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Survival rate in patients with ICU-acquired infections and its related factors in Iran's hospitals



MEDSKorosh Etemad^{1†}, Yousef Khani^{2†}, Seyed-Saeed Hashemi-Nazari^{3*}, Neda Izadi^{1*}, Babak Eshrati⁴ and Yadollah Mehrabi¹

Abstract

Background: Hospital-acquired infections (HAIs) are a well-known cause of morbidity and mortality in hospitalized patients. This study aimed at investigating the survival rate in patients with ICU-acquired infections (ICU-AIs) and its related factors in Iran's hospitals.

Methods: Data were obtained from the Iranian Nosocomial Infections Surveillance (INIS), which registers all necessary information on the main types of infection from different units of each included hospital. One thousand one hundred thirty-four duplicate cases were removed from the analysis using the variables of name, father's name, age, hospital code, infection code, and bedridden date. From 2016 to 2019, 32,998 patients diagnosed with ICU-AI from about 547 hospitals. All patients were followed up to February 29, 2020.

Results: The median age of patients with ICU-Als was 61 (IQR = 46) years. 45.5, 20.69, 17.63, 12.08, and 4.09% of infections were observed in general, surgical, internal, neonatal and pediatric ICUs, respectively. Acinetobacter (16.52%), E.coli (12.01%), and Klebsiella (9.93%) were the major types of microorganisms. From total, 40.76% of infected patients (13,449 patients) died. The 1, 3, 6-months and overall survival rate was 70, 25.72, 8.21 1.48% in ICU-Al patients, respectively. The overall survival rate was 5.12, 1.34, 0.0, 51.65, and 31.08% for surgical, general, internal, neonatal and pediatric ICU, respectively. Hazard ratio shows a significant relationship between age, hospitalization-infection length, infection type, and microorganism and risk of death in patients with ICU-Al.

Conclusions: Based on the results, it seems that the nosocomial infections surveillance system should be more intelligent. This intelligence should act differently based on related factors such as the age of patients, hospitalization-infection length, infection type, microorganism and type of ward. In other words, this system should be able to dynamically provide the necessary and timely warnings based on the factors affecting the survival rate of infection due to the identification, intervention and measures to prevent the spread of HAIs based on a risk severity system.

Keywords: Hospital-acquired infections, Survival rate, Risk factors, Intensive care units, Iran

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Introduction

Hospital-acquired infections (HAIs) are infections that are not present in patients at the time of hospital admission and also are not in the incubation period. These infections occur after hospitalization, especially within 48–72 h after hospital admission and up to 6 weeks later [1].

These infections are a well-known cause of morbidity and mortality in hospitalized patients which in fact complicate hospitalization and treatment processes [2, 3].

These infections include the ventilator-associated events/ respiratory infections/pneumonia (VAE/VAP), central line-associated bloodstream infections/ septicemia (CLABSI), catheter-related urinary tract infection (CAUTI), surgical site infections (SSI), and clostridium difficile infections (CDI) [4]. In addition, the risk factors for these infections include the immunosuppression, older age, longer length of stay in hospital, multiple underlying comorbidities, frequent visits to healthcare facilities, mechanical ventilatory support, recent invasive procedures, indwelling devices, and stay in an intensive care unit (ICU) [5].

The risk of these infections is higher in the intensive care unit, so that in a study of 231,459 patients admitted to the intensive care unit of 947 hospitals in Germany (2015), the point prevalence of ICU-acquired infections (ICU-AIs) was 19.5% [6]. While in study by Magill et al. (2014) on 11,282 patients from 183 U.S. acute care hospitals, the overall point prevalence of these infections was only 4% [7].

Various studies have shown that the incidence of hospital-acquired infections in the intensive care unit is 5 to 10 times higher than in other hospital wards [8]. Some other studies have also shown that 50% of patients admitted to the intensive care unit affected from this infections [9, 10]. Accordingly, these infections are in fact, serious problem which complicate the patients in the intensive care unit [11]. Because the high prevalence of these infections in the intensive care unit, it leads to increase in morbidity and mortality of hospitalized patients. It also increase the economic burden due to higher prescription of antibiotics and longer hospital stay in hospitals [8, 11].

