ONLINE VERSION: ISSN 1028-4818

RPNS-1853

Multimed 2025; 29:e3180

Original article

Characteristics and predictive factors of healthcare-associated infections in critically ill patients

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Characteristics and predictive factors of infections associated with health care in seriously ill patients

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SUMMARY

Introduction: l Healthcare-associated infections are more prevalent in critically ill patients. Contextualized studies are needed to clarify their characteristics and predictive factors.

Aim: Identify the characteristics and predictive factors of healthcare-associated infections.

ONLINE VERSION: ISSN 1028-4818

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Methods: Cohort study in 364 patients. Characteristics were compared between patients with and without infections. To identify predictive factors, infection was considered the dependent variable, and severity, comorbidity, and hospital stay indices were considered independent variables. For data processing, descriptive statistical summary measures were used, along with bivariate and multivariate analyses.

Results: HAIs developed in 7.9% of patients. 62.1% were men (p=0.025). The mean age was estimated at 44.9 years (95% CI 38.0–51.7) (p=0.098). The mean Acute Physiology and Chronic Health Evaluation II score was 15.1 (95% CI 12.7–17.6) and the Sequential Organ Failure Assessment score was 3.0 (95% CI 1.7–4.3). Bacteremia (31.0%) was the main site. The most frequent microorganisms were Staphylococcus aureus (27.5%) and Enterobacter sp (27.5%). Artificial mechanical ventilation (adjusted OR 7.7, 95% CI 2.6-22.8) and length of stay ≥ 7 days (adjusted OR 2.8, 95% CI 1.1-6.9) were identified as predictive factors.

Conclusions: Patients are characterized by older age, severity, organ dysfunction, and comorbidity. Artificial mechanical ventilation and length of stay ≥ 7 days are predictive factors for the development of healthcare-associated infections.

Keywords: Infection; Intensive care units; Prediction.

ABSTRACT

Introduction: healthcare-associated infections (HAIs) have a higher prevalence among critically ill patients. Contextualized studies are needed to clarify their characteristics and predictive factors.

Objective: to identify the characteristics and predictive factors of healthcare-associated infections.

Methods: a cohort study was conducted on 364 patients. Characteristics were compared between patients with and without infections. To identify predictive factors, infection was considered the dependent variable, and severity indices, comorbidity, and length of stay were

considered independent variables. Descriptive statistics, bivariate, and multivariate analyzes were applied.

Results: HAIs developed in 7.9 % of patients. Of these, 62.1 % were male (p = 0.025). The mean age was estimated at 44.9 years (95% CI: 38.0–51.7) (p = 0.098). The average Acute Physiology and Chronic Health Evaluation II score was 15.1 (95% CI: 12.7–17.6), and the Sequential Organ Failure Assessment score was 3.0 (95% CI: 1.7–4.3). The main infection site was bloodstream infection (31.0 %). The most frequent microorganisms were Staphylococcus aureus (27.5 %) and Enterobacter spp. (27.5%). Mechanical ventilation (adjusted OR: 7.7, 95% CI: 2.6–22.8) and length of stay ≥ 7 days (adjusted OR: 2.8, 95% CI: 1.1–6.9) were identified as predictive factors.

Conclusions: Patients are characterized by older age, higher severity, organ dysfunction, and comorbidities. Mechanical ventilation and a length of stay ≥ 7 days are predictive factors for the development of healthcare-associated infections.

Keywords: Infection; Intensive Care Units; Prediction.

SUMMARY

Introduction: Infections associated with health care (IAAS) have a higher prevalence in seriously ill patients. Contextualized studies are only necessary to clarify its characteristics and predictive factors.

Aim: identify the characteristics and predictive factors of infections associated with health care.

Methods: cohort study with 364 patients. The characteristics are compared between patients with semi-infections. To identify the predictive factors, infection is considered as a dependent variable, and the indices of gravity, comorbidities and hospitalization time are considered independent variables. Foram applied summary measures of descriptive statistics, in addition to bivariate and multivariate analyses.

