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Original Article

The incidence and risk factors of nosocomial infections in intensive care unit in China: an epidemiological study of 1718 patients

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Abstract: Objective: This study aims to explore the incidence and risk factors of nosocomial infections (NIs) in the intensive care unit (ICU) in China. Methods: Between January 2011 and December 2013, a total of 1718 patients with a mean age of 59.02 ± 20.71 years in ICU were included. Clinical data of these patients, including gender, age, length of stay, the overall rate of patients with NIs, the distribution of NIs sites and pathogens, were collected. Univariate analysis was used to determine the potential risk factors for NIs in ICU and the multivariate analysis was performed to identify independent risk factors. Results: Among 1,718 patients, the overall NIs rate was 32.48% (558/1,718). Respiratory tract infection (RTI) accounted for 64.75% of total NIs, followed by urinary tract infection (UTI) for 9.4% and bloodstream infection (BSI) for 7.96%. Of the 558 patients with NIs, 2378 pathogens were identified, in which gram-negative aerobic bacilli (71.4%) were the most frequent, and followed by gram-positive aerobic bacilli (19.26%). Univariate analysis showed that length of stay, urinary catheter, blood catheter and and ventilator were associated with NIs in ICU. Multivariate analysis demonstrated that length of stay, urinary catheter and ventilator were independent risk factors for NIs in ICU. Conclusion: There was a relatively high and stable incidence of NIs in ICU. Length of stay, use of urinary catheters and ventilator were independent risk factors for NIs in ICU.

Keywords: Nosocomial infections, intensive care unit, incidence, risk factors

Introduction

Nosocomial infections (NIs), also known as healthcare acquired infection, have become considerable threats to hospitalized patients, which resulting in increasing length of stay, medical costs and complication rates [1, 2]. NIs had risen to be the fourth dominant factor of disease in industrialized countries, as it has been proved in China that the incidence rate of NIs was 26.8% among 1980 patients. Additionally, intensive care units (ICUs) were demonstrated to be highly susceptible areas where NIs occur frequently [3-5]. An epidemiology study of NIs in 125 Italian ICU showed that ICU-acquired infections had a relatively high overall incidence of 27.2% and hospital mortality of 35.1% [6]. Besides, according to an international multicenter study of 28 ICU, NIs are one of the leading causes of death in ICUs despite being largely preventable, 19% of ICU patients suffered from infections, and the estimated frequency was 9.8 outbreaks out of 100,000 admissions [7, 8].

It has been revealed that patients treated in ICU were associated with a higher risk of developing various disease entities, including bloodstream, respiratory, urinary and wound infections, resulting in higher overall morbidity and mortality [8-10]. NIs in ICUs are related to drug-resistant micro-organisms, such pathogens as acinetobacter baumannii, escherichia coli, pseudomonas aeruginosa, and staphylococcus aureus in ICUs are highly resistant to drugs, which pose great threats to therapeutic problems [11-14]. As reported previously, a hospitalized patient had been proved to be

susceptible to infection for many reasons, such as surgery, contact with other patients and hospital staffs, and hospital environment [2, 8]. The etiology that has been confirmed of NIs included immune dysregulation, unavoidable invasive procedures, poor nutritional statuses and serious underlying diseases [3, 15-18]. Previous studies have also demonstrated that there are two main pathophysiological factors for the development of NIs in ICU, namely decreased host defenses and colonization by potentially pathogenic bacteria [19, 20]. In addition, more studies have suggested that the use of invasive devices is one of the major risk factors for the development of NIs in ICU patients, including intracranial pressure monitoring devices, endotracheal tubes and venous and urinary catheters [21-23]. Therefore, we aimed to explore the incidence and potential risk factors of NIs in ICU so as to seek effective intervention measures which can control NIs in ICU.

Materials and methods

Study subjects

This study was conducted in the The First Affiliated Hospital, College of Medicine, Zhejiang University with over 1000 beds and one mixed ICU of 22 beds, which situates in Zhejiang Province, China. Since 2003, the hospital has started the prospective hospital-wide surveillance of NIs in ICU. Between January 2011 and December 2013, a total of 1,718 patients (1,113 males and 605 females) with a mean age of 59.02 ± 20.71 years in ICU were involved. This study was performed with the approval of the Medical Ethics Committee of The First Affiliated Hospital, College of Medicine, Zhejiang University. The beds for all the patients remained unchanged (we have 2500 beds in total, including 29 beds for the integrated ICU. All patients with infections admitted to ICU for more than 48 hours were monitored for NIs. In addition, infections transferred to another apartment or discharged within 48 hours were also treated as ICU-associated infections unless the evidence strongly suggested contrary.