Although the prevalence of HAIs and its related factors have been widely studied, no special study has been conducted in Iran regarding their survival rate of such patients, especially those admitted in ICUs. Therefore, this study aimed at investigating the survival rate in patients with ICU-acquired infections and its related factors in Iran's hospitals.

Methods

In this retrospective cohort study, data were obtained from the Iranian Nosocomial Infections Surveillance (INIS), which uses the standard definitions provided by the national nosocomial infections surveillance system (NNIS). The NNIS registers four main types of infection, including the following: catheter-associated urinary tract infections (CAUTI), ventilator-associated events (VAE), surgical site infections (SSI), central line-associated bloodstream infections (CLABSI) and other infections (bone and joint, central nervous system, chorionic villus sampling, eye, ear, nose, throat and mouth, gastrointestinal system, reproductive tract infection, and skin and soft tissue infections). It also records different types of information in different units of each hospital [12]. For the purpose of this study, following variables were included: age, gender, hospitalization-infection length, duration hospitalization, type of ward, type of infection, device use (different types of catheters include the urinary catheter, artery catheter, umbilical catheter, peripheral venous catheter, temporary central venous and permanent central venous catheter and also ventilator), type of microorganism, type of hospital, and death status. The primary outcome for this study was all cause death among patients with HAIs admitted to the ICU. Follow-up time was considered for one year, whether discharged or death.

Statistical analysis

The median (Interquartile Range = IQR) and count (percentage) were used to describe quantitative and qualitavariables, respectively. The Chi-square test calculated the frequency of different variables among the two groups (alive and dead). The Kaplan Meier was used to compare survival rates between different groups. In addition, we used the Cox proportional hazard regression model to estimate the crude and adjusted hazard ratio (HR) for the risk of death among patients with ICU-acquired infection. To identify the factors related to survival in patients with ICU-acquired infections, all the variables with a P-value less than 0.2 or variables whose most levels are less than 0.2 at the univariable model were included in the multivariable analysis. Data were analyzed by the Stata (version 14.0; Stata Corp, Texas, USA) software. For all statistical tests P < 0.05 was considered statistically significant.

This study was approved by the ethical committee of National Institute for Medical Research Development (IR.NIMAD.REC.1399.074).

Results

One thousand one hundred thirty-four duplicate cases were removed from the analysis by matching name, father's name, age, hospital code, infection code, and bedridden date. Finally, the 32,998 patients diagnosed with ICU-AI from about 547 hospitals between 2016

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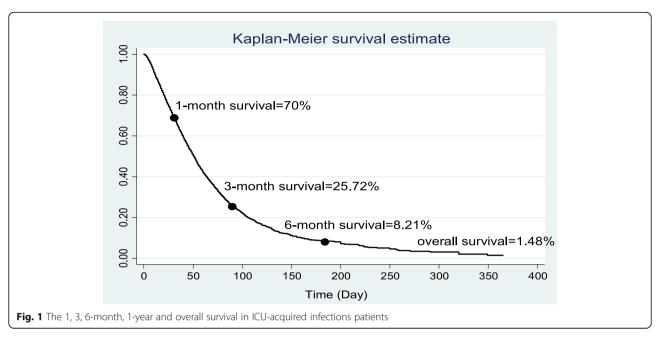
Table 1 Factors associated with the all-cause mortality among ICU-acquired infections patients