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Sequential Organ Failure Assessment was 3.0 (95% CI: 1.7–4.3). The main location of the infection was the bloodstream (31.0%). The most common microorganisms are Staphylococcus aureus (27.5%) and Enterobacter sp. (27.5%). Mechanical ventilation (adjusted OR: 7.7; 95% CI: 2.6–22.8) and hospitalization time ≥ 7 days (adjusted OR: 2.8; 95% CI: 1.1–6.9) were identified as predictive factors.

Conclusões: Patients are characterized by increased ity, pregnancy, organ dysfunction and comorbidities. Mechanical ventilation and hospitalization time ≥ 7 days are predictive factors for the development of infections associated with health care.

Keywords: Infection; Intensive care units; Prediction.

Received: 11/05/2025

Approved: 05/14/2025

Introduction

Healthcare-associated infections (HAIs) develop in patients admitted to a hospital or other health care facility, and are not present or incubating at the time of admission. (1) They currently represent a public health burden by increasing morbidity, mortality, hospital stay, costs, and antimicrobial resistance. (2)

Worldwide, HAIs are common, affecting between 7% and 10% of hospitalized patients. Intensive care units (ICUs) are the hospital wards with the highest prevalence of HAIs, and in high-income countries, up to 30% of critically ill patients in ICUs acquire this type of infection. (3)

In Cuba, the incidence of HAIs is approximately 15%, although a recent specific study confirmed an increase of up to 37.8%. (4,5) In Granma province, Cuba, a study showed that 8.0% of patients admitted to the ICU of a provincial hospital acquired this type of infection. (6)

12.7% of those who remain in an ICU for more than two days have at least one HAI under surveillance, the most common of which are pneumonia, bacteremia, and urinary tract infection. (7) Comorbidity, immunosuppression, catheters, and other invasive devices predispose to these conditions. (8,9)

Despite prior research on the topic, contextualized clinical-epidemiological studies are needed, considering that the prevalence of HAIs is increasing, varies between hospitals and countries, and is related to patient characteristics, epidemiological, and organizational factors. Furthermore, most of these studies have been conducted at the hospital level, and indicators with a close causal relationship to their development are not considered when identifying predictive factors for HAIs in critically ill patients.

The results of the characterization of HAIs and the identification of predictive factors for their occurrence are useful for planning human and material resources and for developing preventive measures aimed at reducing morbidity and mortality from this cause.

Therefore, this study aims to identify the characteristics and predictive factors of HAIs in critically ill patients.

Methods

An observational, analytical, single-cohort study was conducted in the ICU of the Carlos Manuel de Céspedes Provincial General Hospital in Bayamo, Granma. The study was carried out with patients included in the months of November and December of 2016, 2017, 2018, 2019, and 2020, according to the phases of the Multicenter Project "Reduction of Nosocomial Infection in Intensive Care Units" (DINUCI), implemented at the institutional level, from which the cohort was formed.

Inclusion criteria

Patients with a stay of more than 48 hours were successively included and followed until they developed HAIs. The diagnosis of HAIs and their locations were based on the Centers for Disease

Control and Prevention (CDC) guidelines. (10,11) The cohort consisted of 364 subjects, of whom 29 (7.9%) developed HAIs and 335 (91.2%) did not develop HAIs during follow-up.

Exclusion criteria

Patients with a stay of 48 hours or less and those for whom complete follow-up until discharge was not possible were excluded from the cohort.