NIs surveillance and data collection

All patients were monitored in ICU for at least 1 calendar month for NIs that affected specific body sites. An experienced infectious disease specialist was invited to check and verify the reports of NIs cases. Following the American modified Centers for Disease Control (CDC) and Prevention for NI [24], the major NIs, including UTI (urinary tract infection), BSI (primary blood-stream infection), RTI (respiratory tract infection), SSI (surgical site infection) and other infections, were identified. The data collected from patients included baseline characteristics (gender, age and length of stay), the overall rate of patients with NIs, the sites of NIs, pathogens and the discharge status in ICU (dead or alive) and. All patients were divided into two groups: patients with NIs and patients without NIs.

The overall rate of patients with NIs during the defined period of time was calculated by the total number of patients with NIs divided by the total number of patients in ICU (×100). Device-associated infection rates were calculated by the number of device-associated infections divided by the total number of days of relevant devices use (×1,000) for blood-stream, urinary tract and pneumonia infections. The total number of days was calculated by adding up the days of each patient in ICU. In the meantime, dates of admission and discharge from ICU was defined as the total days when a patient stayed in ICU and other departments to which the patient was transferred after the conditions remained stable after leaving ICU. The excess length of stay in ICU was then calculated by the average days of patients with NIs minus the average days of patients without NIs.

A single professional infection control survey was performed during the entire period of study in ICU. The staffs in our ICU were required to complete a specialized knowledge of NIs training program. The intensive care physician (1:3) and the nursing staff (1:2) provided coverage for 24 hours per day. There were no introduction of novel technology and no major changes in physician staffing and in ICU during the study period.

Statistical analysis

SPSS 18.0 software (SPSS, Chicago, USA) was performed for all statistical analysis. The Mann-Whitney nonparametric test for continuous variables and the chi-square test for cate-

Table 1. The incidence rates of NIs of patients in ICU

	Case number (%)	Male (%)	Female (%)	Mean age (%)	Patients with Nis (%)	Patients without Nis (%)	Incidence rate (%)
Year							
2011	500 (29.10)	353 (20.55)	147 (8.56)	58.63 ± 20.27	145 (8.44)	355 (20.66)	29
2012	553 (32.19)	360 (20.95)	193 (11.23)	58.16 ± 20.14	198 (11.53)	355 (20.66)	35.81
2013	665 (38.71)	400 (23.28)	265 (15.42)	60.02 ± 21.49	215 (12.51)	450 (26.19)	32.33
Age							
<20	66 (3.84)	44 (2.56)	22 (1.28)	17.45 ± 1.20	21 (1.22)	45 (2.62)	31.82
20~	277 (16.12)	188 (10.94)	89 (5.18)	29.69 ± 5.88	89 (5.18)	188 (10.94)	32.13
40~	419 (24.39)	258 (15.02)	161 (9.37)	50.39 ± 5.28	131 (7.63)	288 (16.76)	31.26
60~	735 (42.78)	487 (28.35)	248 (14.44)	69.23 ± 5.96	235 (13.68)	500 (29.10)	31.97
≥80	221 (12.86)	136 (7.92)	85 (4.95)	90.60 ± 6.28	82 (4.77)	139 (8.09)	37.1
Length of days							
<5	706 (41.09)	476 (27.71)	230 (13.39)	45.71 ± 17.66	30 (1.75)	676 (39.35)	4.25
5~	429 (24.97)	278 (16.18)	151 (8.79)	60.67 ± 16.50	109 (6.34)	320 (18.63)	25.41
10~	203 (11.82)	122 (7.10)	81 (4.71)	66.52 ± 18.70	116 (6.75)	87 (5.06)	57.14
15~	225 (13.10)	140 (8.15)	85 (4.95)	75.34 ± 11.88	159 (9.25)	66 (3.84)	70.67
30~	94 (5.47)	62 (3.61)	32 (1.86)	76.15 ± 11.60	85 (4.95)	9 (0.52)	90.43
≥60	61 (3.55)	35 (2.04)	26 (1.51)	89.87 ± 6.35	59 (3.43)	2 (0.12)	96.72

NIs: nosocomial infections. ICU: intensive care unit.

gorical variables were used to compare the characteristics of patients in two groups. Two continuous variables within one group were compared by Wilcoxon's test. The association between NIs and potential risk factors was identified by Chi-square test in univariate analysis. Variables significantly different between two groups were analyzed in a forward stepwise logistic-regression model to confirm independent risk factors associated with NIs. Logistic regression analysis was performed to calculate the odds ratio (OR) and 95% confidence interval (CI) by using NIs as a dependent variable and the clinical data (ie. baseline characteristic and use of catheters) as independent variables. For all analyses, $P<0.05$ was considered to indicate a statistical significance.