Variable		Alive (19,549)	Dead (13,449)	Total (32,998)	<i>P</i> -value
		N (%)	N (%)	N	
Gender	Male	11,782 (61.36)	7420 (38.64)	19,202	< 0.001
	Female	7727 (56.2)	6021 (43.8)	13,748	
Hospitalization-infection length	≤8 days	11,241 (65.09)	6030 (34.91)	17,271	< 0.001
	> 8 days	8308 (52.83)	7419 (47.17)	15,727	
Ward type	Surgical ICU	4087 (59.86)	2741 (40.14)	6828	< 0.001
	General ICU	8228 (54.8)	6786 (45.2)	15,014	
	Internal ICU	2743 (47.15)	3075 (52.85)	5818	
	Pediatric ICU	1030 (76.24)	321 (23.76)	1361	
	Neonatal ICU	3461 (86.81)	526 (13.19)	3987	
Infection type	BSI	2470 (58.45)	1756 (41.55)	4226	< 0.001
	PENU & LRTI	3404 (71.66)	1346 (28.34)	4750	
	SSI	1333 (71.13)	541 (28.87)	1874	
	UTI	4008 (61.66)	2492 (38.34)	6500	
	VAE	6421 (48.97)	6690 (51.03)	13,111	
	Other	1913 (75. 4)	624 (24. 6)	2537	
Device use	Yes	11,023 (52.76)	9870 (47.24)	20,893	< 0.001
	No	8526 (70.43)	3579 (29.57)	12,105	
Device type	Catheters	3633 (56.46)	2802 (43.54)	6435	< 0.001
	Ventilators	6820 (50.13)	6784 (49.87)	13,604	
	Other	570 (66.74)	284 (33.26)	854	
	Without device	8526 (70.43)	3579 (29.57)	12,105	
Microorganism	Staphylococcus epidermidis	885 (73.26)	323 (26.74)	1208	< 0.001
	Staphylococcus aureus	995 (62.66)	593 (37.34)	1588	
	Coagulase negative staphylococci	548 (66.26)	279 (33.74)	827	
	Acinetobacter	2617 (48.01)	2834 (51.99)	5451	
	Escherichia coli	2373 (59.89)	1589 (40.11)	3962	
	Enterobacter	901 (63.18)	525 (36.82)	1426	
	Enterococcus	435 (59.92)	291 (40.08)	726	
	Pseudomonas aeruginosa	1474 (58.28)	1055 (41.72)	2529	
	Citrobacter	328 (58.89)	229 (41.11)	557	
	Candida	467 (45.43)	561 (54.75)	1028	
	Candida albicans	284 (55.15)	231 (44.85)	515	
	Klebsiella	1875 (57.23)	1401 (42.77)	3276	
	Klebsiella pneumoniae	921 (48.78)	967 (51.22)	1888	
	Other	1804 (62.6)	1078 (37.4)	2882	
	Unknown	3642 (70.93)	1493 (29.07)	5135	
Hospital type	Government	16,121 (59.45)	10,998 (40.55)	27,119	< 0.001
	Semi-government	581 (43.78)	746 (56.22)	1327	
	Private	2045 (63.14)	1194 (36.86)	3239	
	Other	516 (53.86)	442 (46.99)	958	

^{*}Based on Chi-square test

BSI Blood Stream Infections, PENU & LRI Pneumonia Events & Lower Respiratory Tract Infection, SSI Surgical Site Infection, UTI Urinary Tract Infection, VAE Ventilator Associated Events.

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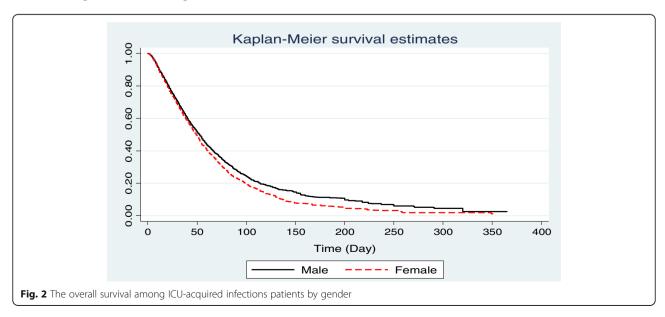


