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ORIGINAL RESEARCH

Clinical Impact and Risk Factors of Intensive Care Unit-Acquired Nosocomial Infection: A Propensity Score-Matching Study from 2018 to 2020 in a Teaching Hospital in China

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Purpose: Nosocomial infection (NI) is associated with poor prognosis. The present study assessed the clinical and microbiological characteristics of NI patients in the intensive care unit (ICU) and investigated the clinical impact and risk factors for NI in ICU patients.

Patients and Methods: An observational study was conducted in an adult general ICU. The electronic medical records of all patients admitted to the ICU for >2 days from 2018–2020 were analyzed retrospectively. Multivariate regression models were used to analyze the risk factors for NI in ICU patients. Propensity score-matching (PSM) was used to control the confounding factors between the case and control groups, thus analyzing the clinical impact of NIs.

Results: The present study included 2425 patient admissions, of which 231 (9.53%) had NI. *Acinetobacter baumannii* (33.0%) was the most common bacteria. Long-term immunosuppressive therapy, disturbance of consciousness, blood transfusion, multiple organ dysfunction syndromes (MODS), treatment with three or more antibiotics, mechanical ventilation (MV), tracheotomy, the urinary catheter (UC), nasogastric catheter, and central venous catheter (CVC) were risk factors for NI in the ICU patients. After PSM, patients with NI had a prolonged length of stay (LOS) in the ICU and hospital, significant hospitalization expenses (all $p<0.001$), increased mortality ($p=0.027$), and predicted mortality ($p=0.007$). The differences in the ICU and hospital LOSs among three pathogens were statistically significant ($p<0.001$); the results of the *Escherichia coli* infection group were lower than the other two pathogenic groups.

Conclusion: NI was associated with poor outcomes. The risk factors for NI identified in this study provided further insight into preventing NI.

Keywords: nosocomial infection, epidemiology, North China, propensity score-matching, intensive care unit, retrospective study

Introduction

Nosocomial infection (NI) is defined as an infection occurring in a patient admitted to a healthcare facility for >48 h but without any evidence that the infection was present or incubating at the time of admission.[1] The incidence rates of NI in China from 2018–2020 were 1.91%, 1.86%, and 1.65%, respectively, which decreased steadily.[2] However, the NI rate in the intensive care unit (ICU) was about 22%.[3] It increased the hospitalization costs for patients, reduced the health-related quality of life, had a substantial effect on morbidity and mortality, prolonged the length of stay (LOS), reduced bed turnover rates, and seriously affected the quality of medical care, thus becoming a major global public health

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concern.[4] Reportedly, 33% of the NIs are preventable.[5] Therefore, studying clinical and preventive medicine related to NI is a challenging issue in modern hospital management but needs to be investigated in depth.

The current studies are primarily focused on the epidemiology and economics of nosocomial infection; however, statistics present a wide variation in the clinical outcomes and methods used for estimation. A few studies on the economic losses of NIs are descriptive studies matching a few variables such as age and gender, which may have a significant confounding bias.[6–8] Therefore, we used a propensity score-matching analysis (PSM) to evaluate the direct economic burden of NIs to minimize the influence of confounding factors. In addition, we also analyzed the risk factors of NI. This would help us comprehend the clinical characteristics of hospital-infected patients in the ICU, quickly and accurately identifying those who are susceptible to the infection and implementing protection and prevention measures to reduce the physical and financial burden of patients while improving the level of diagnosis and treatment of hospital infections.

Materials and Methods

Study Design and Settings

A retrospective observational cohort study was conducted in the ICU of the Second Hospital of Shanxi Medical University, a tertiary hospital in Shanxi Province, China. It is a 2700-bed teaching hospital with an 18-bed ICU. The study complied with the Declaration of Helsinki and was carried out from January 1, 2018 to December 31, 2020. The control group comprised patients without NIs who had a length of stay >48 h and were hospitalized during the same period. This study was approved (2021YX −161) by the Ethics Committee of the Second Hospital of Shanxi Medical University, with a waiver of informed consent from the patients.

Data Collection

NI was developed 48 h after ICU admission and diagnosed according to the standards for NI surveillance issued by the Ministry of Health of China.[1] NI was diagnosed based on the following parameters: (1) Conform to both clinical symptoms and pathogenic diagnosis; (2) Reports by clinicians and pharmacists; (3) Confirmation by staff members of the hospital's infection-control department. The exclusion criteria were as follows: (1) Only culture results of pathogenic bacteria without clinical signs and symptoms; (2) Patients with repeat ICU admissions during a single hospital stay, the first admission information was recorded. Patient data included demographic information, illness severity, comorbidities on ICU admission, invasive procedures, drug usage, and clinical outcomes. Illness severity was evaluated by Acute Physiology and Chronic Health Evaluation (APACHE) II score during the first 24 h of ICU admission. The comorbidities on the ICU admission, including chronic underlying diseases (respiratory diseases, cardiovascular diseases, malignancies, diabetes, hypertension, liver diseases, and renal diseases), consciousness disorder, blood transfusion, surgical operation, trauma, shock, hypoproteinemia, immunological diseases, pneumonia, and multiple organ dysfunction syndrome (MODS), were assessed during the diagnoses. Pneumonia in the comorbidities on ICU admission included both community-associated pneumonia and hospital-acquired pneumonia before ICU admission. The invasive procedures included mechanical ventilation (MV), tracheal intubation, tracheotomy, the urinary catheter (UC), nasogastric catheter, drainage catheter, central venous catheter (CVC), and continuous renal replacement therapy (CRRT).