Results

Baseline characteristics of patients and the overall incidence of NIs in ICU

From 2011 to 2013, of the 1,718 patients (mean age: 59.02 ± 20.71 years) admitted to ICU, 1,113 (64.78%) were males and 605 (35.22%) were females. There were 762 patients (44.35%) less than 60-year-old and 965 patients (55.65%) over 60-year-old. There were a total of 1563 cases whose length of stay was less than 30 days and 155 cases more than 30 days. The overall infection rate was 32.48%. In 2001, there were 353 males and 147 females in 500 patients in which 222 patients were less than 60-year-old and 278 patients were over 60-year-old, with a mean age of 58.63 ± 20.27 years. In 2012, totally 553 patients (360 males and 193 females; mean age: 58.16 ± 20.14 years) were included, with 308 patients over 60-year-old and 245 patients less than 60-year-old. In 2013, 665 patients (400 males and 265 females) with a mean age of 60.02 ± 21.49 years were enrolled in the study. There were 293 patients less than 60-year-old and 372 patients over 60-year-old. By comparing the five age groups (<20, 20~40, 40~60, 60~80, ≥80), it was found that patients over 80 years had the highest rate of infection (37.10%). By the comparison between different length of days (<5 d, 5~10 d, 10~15 d, 15~30 d, 30~60 d and ≥60 d), it was observed that patients who stayed over 60 days in hospital were most likely to be infected, with the rate being 96.72% (**Table 1**).

Table 2. Distribution of NIs sites of patients in ICU

Site	Number of infections	Infection proportion (%)
Respiratory tract	496	64.75
Bloodstream	61	7.96
Urinary tract	72	9.40
Surgical site	40	5.22
Abdominal cavity	11	1.44
Skin and soft tissue	26	3.40
Others	60	7.83

NIs: nosocomial infections. ICU: intensive care unit.

Table 3. Distribution of the main pathogens of NIs in ICU

Pathogen	Number (n)	Proportion (%)
Gram-negative aerobic bacilli	849	71.4
Pseudomonas aeruginosa	187	15.73
Acinetobacter baumannii	132	11.1
Klebsiella pneumoniae	99	8.33
Escherichia coli	75	6.31
Other Gram-negative	356	29.94
Gram-positive aerobic bacilli	229	19.26
Staphylococcus aureus	131	11.02
Staphylococcus epidermidis	24	2.02
Hemolytic streptococcus	23	1.93
Enterococcus	14	1.18
Other Gram-positive	37	3.11
Fungi	111	9.34
Candida albicans	25	2.1
Candida glabrata	10	0.84
Other fungi	76	6.39

NIs: nosocomial infections. ICU: intensive care unit.

Frequency of catheter use in ICU

In 2011, the total days of 1718 patients in hospital was 4274 days. During this period, the urinary catheter, the blood catheter and the ventilator were used for 2029 days, 1903 days and 1814 days, with the utilization ratio being 47.50%, 44.55% and 42.46% respectively. In 2012, the total days was 6358 days in which the urinary catheter was applied for 3489 days, the blood catheter for 2792 days and the ventilator for 2896 days. Their utilization ratios were 54.88%, 43.91% and 45.55% respectively. In the total 8610 days of stay in 2013, the time when the urinary catheter, the blood catheter and the ventilator were used were 4396 days, 4153 days and 3495 days, accounting for 51.06%, 48.23% and 40.59% of utilization ratio respectively.

Incidences and sites of NIs

Among the 558 NIs, RTIs accounted for 64.75%, followed by UTIs (9.4%) and BSIs (7.96%). A total of 69.0% patients with nosocomial RTIs had received tracheotomy before the infections or mechanical ventilation, whereas 52.0% of nosocomial UTIs and 51.3% of nosocomial BSI were catheter associated (**Table 2**).

Pathogen distribution of patients with NIs

Of the 558 NIs, 2378 pathogens were isolated and identified (**Table 3**). In the 849 Gram-negative aerobic bacilli (71.4% of the total pathogens), pseudomonas aeruginosa (187, 15.73%) was the most frequent, followed by acinetobacter baumannii (132, 11.1%), and klebsiella pneumoniae (99, 8.33%). In the 229 Gram-positive aerobic bacilli (19.26% of the total pathogens), staphylococcus aureus (131, 11.02%) was the highest, followed by staphylococcus epidermidis (24, 2.02%) and hemolytic streptococcus (23, 1.93%). Candida albicans (25, 2.1%) accounted for the majority of the total 111 Fungi (9.34% of the total pathogens).