and 2019 were eligible for analysis. The median age of 32,998 patients with ICU-acquired infections was 61 (IQR = 46) years. 58.28% (19,202) of patients were males. The median of hospitalization-infection length and hospitalization duration were 8 (IQR = 16) and 23 (IQR = 29) days, respectively. 45.5, 20.69, 17.63, 12.08, and 4.09% of infections were observed in general, surgical, internal, neonatal and pediatric ICUs, respectively. For 63.32% of patients, the device (catheter and ventilator) was used. The most common ICU-AIs were VAE (13,111 patients; 39.73%). The major type of microorganisms were Acinetobacter (16.52%), E.coli (12.01%), and Klebsiella (9.93%). From total, 40.76% of infected patients (13,449 patients) died. Variables

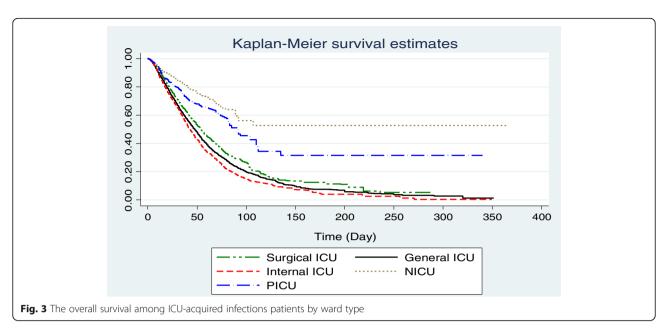
associated with death of such patients were investigated and have been shown in Table 1.

The survival rate

The 1, 3, 6-months and overall survival rate was 70, 25.72, 8.21 1.48% in ICU-acquired infections patients, respectively (Fig. 1). The 1, 3, 6-months and overall survival rates in males were higher than females (Fig. 2). The overall survival rate was 5.12, 1.34, 0.0, 51.65, and 31.08% for surgical, general, internal, neonatal and pediatric ICU, respectively. Also, the 6-months and the overall survival rate among neonates (51.65%) was significantly higher compared to other age groups (Fig. 3).



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The risk of death in patients with ICU-acquired infection

The association between different variables and risk of death were investigated and have been presented in Appendix 1, Table 2.

General ICU

Based on multivariable Cox regression, with increasing one year of age, the risk of death in ICU-AI patients increases by 1% (HR = 1.01; 95% CI: 1.009-1.01). The risk of death was 6% higher in women than men (HR = 1.06; 95% CI: 1.01-1.011). The hospitalization-infection length > 8 days was associated with a 64% decrease in the number of deaths in ICU-acquired infections (HR = 0.36; 95% CI: 0.34-0.38). The use of a device (catheter and ventilator) was also associated with a 16% increase in death risk (HR = 1.16; 95% CI: 1.1-1.23). Considering the types of microorganisms, the largest increase in death risk was related to the Acinetobacter (HR = 1.25; 95% CI: 1.06-1.48) (Table 2).

Internal ICU

The risk of death in ICU-AI patients increases by 0.9% (HR = 1.009; 95% CI: 1.007–1.01) with increasing 1 year of age. The hospitalization-infection length > 8 days was associated with a 63% decrease in the number of death in ICU-acquired infections patients (HR = 0.37; 95% CI: 0.34–0.4). In addition, the risk of death was 34% (HR = 1.34; 95% CI: 1.09–1.64) and 50% (HR = 1.5; 95% CI: 1.16–1.92) higher in government and semi-government hospitals compare to private hospitals. Considering the types of microorganisms, the largest increase in the risk of death was related to the Candida (HR = 2.76; 95% CI: 1.95–3.9),

Enterococcus (HR = 2.09; 95% CI: 1.44–3.03), and Acinetobacter (HR = 1.97; 95% CI: 1.45–2.68) (Table 2).