Definition of Outcome Indicators

The clinical outcomes consist of the LOS in the ICU and hospital, costs of hospitalization and antimicrobial drugs, death in the ICU (all-cause mortality), and predicted death in the ICU. Hospitalization costs are the direct medical costs incurred by patients during their stay in the hospital. Predicted death in the ICU included death in the ICU and after discharge against medical advice because of critical conditions and the patient's desire to die at home.[9] Hospitalization costs are the direct medical costs incurred by patients during their stay in the hospital.

PSM

To minimize the impact of potential confounding variables, we employed PSM using R Package Matching version 4.0.4 (CRAN.R-project.org/package = Matching). Based on previous reports, consultation with the relevant experts, and in conjunction with the ICU-targeted monitoring database, factors that may affect patient prognostic indicators were identified for inclusion as adjustment factors. Herein, we input variables that included the patient's demographics (age and sex), APACHE II score on ICU admission, malignancies, a disorder of consciousness, surgical operation, trauma, shock, MV, CVC, CRRT, and MODS.[9,10] We also used the predicted probabilities of each potential confounding variable for PSM. The propensity score was balanced between the two groups; therefore, nearest-neighbor matching was employed to obtain the matched pairs of subjects and controls at a 1:2 ratio and a 0.02 calipers value. Variables with an absolute value of standard deviation (SD) ≤0.1 after PSM indicated a balance between the groups. The resultant pairs were subjected to additional clinical outcome analyses.

Statistical Analysis

Statistical analyses were performed using SPSS 25.0. Continuous variables were described as means and standard deviations (SD) when fitting a normal distribution, otherwise as medians and interquartile range (IQR), while categorical variables were expressed as percentages. Chi-square and Fisher's exact tests were used to compare the categorical variables. If the two groups of continuous variables showed normal distribution, the independent sample's *t*-test was used; otherwise, the non-parametric test of two independent samples (Mann–Whitney *U*-test) was employed. Kruskal–Wallis test was used to analyze the differences in clinical outcomes between groups of infection sites and causative organisms. For evaluating the risk factors of NIs, the variables with a p-value <0.05 in the univariate analysis were selected for multivariate logistic regression models. All tests were two-sided, and p<0.05 was considered statistically significant.

Results

Population

A total of 2425 patients, including 1298 patients who stayed at least 48 h in our ICUs, were enrolled during the study period. A total of 231 patients acquired NIs after ICU admission, at a rate of 9.53%. The baseline characteristics of the

Table 1 Comparison of Patients with Nosocomial Infections and Without Nosocomial Infections Groups in Terms of the Baseline Characteristics and Risk Factors

	Univariate Analysis			Multivariate Analysis	
	Patients with NIs (N=231)	**Patients Without NIs (N=1067)**	**p-value**	**OR (95% CI)**	**p-value**
Gender, No. male (%)	163 (70.6)	613 (57.5)	**p<0.001**		
Age (years), median [IQR]	60.0 [47.0,74.0]	59.0 [45.0,72.0]	p=0.163		
Smoking history, No. (%)	83 (35.9)	302 (28.3)	**p=0.021**		
Long-term immunosuppressive therapy, No. (%)	18 (7.8)	31 (2.9)	**p<0.001**	2.57 (1.21,5.50)	**p=0.015**
APACHE II score on ICU admission, median [IQR]	19.0 [13.0, 27.0]	14.0 [9.0, 19.0]	**p<0.001**		
Chronic underlying diseases					
Respiratory diseases, No. (%)	31 (13.4)	93 (8.7)	**p=0.027**		
Cardiovascular diseases, No. (%)	66 (28.6)	322 (30.2)	p=0.629		
Malignancies, No. (%)	22 (9.5)	152 (14.2)	p=0.056		
Diabetes, No. (%)	30 (13.0)	168 (15.7)	p=0.290		
Hypertension, No. (%)	75 (32.5)	382 (35.8)	p=0.336		
Liver diseases, No. (%)	32 (13.9)	171 (16.0)	p=0.410		
Renal diseases, No. (%)	22 (9.5)	99 (9.3)	p=0.907		
Disorder of consciousness, No. (%)	73 (31.6)	112 (10.5)	**p<0.001**	1.80 (1.20,2.71)	**p=0.005**
Blood transfusion, No. (%)	148 (64.1)	436 (40.9)	**p<0.001**	1.91 (1.31,2.78)	**p=0.001**
The surgical operation, No. (%)	109 (47.2)	671 (62.9)	**p<0.001**	0.50 (0.35,0.71)	**p<0.001**

(*Continued*)

Table 1 (Continued).