Univariate and multivariate analyses

Of the 1,718 patients, 570 (232 infected and 338 uninfected) died during ICU stay with mortality rate of 33.18%. The overall fatality rate among the infected patients was 41.58% (232/558) compared to 29.14% (338/1160) in the uninfected group. A stepwise logistic regression analysis was performed to identify the variables associated with NIs rates. With NIs status in ICU as the dependent variable and potential NIs-related indices (gender, age, length of stay, urinary catheter, blood catheter and ventilator) as the independent variables, univariate analysis was performed. The results suggested that gender (male vs. female), age (<60 vs. ≥60) were not related to NIs in ICU (all $P>0.05$), but the length of stay (≥30 d vs. <30 d; 95% CI=15.842~18.099; $P<0.05$), urinary catheter (used vs. unused; 95% CI=6.815~7.783; $P<0.05$), blood catheter (used vs. unused; 95% CI=7.385~8.371;

P<0.05) and ventilator (used vs. unused; 95% CI=6. 842~7.730; *P*<0.05) were factors associated with NIs in ICU. Regarding NIs status in ICU as the dependent variable and NIs-related indices (length of stay, urinary catheter, blood catheter and ventilator) as the independent variables, multivariate analysis was conducted. The results demonstrated that length of stay (≥30 d vs. <30 d; OR=1.052; 95% CI=1.014~1.090; *P*<0.05), urinary catheter (used vs. unused; OR=1.091; 95% CI=1.028~1.158; *P*<0.05) and ventilator (used vs. unused; OR=1.187; 95% CI=1.122~1.256; *P*<0.05) were the independent risk factors for NIs in ICU.

Discussion

Along with development of modern medical techniques and the clinical application of a variety of surgical operations, NIs was considered to be an important risk factor for the prognosis of patients, which has been widely accepted by various medical personnel and medical researchers [25]. On the other hand, the patients in ICU have been reported to be more easily suffered from NIs, which may be caused by the invasive operations or low immunity ability [26]. It was worthwhile to note that NIs might not only directly or indirectly cause the death of critical patients, but also directly influence the treatment or operation of patients, prolong the hospitalization time and increase the hospitalization costs, which may largely increase the social-economic burden and have negative effects on the prognosis of patients [27]. The primary objective of this study was to investigate the actual state and the characteristics of nosocomial infections (NIs) in ICU, and to analyze the related risk factors for NIs in order to supply scientific evidences for intervening measures to reduce the incidence of NIs in ICU. In our study, we monitored totally 1718 critical patients in ICU from 2011 to 2013, and we found that the overall incidence of patients with NIs was up to 32.48%, which was significantly high. As we all know, the critical patients in ICU may be considered to be suffered from serious diseases and has invasive operations with low immunity ability, which may be sensitive to the viral and bacterial infections resulted in the incidence of NI [28, 29]. Previous studies have demonstrated that critical patients in ICU were often associated with longer length of stay and may have higher hospital mortality rate compared with other patients [30, 31]. Notably, the immunity of patients was obviously decreased and may be sensitive to the pathogenic microorganisms along with the progression of disease, which may cause more serious issues and result in poor prognosis of patients [32]. On the other hand, infants and elderly people have been reported to be susceptible population with lower immunologic function or hypofunction of organs, which was in consistent with the findings in our study [33-35].

In addition, we observed that a variety of risk factors may be associated with the occurrence and development of NIs, including length of stay, use of catheters (urinary catheter and blood catheter) and ventilator. We should pay more attention to the influencing factors of the critical patients in ICU, who was considered to be the group with high risk of NIs. Numerous studies have shown that the incidence of NIs was closely related to the process of various invasive operations and virus infections [36, 37]. Rosenthal VD et al. have revealed that device-associated infections in ICUs was regarded as one of the most important influencing factors in the occurrence and development of NIs, and it's more serious in developing countries when compared with the developed countries, which may largely affect the prognosis of patients [38]. In our study, we found that the rate of ventilator-related RTIs was up to 46.24%, blood catheter-associated BSIs was up to 7.07%, and the catheter-associated UTIs was 4.09%. These results have implied that the device-associated infection rates were significantly high in ICU patients, and the ventilator may be the major influencing factor leading to the incidence of NIs. In this regard, to further reduce the incidence of NIs, we should pay more attention to reducing the frequency of invasive operations as possible as we can or attempt to downregulate the usage time when possible [39, 40]. Another important finding in our study have revealed that the lower respiratory tract was the uppermost infected area of patients in ICU, with the infection rate of 64.75%, which was significantly higher than other infected areas. Due to the serious conditions, patients in ICU was considered to be more likely suffered from microbial infections, which may be resulted from serious wound infection, pneumonia, alimentary infection and so on [11, 40,

41]. In this regard, the effective measures and targeted intervention should be undertaken to reduce the incidence of NIs.

In summary, our results supported the view that there was a relatively high and stable incidence of NIs in ICU. Length of stay, use of urinary catheters and ventilator were independent risk factors for NIs in ICU, which may be related to the occurrence of NIs. Thus, we should pay more attention to more the influencing factors and take targeted intervention and effective measures to reduce the morbidity of patients with NIs in ICU.

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Disclosure of conflict of interest

None.

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