Study variables

The following variables were defined: sex: according to biological sex (male or female), age (in years), Acute Physiology and Chronic Health Evaluation II (APACHE II) prognostic score: to quantify severity, (12) Sequential Organ Failure Assessment (SOFA) score on admission: to evaluate the alteration of organ functions (13), sepsis stage: Systemic Inflammatory Response Syndrome (SIRS), sepsis and septic shock (according to the SIRS criteria of the Consensus Conference of Chest Physicians/Society of Critical Care Medicine); and sepsis and septic shock according to the Sepsis-3 consensus. (14) Comorbidity was also recorded: a) Immunosuppression: patients with radiation, chemotherapy, high-dose and prolonged steroids, advanced diseases, HIV or congenital or acquired immunodeficiency; b) History of chronic diseases: Diabetes mellitus, chronic kidney disease (CKD), neoplasia, liver cirrhosis and Chronic Obstructive Pulmonary Disease (COPD). Artificial mechanical ventilation (AMV), renal cleansing methods (RDM), parenteral nutrition (PNT) and antimicrobial treatment upon admission were determined as therapeutic procedures. Central venous catheter (CVC) implantation was used as a device. Other variables taken into account in the characterization were: ICU stay (in days), status at discharge (alive or deceased), location of infection according to the guidelines established by the Centers for Disease Control and Prevention (CDC), (10,11) and causative microorganism isolated in the microbiological culture. To identify predictive factors, the dependent variable was defined as HAI (yes or no) and independent variables were defined as predictive factors whose influence is evaluated on the development of HAI: APACHE II, SOFA, comorbidity, CVC, AMV and ICU stay.

Statistical analysis

Percentages were estimated for qualitative variables such as sex, sepsis stage, comorbidity, therapeutic procedures and implanted device, discharge status, infection site, and causative microorganism. For the analysis of quantitative variables (age, APACHE II, SOFA, ICU stay), the arithmetic mean and their 95% confidence intervals (95% CI) were calculated.

To determine the differences between the means of patients with and without HAIs, the parametric Student t test was used for independent data; and the chi-square test was used to compare categorical variables. The level of statistical significance was $\alpha < 0.05$.

A bivariate analysis was performed to identify predictive factors. The relative risk (RR) and its 95% confidence interval (95% CI) were calculated. Each factor was considered to be associated with the development of HAIs when the RR was greater than 1 and statistical significance was equal to or greater than 0.05. The cutoff points for quantitative variables were estimated by inspecting the box plots, starting from the point that marked the difference between patients with and without HAIs.

A multivariate data analysis technique was also applied using a binary logistic regression statistical model. The maximum likelihood method and the Hosmer-Lemeshow goodness-of-fit and Nagelkerke R2 statistics were used for this purpose. SPSS version 27.0 was used for statistical processing.

Ethical regulations

The ethical provisions of the Declaration of Helsinki for studies involving human subjects were observed. The information necessary for the research was obtained from clinical practice, and its confidentiality was guaranteed. No new therapeutic measures were tested.

Results

Twenty-nine patients were diagnosed with HAIs, representing 7.9% of the total population. Table 1 shows the characteristics of patients with HAIs by sex, sepsis stage, and comorbidity. In the series, 210 patients (57.7%) were female. Among those who developed HAIs, 62.1% were

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male; significant differences were found between patients with and without HAIs by sex (p=0.025).

SIRS was documented in 35.1% of patients; however, it was identified in 62.0% of those with HAIs and 32.8% without HAIs, with significant differences between the two groups (p=0.002). The sepsis/septic shock stage was confirmed in 27.6% of those who acquired the infection and in 5.1% of patients without infection (p=0.001) (Table 1).

89.7% of patients with HAIs had neoplasia; this frequency was significantly higher compared with those who did not develop infection (p=0.022). 10.3% of patients were on immunosuppression; this condition was not significantly associated with HAIs (p=0.531) (Table 1).

Table 1. Patient characteristics by sex, sepsis stages, and comorbidity.