	Univariate Analysis			Multivariate Analysis	
	Patients with NIs (N=231)	**Patients Without NIs (N=1067)**	**p-value**	**OR (95% CI)**	**p-value**
Trauma, No. (%)	108 (46.8)	443 (41.5)	p=0.144		
Shock, No. (%)	61 (26.4)	156 (14.6)	**p<0.001**		
Hypoproteinemia, No. (%)	180 (77.9)	692 (64.9)	**p<0.001**		
Immunological diseases, No. (%)	22 (9.5)	73 (6.8)	p=0.156		
Pneumonia, No. (%)	106 (45.9)	272 (25.5)	**p<0.001**		
MODS, No. (%)	21 (9.1)	16 (1.5)	**p<0.001**	3.29 (1.51,7.17)	**p=0.003**
Invasive procedures					
MV, No. (%)	204 (88.3)	479 (44.9)	**p<0.001**	3.67 (2.26,5.96)	**p<0.001**
Tracheal intubation, No. (%)	156 (67.5)	403 (37.8)	**p<0.001**		
Tracheotomy, No. (%)	74 (32.0)	56 (5.2)	**p<0.001**	4.07 (2.56,6.48)	**p<0.001**
UC, No. (%)	228 (98.7)	967 (90.6)	**p<0.001**	3.79 (1.08,13.33)	**p=0.038**
Nasogastric catheter, No. (%)	199 (86.1)	491 (46.0)	**p<0.001**	2.442 (1.57,3.81)	**p<0.001**
Drainage catheter, No. (%)	119 (51.5)	584 (54.7)	p=0.374		
CVC, No. (%)	175 (75.8)	554 (51.9)	**p<0.001**	1.61 (1.07.2.44)	**p=0.024**
CRRT, No. (%)	29 (12.6)	51 (4.8)	**p<0.001**		
Prior antibiotics use					
Time of antibiotic use (days), median [IQR]	9.0 [5.0,14.0]	5.0 [3.0,9.0]	**p<0.001**		
Treatment with three or more antibiotics, No. (%)	110 (47.6)	236 (22.1)	**p<0.001**	1.84 (1.28,2.63)	**p<0.001**
Clinical result					
Deaths in ICU (mortality), No. (%)	28 (12.1)	23 (2.2)	**p<0.001**	-	-
Predicted deaths in ICU (predicted mortality), No. (%)	82 (35.5)	98 (9.2)	**p<0.001**	-	-

Note: P value in bold shows that the variables are statistically significant.
Abbreviations: NIs, Nosocomial infections; MODS, Multiple organ dysfunction syndromes; MV, Mechanical ventilation; UC, Urinary catheter; CVC, Central venous catheter; CRRT, Continuous renal replacement therapy; IQR, Interquartile range; OR, Odds Ratio.

study patients are shown in Table 1. The 231 patients with NI were 60-years-old, mostly males (163/231, 70.6%), and had a median APACHE II score of 10.0 at the time of ICU admission. Compared to the patients without NIs, those with NIs had a significantly higher in-ICU mortality rate (12.1% vs 2.2%, p<0.05).

Acquired Infection

A total of 389 pathogens were isolated from 231 infections: 293 Gram-negative bacilli, 78 Gram-positive cocci, and 18 fungi. The respiratory tract, bloodstream, urinary tract, and intra-abdominal events accounted for the majority of the ICU-acquired infections (56.3%, 22.4%, 6.2%, and 6.2%, respectively). *Acinetobacter baumannii* (31.6%), *Pseudomonas aeruginosa* (13.4%), and *Escherichia coli* (8.2%) were the most frequently isolated pathogens and *A. baumannii* had the highest rate of drug resistance (Table 2). *Enterobacter cloacae* also ranked in the top 10 in terms of isolation rate (Figure 1).

Risk Factors for NIs

The risk factors associated with NIs in the ICU patients were long-term immunosuppressive therapy [odds ratio (OR) 2.57, 95% confidence interval (CI): 1.21–5.50, p=0.015)], surgical operation (OR 0.50, 95% CI: 0.35–0.71, p<0.001), disturbance of consciousness (OR 1.80, 95% CI: 1.20–2.71, p=0.005), blood transfusion (OR 1.91, 95% CI: 1.31–2.78, p=0.001), MODS (OR 3.29, 95% CI: 1.51–7.17, p<0.001), and treatment with three or more antibiotics (OR 1.84, 95% CI: 1.28–2.63, p<0.001). Moreover, patients with invasive procedures were at high risk for developing NIs. These included MV (OR 3.67, 95% CI: 2.26–5.96, p<0.001), tracheotomy (OR 4.07, 95% CI: 2.56–6.48, p<0.001), UC (OR 3.79, 95% CI: 1.08–13.33, p=0.038), a nasogastric catheter (OR 2.44, 95% CI: 1.57–3.81, p<0.001), and CVC (OR 1.61, 95% CI: 1.07–2.44, p=0.024). Finally, the current results showed that surgical operations have advantages in these patients in lowering the risk of infection (OR 0.5, 95% CI: 0.35–0.71, p<0.001) (Table 1).