Surgical ICU

With increasing 1 year of age, the risk of death in ICU-AI patients increases by 1.7% (HR = 1.017; 95% CI: 1.015-1.019). The risk of death was 13% higher in women than men (HR = 1.13; 95% CI: 1.05-1.22). The hospitalization-infection length > 8 days was associated with a 58% decrease in the number of deaths in ICUacquired infections (HR = 0.42; 95% CI: 0.39-0.46). In addition, based on type of infection, BSI, VAE and other type of infections increase the risk of death by 50% (HR = 1.5; 95% CI: 1.26–1.78), 33% (HR = 1.33; 95% CI: 1.14–1.54), and 90% (HR = 1.9; 95% CI: 1.54–2.34), respectively. Considering the types of microorganisms, the largest increase in the risk of death was related to the Candida (HR = 1.54; 95% CI: 1.15-2.06), Coagulase negative staphylococci (HR = 1.54; 95% CI: 1.08-2.19), and Escherichia coli (HR = 1.41; 95% CI: 1.1-1.82) (Table 2).

Pediatric ICU

The risk of death in PICU was only associated with hospitalization-infection length (HR = 0.45; 95% CI: 0.35-0.57) (Table 2).

Neonatal ICU

The hospitalization-infection length > 8 days was associated with a 61% decrease in the number of death in ICU-acquired infections patients (HR = 0.39; 95% CI: 0.32–0.48). Based on the type of infection, BSI and VAE increase death risk (HR = 2.35; 95% CI: 1.3–4.26) and (HR = 2.05; 95% CI: 1.09–3.87). In addition, the use of a device (catheter and ventilator) was also associated with

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Table 2 Multiple Cox regression analysis of survival of ICU-acquired infection patients by ward type

Variable		Adjusted HR (95% CI)					
		General ICU	Internal ICU	Surgical ICU	Pediatric ICU	Neonatal ICU	
Age	Year	1.01* (1.009– 1.01)	1.009* (1.007– 1.01)	1.017* (1.015– 1.019)	0.99 (0.98–1)	_	
Gender	Male	1	1	1	1	1	
	Female	1.06* (1.01– 1.11)	1.06 (0.99–1.14)	1.13* (1.05–1.22)	-	_	
Hospitalization-infection length	≤8 days	1	1	1	1	1	
	> 8 days	0.36* (0.34– 0.38)	0.37* (0.34–0.4)	0.42* (0.39–0.46)	0.45* (0.35– 0.57)	0.39* (0.32– 0.48)	
Infection type	BSI	-	1.5* (1.15–1.95)	1.5* (1.26–1.78)	-	2.35* (1.3– 4.26)	
	PENU & LRI	-	1.35* (1.02–1.77)	0.96 (0.79–1.17)	_	1.26 (0.69– 2.31)	
	SSI	1	1	1	1	1	
	UTI	=	1.23 (0.95–1.59)	1.04 (0.87–1.24)	_	0.56 (0.27– 1.18)	
	VAE	-	1.51* (1.19–1.93)	1.33* (1.14–1.54)	_	2.05* (1.09– 3.87)	
	Other	_	1.43* (1.07–1.92)	1.9* (1.54–2.34)	_	0.62 (0.33– 1.17)	
Device use	No	1	1	1	1	1	
	Yes	1.16* (1.1–1.23)	-	_	1.19 (0.95– 1.48)	1.26* (1.02– 1.56)	
Microorganism	Staphylococcus epidermidis	1	1	1	1	1	
	Staphylococcus aureus	0.98 (0.81– 1.19)	1.31 (0.99–1.74)	1.56* (1.1–2.2)	_	0.52 (0.21– 1.27)	
	Coagulase negative staphylococci	1.1 (0.88–1.38)	1.54* (1.08–2.19)	1.5* (1.01–2.21)	_	0.76 (0.4–1.46)	
	Acinetobacter	1.25* (1.06– 1.48)	1.31* (1.03–1.66)	1.97* (1.45–2.68)	_	2.91* (1.86– 4.54)	
	Escherichia coli	1.09 (0.92–1.3)	1.41* (1.1–1.82)	1.77* (1.29–2.42)	_	1.41 (0.83– 2.39)	
	Enterobacter	1.04 (0.85– 1.27)	1.27 (0.96–1.69)	1.32 (0.91–1.9)	_	2.92* (1.77– 4.81)	
	Enterococcus	0.97 (0.77– 1.23)	1.26 (0.9–1.76)	2.09* (1.44–3.03)	_	1.74 (0.84– 3.61)	
	Pseudomonas aeruginosa	0.9 (0.75–1.08)	1.02 (0.78–1.33)	1.41* (1.01–1.95)	_	2.13* (1.21– 3.75)	
	Citrobacter	1.05 (0.73– 1.32)	1.19 (0.75–1.88)	1.49* (1.01–2.2)	_	2.25 (0.97– 5.17)	
	Candida	1.23* (1.01– 1.51)	1.54* (1.15–2.06)	2.76* (1.95–3.9)	-	4.9* (2.22– 10.81)	
	Candida albicans	1.26 (0.99– 1.61)	1.42 (0.99–2.05)	1.64* (1.09–2.47)	=	2.95* (1.33– 6.5)	
	Klebsiella	0.97 (0.82– 1.16)	1.4* (1.09–1.8)	1.62* (1.17–2.24)	-	2.52* (1.56– 4.04)	
	Klebsiella pneumoniae	0.96 (0.8–1.15)	1.29 (0.98–1.69)	1.77* (1.29–2.45)	_	2.3* (1.3–4.08)	
	Other	0.99 (0.83– 1.19)	1.16 (0.89–1.52)	1.61* (1.36–2.56)	-	1.56 (0.96– 2.55)	
	Unknown	1.25* (1.05–	1.4* (1.08–1.81)	1.87* (1.17–2.22)	_	1.86* (1.19–	