Variable	All patients (n=364)		With IAAS (n=29)		Without IAAS (n=335)		p*
	No.	%	No.	%	No.	%	
Sex							
Female	210	57.7	11	37.9	199	59.4	0.025
Male	154)	42.3	18	62.1	136	40.6	
SRIS							0.002
Yeah	128	35.1	18	62.0	110	32.8	
No	236	64.9	11	38.0	225	67.2	
Sepsis/Septic Shock							0.001
Yeah	25	6.9	8	27.6	17	5.1	
No	339	93.1	21	72.4	318	94.9	
Diabetes mellitus							0,099
Yeah	29	7.9	0	0.0	29	8.6	
No	335	92.1	29	100.0	306	91.4	
Neoplasia							0.022
Yeah	32	8.8	3	10.3	29	8.7	
No	332	91.2	26	89.7	306	91.3	
Immunosuppression							0.531
Yeah	27	7.4	3	10.3	24	7.1	
No	337	92.6	26	89.7	311	92.9	

* $p < 0.05$

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15.6% of patients required AMI (Table 2), but this procedure was applied to 68.9% of patients with HAIs, corroborating differences in frequency compared to those who did not acquire HAIs (p=0.000). TPN treatment was significantly associated with HAIs, being indicated in 10.3% of patients who developed them (p=0.016). A central venous catheter was placed in 41.8% of patients in the series; in 79.3% of those who acquired infection and 38.5% without infection (p=0.001) (Table 2).

The mean age was 40.5 years (95% CI 38.6-42.5); in those who developed HAIs, the age was estimated at 44.9 years (95% CI 38.0-51.7) compared with 40.2 years in patients without infection (95% CI 38.1-42.4) (p=0.098). (Table 2)

The mean APACHE II score was 10.2 (95% CI 9.5-10.8). In patients with HAIs, it was 15.1 (95% CI 12.7-17.6) and 9.7 without HAIs (95% CI 9.1-10.4) (p=0.000). The mean SOFA score was 1.1 (95% CI 0.9-1.4) and in those with infection, 3.0 (95% CI 1.7-4.3) (p=0.000). The mean length of stay was 6.7 days (95% CI 5.1-6.3); 11.4 days in those with infection (95% CI 5.1-6.3) and 6.3 in patients without infection (p=0.001) (Table 1). 8.6% of patients were discharged dead; in the HAI group, mortality was 17.3% (p=0.079). (Table 2)

Table 2. Characteristics according to procedures, device and values of quantitative variables.

Variable	All patients (n=364)		With IAAS (n=29)		Without IAAS (n=335)		p*
	No.	%	No.	%	No.	%	
VMA							0.000
Yeah	57	15.6	20	68.9	37	11.1	
No	307	84.3	9	31.1	298	88.9	
MDR							0.072
Yeah	8	2.2	2	6.9	6	1.7	
No	356	97.8	27	93.1	329	98.2	
Parenteral nutrition							0.016
Yeah	11	3.1	3	10.3	8	2.4	
No	353	96.9	26	89.7	327	97.6	
Previous antibiotic							0.333
Yeah	145	39.8	14	48.3	131	39.1	
No	219	60.2	15	51.7	204	60.9	
Central venous							0.001

catheter							
Yeah	152	41.8	23	79.3	129	38.5	
No	212	58.2	6	20.7	206	61.5	
Quantitative variables	Avera ge	(95% CI)	Average	95% CI)	Average	95% CI	
Middle Ages	40.5	38.6-42.5	44.9	38.0-51.7	40.2	38.1-42.4	0.098
APACHE II	10.2	9.5-10.8	15.1	12.7-17.6	9.7	9.1-10.4	0.000
COUCH	1.1	(0.9-1.4)	3.0	1.7-4.3	1.0	0.7-1.2	0.000
Stay	6.7	(6,1-7,4)	11.4	8.4-14.3	6.3	5.7-7.0	0.001

*p < 0.05 **Artificial mechanical ventilation; ***Renal cleansing methods

Table 3 shows that bacteremia (31.0%), VMA-associated tracheobronchitis (27.6%), and VMA-associated pneumonia (VAP) were the main sites of HAIs. The most frequent causative microorganisms were Staphylococcus aureus (27.5%), Enterobacter sp (27.5%), and Escherichia coli (20.6%).