Table 2 Pathogens Associated with Selected Nosocomial Infection Types

Pathogen Type	Clinical Forms of NIs						MDR Bacteria (n=188)	Total (n=389)
	RTI (n=219)	BSI (n=87)	UTI (n=24)	IAI (n=24)	SSI (n=21)	Others (n=14)		
Gram-negative bacteria								
Acinetobacter baumannii, No. (%)	89 (40.6)	17 (19.5)	1 (4.2)	6 (25.0)	8 (38.1)	2 (14.3)	114 (60.6)	123 (31.6)
Pseudomonas aeruginosa, No. (%)	39 (17.8)	4 (4.6)	5 (20.8)	2 (8.3)	2 (9.5)	–	10 (5.3)	52 (13.4)
Escherichia coli, No. (%)	12 (5.5)	5 (5.7)	4 (16.7)	3 (12.5)	3 (14.3)	5 (35.7)	11 (5.9)	32 (8.2)
Klebsiella pneumoniae, No. (%)	15 (6.8)	3 (3.4)	2 (8.3)	3 (12.5)	2 (9.5)	2 (14.3)	7 (3.7)	27 (6.9)
Stenotrophomonas maltophilia, No. (%)	13 (5.9)	3 (3.4)	–	1 (4.2)	–	–	–	17 (4.4)
Miscellaneous Gram-negative bacilli, No. (%)	22 (10.0)	9 (10.3)	3 (12.5)	2 (8.3)	2 (9.5)	4 (28.6)	7 (3.7)	42 (10.8)
Gram-positive bacteria								
Coagulase-negative staphylococci, No. (%)	–	29 (33.3)	2 (8.3)	–	–	–	27 (14.4)	31 (8.0)
Enterococcus faecium, No. (%)	2 (0.9)	5 (5.7)	6 (25.0)	5 (20.8)	2 (9.5)	1 (7.1)	2 (1.1)	21 (5.4)
Corynebacterium striatum, No. (%)	9 (4.1)	2 (2.3)	–	–	–	–	1 (0.5)	11 (2.8)
Staphylococcus aureus, No. (%)	6 (2.7)	–	–	–	1 (4.8)	–	5 (2.7)	7 (1.8)
Miscellaneous Gram–positive cocci, No. (%)	1 (0.5)	5 (5.7)	–	1 (4.2)	1 (4.8)	–	4 (2.1)	8 (2.1)
Fungi								
Candida albicans, No. (%)	5 (2.3)	4 (4.6)	1 (4.2)	1 (4.2)	–	–	–	11 (2.8)
Non-*albicans Candida spp*., No. (%)	6 (2.7)	1 (1.1)	–	–	–	–	–	7 (1.8)

Abbreviations: MDR, Multi-drug resistant; NIs, Nosocomial infections; RTI, Respiratory tract infection; BSI, Bloodstream infection; UTI, Urinary tract infection; IAI, Intra-abdominal infection; SSI, Surgical site infection.

Impact of NIs on the Outcomes

After PSM, 196 cases in the case group were successfully matched (Table 3), and the distributions of covariates in the NIs group and the non-infection group were balanced (Figure 2). Compared with the control group, patients with NIs have prolonged LOS in the ICU (median 12.0 days, p<0.001) and hospital (median 14.0 days, p<0.001) and increased