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Table 2 Multiple Cox regression analysis of survival of ICU-acquired infection patients by ward type (Continued)

Variable		Adjusted HR (95% CI)					
		General ICU	Internal ICU	Surgical ICU	Pediatric ICU	Neonatal ICU	
Hospital type	Government	-	1.34* (1.09–1.64)	_	-		
	Semi-government	-	1.5* (1.16–1.92)	_	_	_	
	Private	1	1	1	1	1	
	Other	-	1.07 (0.84–1.37)	-	-	-	

*P < 0.05

HR Hazard Ratio, CI Confidence Interval, BSI Blood Stream Infections, PENU & LRI Pneumonia Events & Lower Respiratory Tract Infection, SSI Surgical Site Infection, UTI Urinary Tract Infection. VAE Ventilator Associated Events.

a 26% increase in the risk of death (HR = 1.26; 95% CI: 1.02-1.56). Considering the types of microorganisms, the largest increase in the risk of death was related to the Candida (HR = 4.9; 95% CI: 2.22-10.81), Candida Albicans (HR = 2.95; 95% CI: 1.33-6.5), Enterobacter (HR = 2.92; 95% CI: 1.77-4.81), and Acinetobacter (HR = 2.91; 95% CI: 1.86-4.54) (Table 2).

Discussion

Our study showed that the survival rate in HAIs patients decreases over time. The reason for such decrease is multifactorial and is at least partly due to the possible change of pattern of infection over time, in which more than one organism may contribute to occurrence of HAIs. This in turn might be due to improper treatment of HAIs, multi-drug resistance, low quality of care for patients after their discharge from hospital [13–16].

According to the results of this study, the risk of death in women with HAIs admitted to the intensive care unit in general and surgical ICUs was higher than men. This result needs further investigation because the results from elsewhere is not consistent [8, 17]. However, the results of our study seem to be more reliable considering that its sample size is larger than most of other reports. Our results, are in fact, based on a national registration system.

In terms of type of ICU, the survival rate was higher in neonatal and pediatric ICUs and it may be because of the effect of age which is the main variable differed among such patients. Our finding is consistent with reports from elsewhere [18–21].

