43**(2):171–3. doi: 10.1016/j.ajic.2014.10.022. [PubMed: 25516219].
7. Rosenthal VD, Guzman S, Orellano PW. Nosocomial infections in medical-surgical intensive care units in Argentina: Attributable mortality and length of stay. *American J Infect Control.* 2003;**31**(5):291–5. doi: 10.1067/mic.2003.1.
8. Chen Y, Xu X, Liang J, Lin H. Relationship between climate conditions and nosocomial infection rates. *African Health Sci.* 2013;**13**(2):339–43. doi: 10.4314/ahs.v13i2.20.
9. Rosenthal VD, Guzman S, Safdar N. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. *Am J Infect Control.* 2005;**33**(7):392–7. doi: 10.1016/j.ajic.2004.08.009. [PubMed: 16153485].
10. Pronovost PJ, Goeschel CA, Colantuoni E, Watson S, Lubomski LH, Berenholtz SM, et al. Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study. *Bmj.* 2010;**340**(c309):1–6. doi: 10.1136/bmj.c309.
11. Kwak YG, Lee SO, Kim HY, Kim YK, Park ES, Jin HY, et al. Risk factors for device-associated infection related to organisational characteristics of intensive care units: findings from the Korean Nosocomial Infections Surveillance System. *J Hosp Infect.* 2010;**75**(3):195–9. doi: 10.1016/j.jhin.2010.01.014. [PubMed: 20434798].
12. Kubler A, Duszynska W, Rosenthal VD, Fleischer M, Kaiser T, Szewczyk E, et al. Device-associated infection rates and extra length of stay in an intensive care unit of a university hospital in Wroclaw, Poland: International Nosocomial Infection Control Consortium's (INICC) findings. *J Crit Care.* 2012;**27**(105):ee5–e10. .
13. Leblebicioglu H, Ozturk R, Rosenthal VD, Akan OA, Sirmatel F, Ozdemir D, et al. Impact of a multidimensional infection control approach on central line-associated bloodstream infections rates in adult intensive care units of 8 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). *Ann Clin Microbiol Antimicrob.* 2013;**12**:10. doi: 10.1186/1476-0711-12-10. [PubMed: 23641950].
14. Peng H, Tao XB, Li Y, Hu Q, Qian LH, Wu Q, et al. Health care-associated infections surveillance in an intensive care unit of a university hospital in China, 2010-2014: Findings of International Nosocomial Infection Control Consortium. *Am J Infect Control.* 2015;**43**(12):e83–5. doi: 10.1016/j.ajic.2015.07.023. [PubMed: 26315060].
15. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med.* 2006;**355**(26):2725–32. doi: 10.1056/NEJMoa061115. [PubMed: 17192537].
16. 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**(10):783–805. doi: 10.1016/j.ajic.2009.10.001. [PubMed: 20004811].
17. Chang R, Greene MT, Chenoweth CE, Kuhn L, Shuman E, Rogers MA, et al. Epidemiology of hospital-acquired urinary tract-related bloodstream infection at a university hospital. *Infect Control Hosp Epidemiol.* 2011;**32**(11):1127–9. doi: 10.1086/662378. [PubMed: 22011543].

18. Silvestri L, Monti Bragadin C, Milanese M, Gregori D, Consales C, Gullo A, et al. Are most ICU infections really nosocomial? A prospective observational cohort study in mechanically ventilated patients. *J Hosp Infect.* 1999;**42**(2):125–33. [PubMed: 10389062].
19. Meric M, Willke A, Caglayan C, Toker K. Intensive care unit-acquired infections: incidence, risk factors and associated mortality in a Turkish university hospital. *Jpn J Infect Dis.* 2005;**58**(5):297–302. [PubMed: 16249625].
20. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial Infections in Pediatric Intensive Care Units in the United States. *Pediatr.* 1999;**103**(4):1–7.
21. Decoster A, Grandbastien B, Demory MF, Leclercq V, Alfandari S, Regional Network 'Review of nosocomial infection-related M. A prospective study of nosocomial-infection-related mortality assessed through mortality reviews in 14 hospitals in Northern France. *J Hosp Infect.* 2012;**80**(4):310–5. doi: 10.1016/j.jhin.2011.11.016. [PubMed: 22365323].
22. Balaban I, Tanir G, Timur OM, Nur Oz F, Teke TA, Bayhan G. Nosocomial Infections in the General Pediatric Wards of a Hospital in Turkey. *Japanese J Infect Dis.* 2012;**65**(4):318–21. doi: 10.7883/yoken.65.318.
23. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *JAMA.* 1995;**274**(8):639–44. [PubMed: 7637145].
24. Faria S. , Sodano L, Gjata A, Dauri M, Sabato AF, Bilaj A, et al. The first prevalence survey of nosocomial infections in the University Hospital Centre 'Mother Teresa' of Tirana, Albania. *J Hospital Infect.* 2007;**65**(3):244–50.
25. Girou E, Schortgen F, Delclaux C, Brun-Buisson C, Blot F, Lefort Y, et al. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. *JAMA.* 2000;**284**(18):2361–7. [PubMed: 11066187].
26. Kaoutar B, Joly C, L Heriteau F, Barbut F, Robert J, Denis M, et al. Nosocomial infections and hospital mortality: a multicentre epidemiological study. *J Hospital Infect.* 2004;**58**(4):268–75. doi: 10.1016/j.jhin.2004.06.006.