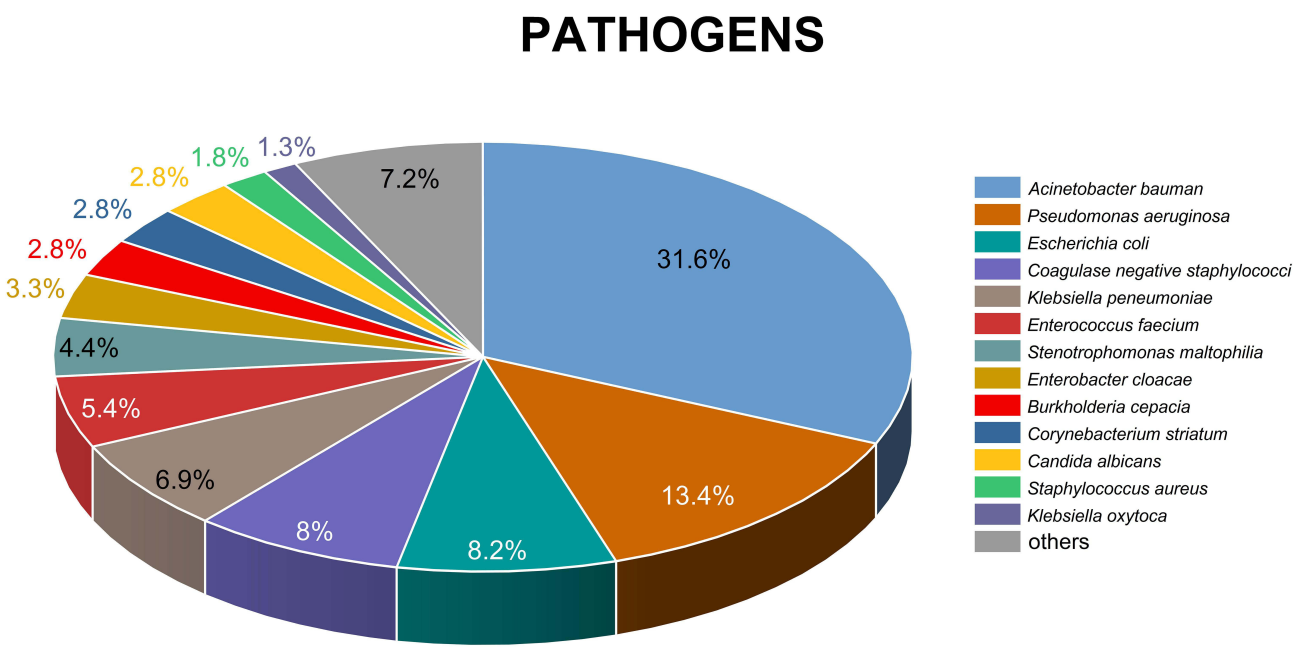

Figure 1 Pathogens cultured from nosocomial infections (NIs). The top thirteen hospital-acquired pathogenic bacteria are dominated by Gram-negative bacteria. The top five bacteria are *Acinetobacter baumannii* (31.6%), *Pseudomonas aeruginosa* (13.4%), *Escherichia coli* (8.2%), *Coagulase negative staphylococci* (8%), *Klebsiella pneumoniae* (6.9%).

Table 3 The Baseline Charities of the Two Groups of Patients Before and After Matching

Feature	Before PS Matching			After PS Matching		
	NIs (n=231)	Without NIs (n=1067)	p-value	NIs (n=196)	Without NIs (n=325)	p-value
Gender (male), No. (%)	163 (70.6)	613 (57.5)	p<0.001	136 (69.4)	223 (68.6)	p=0.854
Age, mean ± SD	59.81 ± 18.02	57.76 ± 18.63	p=0.128	59.33 ± 18.05	59.11 ± 17.09	p=0.890
APACHE II score, mean ± SD	19.88 ± 9.18	15.02 ± 7.62	p<0.001	18.96 ± 8.53	18.18 ±8.52	p=0.312
Malignancies, No. (%)	22 (9.5)	152 (14.2)	p=0.056	21 (10.7)	39 (12.0)	p=0.656
Disorder of consciousness, No. (%)	73 (31.6)	112 (10.5)	p<0.001	49 (25.0)	73 (22.5)	p=0.507
The surgical operation, No. (%)	109 (47.2)	671 (62.9)	p<0.001	99 (50.5)	191 (58.8)	p=0.066
Trauma, No. (%)	108 (46.8)	443 (41.5)	p=0.144	90 (45.9)	148 (45.5)	p=0.933
Shock, No. (%)	61 (26.4)	156 (14.6)	p<0.001	47 (24.0)	76 (23.4)	p=0.877
MODS, No. (%)	21 (9.1)	16 (1.5)	p<0.001	5 (2.6)	6 (1.8)	p=0.588
MV, No. (%)	204 (88.3)	479 (44.9)	p<0.001	169 (86.2)	282 (86.8)	p=0.860
CVC, No. (%)	175 (75.8)	554 (51.9)	p<0.001	142 (72.4)	232 (71.4)	p=0.794
CRRT, No. (%)	29 (12.6)	51 (4.8)	p<0.001	18 (9.2)	19 (5.8)	p=0.151

Abbreviations: PS matching, Propensity score matching; SD, standard deviation; NIs, Nosocomial infections; MODS, Multiple organ dysfunction syndromes; MV, Mechanical ventilation; CVC, Central venous catheter; CRRT, Continuous renal replacement therapy.

hospitalization (median 73,596.62-yuan, p<0.001), antibacterial drug costs (median 7612.44-yuan, p<0.001), mortality in the ICU (5.8%, p=0.005), and predicted mortality in the ICU (11.3%, p=0.003) compared to those without NI. The antimicrobial drug costs account for 1/10th of the overall hospital costs (Table 4).

Impact of Different Infection Sites and Pathogens on the Outcomes

Several studies have identified the association of NI with poor clinical outcomes, including LOS in hospitals, healthcare costs, and mortality. As shown in Table 5, the length of ICU stay in the *A. baumannii, P. aeruginosa*, and the *E. coli* groups were 20.0, 35.0, and 16 days, respectively. The length of hospital stay in the *A. baumannii* group, the *Pseudomonas aeruginosa* group and the *Escherichia coli* group were 33.5, 49, and 24 days, respectively. The differences in the ICU and hospital LOSs among the three pathogens were statistically significant (p<0.001), and that in the *E. coli* infection group was lower than in the other two pathogenic groups (LOS in ICU: *E. coli* vs *A. baumannii*, p<0.001, *E. coli* vs *P. aeruginosa*, p<0.001; LOS in hospital: *E. coli* vs *A. baumannii*, p<0.001, *E. coli* vs *P. aeruginosa*, p=0.001).