Table 3. Frequency distribution by location and microorganisms of healthcare-associated infections.

Variable	No.	%
Location		
Bacteremia	9	31.0
VMA-associated tracheobronchitis	8	27.6
VMA-associated pneumonia	6	20.6
Urinary infection	5	17.2
Other	1	3.4
Microorganisms		
Staphylococcus aureus	8	27.5
Enterobacter sp	8	27.5
Escherichia coli	6	20.6
Pseudomona aeruginosa	4	13.7
Enterococcus sp.	2	6.8
Staphylococcus epidermidis	1	3.4

Bivariate analysis confirmed that an APACHE score ≥ 11 increases the likelihood of developing the infection approximately sevenfold (RR 7.5% CI 95% 3.1-18.1 p=0.000). The SOFA score ≥ 2 (RR 5.7% CI 95% 2.5-12.6 p=0.000) and the use of a central venous catheter (RR 5.7% CI 95% 2.5-12.6 p=0.000) increase the risk of developing it almost sixfold. An AMV (RR 17.8% CI 95% 7.5-42.1 p=0.000) increases the risk approximately 18-fold, and a length of stay ≥ 7 (RR 5.3% CI 95%

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2.4-11.8 p=0.000) increases it fivefold. These factors were associated with the development of HAIs (Table 4).

Table 4. Bivariate analysis of predictors of healthcare-associated infection.

Variables	With IAAS n=29		Without IAAS n=335		Relative risk (RR)	95% confidence interval (95% CI)		p*
	No	%	No	%		Lower limit	Upper limit	
APACHE II								
<11	7	24.1	236	70.4				
≥11	22	75.9	99	29.6	7.5	3.1	18.1	0.000
COUCH								
<2	15	51.7	288	86.0				
≥ 2	14	48.3	47	14.0	5.7	2.5	12.6	0.000
Comorbidity								
Yeah	7	24.1	75	22.4				
No	22	75.9	260	77.6	1.1	0.4	2.6	0.829
Central venous catheter								
Yeah	23	79.3	129	38.5				
No	6	20.7	206	61.5	6.1	2.4	15.4	0.000
Artificial mechanical ventilation								
Yeah	20	69.0	37	11.0				
No	9	31.0	298	89.0	17.8	7.5	42.1	0.000
Stay (days)								
< 7	18	62.1	257	76.7	5.3	2.4	11.9	0.000
≥ 7	11	37.9	78	23.3				

*p < 0.05

The VMA (adjusted odds (OR) 7.7, 95% CI 2.6-22.8, p=0.000) and length of stay ≥ 7 days (adjusted OR 2.8, 95% CI 1.1-6.9) were identified as independent predictors of HAIs in the binary logistic regression statistical model, when other hypothesized influential variables were present. (Table 5).

Table 5. Logistic regression model of predictors of healthcare-associated infection.

Variables	B*	Mistake Standard	Wald	Next. †	Exp(B) ‡	95% CI §	
						Lower	Superior
Artificial mechanical ventilation	2,042	0.55	13.59	0.000	7.7	2.6	22.8
Stay ≥ 7 days	1,040	0.46	5.10	0.024	2.8	1.1	6.9
Central venous catheter	0.673	0.550	1.49	0.222	1.9	0.6	5.7
APACHE II ≥ 11	0.425	0.583	0.53	0.466	1.5	0.4	4.7

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SOFA ≥ 2	0.225	0.517	0.18	0.663	1.2	0.4	3.4

Hosmer and Lemeshow test: 0.526; Nagelkerke R2: 0.339;
*Model coefficients † Statistical significance;
‡ Adjusted Odd Ratio (OR) § 95% Confidence Interval

Discussion

The frequency of HAIs is lower than in other series. Despotovic MD et al. (8) confirmed the infection in 32.6% of those admitted. Blonch N et al. (15) corroborated HAIs in 56.3% of patients with COVID-19, and in 18.9% without COVID-19. A prevalence study in Cuba showed an increase in HAIs from 23.1% in 2019 to 37.8% in 2020. (5). The implementation of a package of prophylactic measures, as part of the DINUCI project, in the study ICU, could explain the described results.