Studies have shown that increasing the length of hospitalization in the ICUs, increases the risk of HAIs. However, they do not necessarily increase the risk of death [22–25]. The main finding of this study was that hospitalization in the ICU for more than 8 days increases the survival in patients with nosocomial infections. The reason for such improvement in survival might be due to better care given to such patients which in turn lead to have a better condition for them [13]. Of course, it's worthwhile to mention that the overall survival rate decreases with the prolong hospitalization in ICUs which is different based on type of microorganism.

Based on our study, blood stream infections (BSI) and infections associated with ventilator and catheter events lead to an increased risk of death and decreased survival rate in patients with HAIs admitted to the ICU. In our study, the most common microorganisms that increased the risk of death and decreased survival rate were: Candida Albicans, Candida, Acinetobacter, Enterococcus and Enterobacter. These findings are consistent with the results of other reports [13, 26–29]. Therefore, it is of high importance to pay special attention to these microorganisms, while trying to prevent their occurrence, considering appropriate and adequate treatment for each of these cases are essential.

This study was the first comprehensive and national study conducted on the survival rate in patients with ICU-acquired infections and its related factors in Iran's hospitals using a nationwide registered data. Although, its coverage is about 83.5% and therefore it is not generalizable to not cover hospitals, but a random selection of all included hospitals almost represent the national situation of ICU-AIs and provide a national view.

On the other hand, the surveillance data are often limited in terms of recorded variables. Different scoring systems based on clinical and laboratory findings that predict the mortality in patients with critical situations such as the acute physiology and chronic health evaluation (APACHE) score, sequential organ failure assessment (SOFA), mortality in emergency department sepsis (MEDS), and other similar scoring systems are not covered in the INIS dataset. Therefore, we were not able to assess the effect of such variables on mortality at ICU admission.

Conclusions

Despite the above mentioned limitations of the nosocomial infection surveillance system, the results of our report, provided a general picture for the survival rate and its related risk factors among ICU-AIs. It seems that the nosocomial infections surveillance system should be more intelligent. This intelligence should act differently based on related factors such as the age of patients, hospitalization-infection length, infection type,

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microorganism and type of ward. In other words, this system should be able to dynamically provide the necessary and timely warnings based on the factors affecting the survival rate of infection due to the identification, intervention and measures to prevent the spread of HAIs based on a risk severity system.

Abbreviations

CAUTI: Catheter-related urinary tract infection; CLABSI: Central line-associated bloodstream infections / septicemia; HAIs: Hospital-acquired infections; ICU-AIs: ICU-acquired infections; ICUs: Intensive care units; INIS: Iranian nosocomial infections surveillance; IQR: Interquartile range; VAE/VAP: Ventilator-associated events / respiratory infections / pneumonia; HR: Hazard ratio; Cl: Confidence interval; SSI: Surgical site infections; CDI: Clostridium difficile infections; APACHE: Acute physiology and chronic health evaluation; SOFA: Sequential organ failure assessment; MEDS: Mortality in emergency department sepsis; NNIS: National nosocomial infections surveillance system; PENU & LRI: Pneumonia events & lower respiratory tract infection

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-021-10857-y.

Additional file 1: Appendix 1. Univariable Cox regression analysis of survival of ICU-acquired infection patients by ward.

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Authors' contributions

K. E: Contribution to study concept and design, drafting of the manuscript. Y. Kh: Contribution to study concept and design, drafting of the manuscript. SS. HN: Contribution to study concept and design, acquisition, analysis and interpretation of data, drafting of the manuscript. N. I: Contribution to study concept and design, acquisition, analysis and interpretation of data, drafting of the manuscript. B. E: Contribution to study concept, design, and interpretation of data. Y. M: Contribution to analysis and interpretation of data. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All procedures performed in the study were approved by the ethical committee of the National Institute for Medical Research Development. Also informed consent was obtained from all participants. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable. The manuscript does not contain patient identifiable data.

Competing interests

The authors declare that they have no competing interests.

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