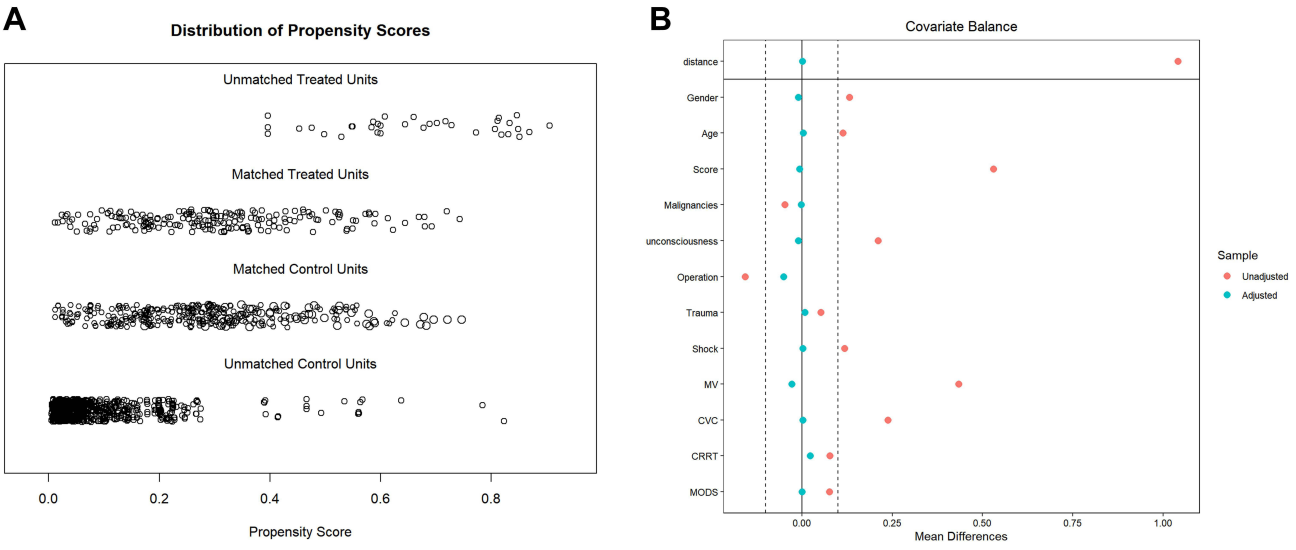

Figure 2 (**A**) Jitter plot of propensity score distribution. The distribution of propensity score between the control and infected groups before and after matching is indicated to understand the effect of matching. (**B**) Standardized difference scatter plot of each covariable. After matching, the corresponding point of the variable falls between −0.1 and 0.1, indicating that the variable reaches equilibrium.

Table 4 Excess Outcomes of Nosocomial Infection After PS Matching

Outcomes	NIs (n=196)	Without NIs (n=325)	Excess Values†	p-value
Hospitalization costs (CNY), median (IQR)	154,511.48 (108,377.07–213,081.81)	80,914.86 (49,894.51–130,853.22)	73,596.62	**p<0.001**
Antibacterial drug costs (CNY), median (IQR)	10,635.34 (4727.39–18,835.48)	3022.90 (1509.72–6137.23)	7612.44	**p<0.001**
LOS in ICU (days), median (IQR)	17 (11.0–28.75)	5.0 (4.0–10.0)	12.0	**p<0.001**
LOS in hospital (days), median (IQR)	30.0 (19.0–45.0)	16.0 (10.0–29.0)	14.0	**p<0.001**
Deaths in ICU (mortality)	18 (9.2%)	11 (3.4%)	5.8%	**p=0.005**
Predicted deaths in ICU (predicted mortality)	57 (29.1%)	58 (17.8%)	11.3%	**p=0.003**

Notes: † Excess values are the median difference between nosocomial and non-nosocomial infections. P value in bold shows that the variables are statistically significant.
Abbreviations: PS matching, Propensity score matching; NIs, Nosocomial infections; CNY, China Yuan; LOS, Length of stay; ICU, Intensive Care Unit; IQR, Interquartile range.

Discussion

A targeted surveillance of NI in the ICU is beneficial for decreasing the incidence of NI. Compared to other domestic studies, this survey based on the retrospective cohort data showed that the proportion (9.53%) of NIs was significantly higher than in studies from Jiangsu Province (7.23%),[11] Inner Mongolia Autonomous Region (3.62%),[12] and Hubei Province (5.51%)[13] and lower than in studies from Heilongjiang Province (12.87%)[14] and Anhui Province (15.11%).[15] The incidence of NIs in our hospital was much lower than in other countries.[3,16,17] The primary causes of infection rates vary according to the characteristics of the patient's condition, regional economic conditions, hospital size, medical treatment capacity, application of antimicrobial drugs, infection control, and case diagnosis level. Thus, our hospital should take comprehensive measures to reduce the incidence of NIs, such as enhanced training, information disclosure, and supervisory feedback.