A systematic review with meta-analysis developed by Liu X and colleagues, (16) found a significant difference in the development of infection between men and women, which is close to that observed in the present case series. The probability was 1.33 (95% CI 1.20-1.47) in favor of men. Epidemiological studies show sexual dimorphism in infectious diseases; with lower risk in women. Sex disparities influence hormonal and chromosomal control of immunity. Furthermore, differences in occupational activities, lifestyle and comorbidity play an important role in exposure to pathogens. (17)

Elderly patients are identified as a high-risk group for HAIs due to immunosenescence, which was not evident in the series due to the study's ICU admission criteria; despite a higher age in those with HAIs. (18)

The APACHE II and SOFA scores and sepsis staging results are similar to those reported by He et al. (19) The authors confirmed a mean APACHE II score of 12.5, a SOFA score of 4.05, a higher mean SIRS criteria, and septic shock in 28.7% of patients. Consequently, sepsis risk and staging indices are key indicators for characterizing the severity and degree of organ dysfunction.

Patients with malignancies have a 3- to 5-fold increased risk of sepsis and HAIs due to resistant bacteria and are associated with increased therapeutic failure. (20) They also experience higher

rates of central venous catheter-associated bacteremia and more severe infections at other sites, supporting the study's findings regarding comorbidity. (21)

A meta-analysis showed that the incidence of VAP is 30% (95% CI 24-37%). (22) Another study reported that approximately 11.0% of patients with VMA develop trachoebronchitis, and 12% of these cases progress to pneumonia, supporting the increased association of this procedure with HAI. (23)

The average length of stay identified is close to that of the study by Tomazini et al. (23) who showed that it increases 3.5 times more in patients with HAIs. The increase in the length of hospital stay is a useful measure of the cost burden of HAIs and is used to increase investments in their prevention and control. (24)

The main sites of infection generally coincide with those detected in several studies, although pulmonary infection predominates in most, especially VAP. (1,7,16,19) In the report on the epidemiological trend of HAIs in Cuban ICUs, VAP developed in 47.5% of patients; tracheobronchitis in 14.6% and bacteremia in 11.5%; statistics more similar to ours. (4) In the package of measures applied, those aimed at preventing VAP and tracheobronchitis predominated, hence the result.

The microorganisms identified are specific to the main locations and are consistent with those reported in national (4,5) and international (1,8,16,19) studies. Emphasis is placed on the contribution of gram-positive and -negative bacteria to the etiology of HAIs.

The VMA as an independent predictive factor of HAI was confirmed in the multivariate analysis estimated by Wang L et al., (24) with an adjusted OR of 2.70 (95% CI 1.33-5.35); a value close to that obtained in the logistic model of this study. Authors such as Blonch N et al., (15) Shrestha SK et al., (25) and Pereira PPS et al., (26) identified it as an associated risk factor. The VMA involves the use of invasive devices on the airway; antimicrobials, gastric mucosal protectors, urinary catheter and leads to a prolonged stay, which increases the risk of HAI.

Multivariate analyses also consider length of stay as a predictor of infection; when it exceeds 7 days, the risk may be significantly higher (RR 6.98, 95% CI 1.42-34.15). (26)

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Conclusions

Patients with HAIs are characterized by older age, severity, organ dysfunction, and comorbidity. Artificial mechanical ventilation and a hospital stay of ≥7 days are independent predictors of the development of HAIs.

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Conflicts of interest

The authors declare no conflicts of interest.

Authorship contribution

Julio César González Aguilera: Conceptualization, research, methodology, writing, review and editing.

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I, Julio César González Aguilera, on behalf of all the co-authors, declare the veracity of the content of the article.