The current study showed that respiratory tract infection is the most common type of infection, which is in accordance with the data published in the National Bacterial Resistance Surveillance Report in 2020.[18] Gram-negative bacteria were dominant, and *A. baumannii* (31.6%), *P. aeruginosa* (13.4%), and *E. coli* (8.2%) were the main pathogens. Consistent with other studies, *A. baumannii* is becoming a major cause of NIs in critically ill patients.[19,20] Previously, *Acinetobacter* was recognized as a low-virulent organism that causes infections primarily among immunocompromised hosts. Nonetheless, it has also acquired resistance to antibiotics over the past several years, and therefore its virulence is becoming an increasing concern. Multidrug-resistant *A. baumannii* (MDR-AB) has been reported worldwide and is now recognized as one of the most difficult NIs to be treated and controlled.[21,22]

Long-term immunosuppressive therapy, comorbidities on ICU admission, invasive procedures, and using three or more antibiotics were the main factors associated with a high prevalence of NIs among ICU patients in this study. A single-center point-prevalence survey in an American hospital showed that 96.8% of the hospitalized adult patients had at least one indwelling device;[23] however, the invasive operation destroys the normal defense of the body barrier, facilitating pathogen invasion and colonization.[24] The current study pointed out that tracheotomy with OR 4.07 and urinary catheters (UC) with OR 3.79 were the strongest independent risk factors for NI; these results were similar to the previously reported conclusions in adults about the risk factors of NIs.[25,26] In addition, the long-term use of a variety of antibiotics will inhibit the immune function of the body, disturb the normal flora of the patient body, affect the stability of the internal environment, provide adequate conditions for the breeding and reproduction of pathogens, and increase the possibility of NI occurrence.[27,28] However, some studies showed that previous broad-spectrum antibiotics are associated with the acquisition of MDR bacterial infections.[29,30] This phenomenon indicated that prudent and high-quality antibiotics prescription and rational use of antibiotics are essential to restrict the overuse of antibiotics, thereby reducing the occurrence of NIs among ICU patients. Some studies have shown that a large number of blood transfusions and stale storage components in the blood can promote the activation of inflammatory cytokines in the lung endothelium and induce NIs.[31] Several studies have shown an association between blood transfusions and subsequent ICU-acquired infections,[32–34] with platelet transfusions having a higher risk than other blood components.[35,36] A meta-analysis by Rohde et al demonstrated that a restrictive blood transfusion policy significantly reduces the incidence of infection.[37] Therefore, restrictive transfusion strategies are essential for preventing and controlling hospital infections. Furthermore, patients with consciousness disorders have an increased risk of aspiration due to long-term bed rest, the disappearance of

Table 5 Clinical Outcomes of Nosocomial Infection with Different Clinical Forms and Pathogens After PS Matching

	Hospitalization Costs (CNY), Median (IQR)		Antibacterial Drug Costs (CNY), Median (IQR)		LOS in ICU (Days), Median (IQR)		LOS in Hospital (Days), Median (IQR)		Deaths in ICU (Mortality)		Predicted Deaths in ICU (Predicted Mortality)	
	NIs	Excess Values[†]	NIs	Excess Values[†]	NIs	Excess Values[†]	NIs	Excess Values[†]	NIs	Excess Values[†]	NIs	Excess Values[†]
Clinical forms of NIs												
RTI	154306.67 (101,898.14–224,490.40)	73,917.06*	10,750.06 (3831.29–219,622.42)	7727.16*	18.0 (11.0–31.5)	13.0*	32.0 (18.5–45.0)	16.0*	10.1%	6.2%*	32.6%	13.0%*
BSI	154721.37 (118,175.07–243,561.31)	63,542.07*	13,886.05 (7032.21–21,189.34)	10,818.96*	18.0 (12.0–31.0)	12.0*	33.0 (21.0–47.0)	16.0*	10.2%	8.1%*	30.5%	12.8%
UTI	157989.98 (117,470.02–213,772.21)	78,715.35*	9792.95 (5466.29–19,587.44)	6770.05*	31.0 (14.0–48.0)	26.0*	36.0 (20.0–50.0)	19.0*	17.4%	14.8%*	30.4%	20.1%*
Pathogen types of NIs												
Acinetobacter baumannii	168,007.51 (107,875.63–239,758.31)	83,887.69*	12,823.32 (5824.70–24,739.18)	10,185.81*	20.0 (12.75–34.0)	14.0*	33.5 (18.75–46.5)	17.5*	11.0%	7.2%*	32.9%	7.1%
Pseudomonas aeruginosa	21,377.21 (154,725.89–316,503.82)	135,248.97*	16,106.96 (7815.02–23,021.48)	12,027.96*	35.0 (20.0–63.0)	29.0*	49.0 (39.0–77.0)	34.0*	20.0%	11.2%	45.7%	26.4%*
Escherichia coli	154,721.37 (116,483.76–198,699.56)	79,697.37*	11,495.36 (8101.03–18,725.63)	8949.20*	16.0 (10.5–19.5)[ab]	11.0*	24.0 (19.5–41.5)[cd]	9.0*	12.0%	12.0%*	32.0%	29.7%*

Notes: [a]Compared with *Acinetobacter baumannii*, p < 0.001. [b]Compared with *Pseudomonas aeruginosa*, p < 0.001. [c]Compared with *Acinetobacter baumannii*, p < 0.001. [d]Compared with *Pseudomonas aeruginosa*, P = 0.001. [†] Excess values are the median difference between nosocomial and non-nosocomial infections. *p-value is < 0.05.

Abbreviations: NIs, Nosocomial infections; CNY, China Yuan; LOS, length of stay; BSI, Bloodstream infection; RTI, Respiratory tract infection; UTI, Urinary tract infection; IQR, Interquartile range.

cough reflex, and insufficient food intake, which become high-risk factors for nosocomial infection.[38,39] Finally, patients with MODS have a combination of risk factors. Therefore, in all patients, MODS is associated with exceptionally high rates of infection.[40,41]

Conversely, surgical operations exhibited a protective effect on ICU inpatients to prevent NIs. Tai showed that compared to the non-surgery group, the surgery group has less diabetes, tracheotomy, and ICU LOS, lower APACHE II score, and younger age.[42] In the current study, we found that the number of patients with disturbed consciousness and tracheotomy in the surgery group was significantly lower than that in the non-surgery group. In summary, the risk of NIs was lower due to fewer comorbidities and risk factors. In addition, surgical site infections (SSIs) are the most common type of infection in surgical patients;[43] and the surgeries in our study were mainly orthopedic surgeries, hence, clinical active debridement surgery and the application of local bone cement can effectively reduce the occurrence of NI.[44,45] Nevertheless, the protective factors of surgery in ICU infection during hospitalization need to be substantiated in the future.

Several studies have shown that NIs prolong the LOS of patients from 10–20 days, with additional hospital costs ranging from $7000–$15,000 and mortality rates 20–30%.[46–48] PSM is one of the most commonly used clinical tools to analyze the economic burden of hospital-acquired infections and avoid the impact of confounding factors on the economic burden and provide an objective and accurate assessment.[49,50] Therefore, in the present study, the economic burden of hospital-acquired infections on ICU patients was analyzed using PSM in a 1:2 matching exercise. In the present study, the direct economic burden of hospital-acquired infections was 73,596.62 yuan, which was much higher than that reported previously. The mortality rate (9.2%) was significantly lower in this study but similar to the predicted mortality rate (29.1%). This phenomenon could be attributed to the serious condition of hospitalized patients in China and poor prognosis. Moreover, due to the economic level and the traditional concept of dying at home, many patients and their families choose to give up treatment and be discharged from the hospital; however, these patients are likely to die in the short term. A few studies have estimated the difference in the clinical outcomes between different sites and pathogens of infection. The current study showed that LOS in the hospital, the cost of hospitalization, and the mortality for UTIs were higher than those of the other two types. This finding was not consistent with that of the other studies.[47,51,52] Another review showed that all SSIs were not similar. Although by definition, all SSIs were costly; however, the principal determinants of the cost of an SSI were geographic locale, the type of surgery performed, and the depth of the infection.[53] Next, we analyzed the clinical outcomes of different pathogens, which showed that *E. coli* is less abundant compared to the other two pathogens and *P. aeruginosa* has poor clinical outcomes. Moreover, the extra economic burden of NIs caused by MDR bacteria deserves significant attention. Although the current study did not match MDR bacteria, a retrospective study in Spain found that the hospitalization costs for patients hospitalized with MDR *P. aeruginosa* were 1.7 times more than those for non-NI patients.[54] Therefore, NI should be under intensive focus, especially in ICU patients.

Nevertheless, the current study has several limitations. First, we used retrospective data in a single hospital, which caused inevitable biases. Secondly, this study assessed the overall cost of hospitalization to NI patients in the ICU but did not evaluate the classified costs, such as the treatment, nursing, or direct expenses after developing NI. Finally, the generalizability of our findings could be limited by the type of ICU (a general ICU always admits critically ill patients) and the high prevalence of NIs in this unit.

Conclusions

In conclusion, NI has a high prevalence in ICU patients and is associated with poor clinical outcomes, which include LOS in the ICU and the hospital, hospitalization costs, and all-cause mortality in the ICU. Long-term immunosuppressive therapy, disturbance of consciousness, blood transfusion, MODS, three or more antibiotics treatment, MV, tracheotomy, UC, nasogastric catheter, and CVC were risk factors for developing NI in ICU patients. These factors provided potential measures for preventing NI, such as aseptic techniques, promoting the rational use of antimicrobial drugs, and the importance of accurate determination of the underlying disease status.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University (Reference Number 2021YX −161). The Ethics Committee granted permission to access the raw data and approved the waiver of informed consent to participate in this study due to its retrospective design. All patient data were anonymous prior to the analysis.

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Disclosure

The authors declare that they have no competing interests in this work.

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