ABSTRACT

Objectives: to evaluate hospitalization costs of patients with and without Healthcare-Associated Infections in an Intensive Care Unit. Methods: a retrospective case-control study. Data collection was retrieved from the medical records of Intensive Care Unit of a medium-sized public hospital in Goiás-Brazil. For each case, two controls were selected. Data on socioeconomic, clinical, and hospital costs were collected. To verify associations between variables, Odds Ratio and linear regression were calculated. Results: a total of 21 patients diagnosed with Healthcare-Associated Infections and 42 controls were evaluated. The hospitalization cost for patients with infection was four times higher than for non-infection patients (p-value<0.001). There was an association between infection and higher mortality (p-value<0.001), longer hospital-stay (p-value=0.021), and higher hospital costs (p-value=0.007). Conclusions: hospitalization costs of diagnosed Healthcare-Associated Infections patients are high compared to those who do not have this diagnosis.

Descriptors: Intensive Care Units; Health Care Costs; Infections; Delivery of Health Care; Critical Care.

RESUMO

Objetivos: avaliar custos de internação hospitalar de pacientes com e sem Infeção Relacionada à Assistência em Saúde em uma Unidade de Terapia Intensiva. Métodos: estudo caso-controle retrospectivo. Os dados foram coletados dos prontuários dos pacientes de Unidade de Terapia Intensiva de um hospital público de médio porte em Goiás-Brasil. Para cada caso foram selecionados dois controles. Foram coletadas informações econômicas, clínicas e custos hospitalares. Para verificar associações entre variáveis foram calculados Odds Ratio e regressão linear. Resultados: foram avaliados 21 pacientes com diagnóstico de Infecção Relacionada à Assistência em Saúde e 42 controles. O custo de internação de pacientes com infecção foi quatro vezes maior em relação aos pacientes sem infecção (p-valor<0,001). Houve associação entre infecção e maior mortalidade (p-valor<0,001), maior permanência hospitalar (p-valor=0,021) e maior custo hospitalar (p-valor=0,007). Conclusões: custos financeiros de internação de pacientes diagnosticados com Infeção Relacionada à Assistência em Saúde são elevados em relação àqueles sem este diagnóstico.

Descritores: Unidades de Terapia Intensiva; Custos de Cuidados de Saúde; Infeções; Prestação de Atendimento de Saúde; Cuidados Críticos.
INTRODUCTION

Hospital infection is an infection related to a hospitalization or hospital procedures and can occur after the patient's hospital admission, during hospitalization or after discharge\(^1\). The term “hospital infections” has been replaced by “Health Care-Associated Infections” (HAIs), a term that encompasses infections acquired and related to care in any environment\(^2\).

HAIs are among the most recurrent complications of hospitalization. They are associated with the use of invasive devices (venous accesses, probes, tubes and others), surgical procedures and infections by multidrug-resistant microorganisms, which currently represent a serious threat to the patient's health, as they make rehabilitation difficult, especially for patients who are already under intensive care\(^3\).

According to the World Health Organization (WHO), HAIs are one of the most common adverse events in hospital care with an impact on mortality and quality of life for the population. The risk of acquiring at least one type of HAIs is present in up to 7% and 10% of patients in developed and developing countries, respectively\(^4\).

In the United States, the Centers for Disease Control and Prevention (CDC) of Atlanta, through the SENIC study (Study on the Efficacy of Nosocomial Infection Control), evaluated the effectiveness of HAIs control programs active in the country. It was verified that HAIs extend hospital stay by at least four days and increase additional costs\(^5\).

Guest and collaborators\(^6\) estimated the HAIs annual economic impact (2016/2017) served by the National Health Service (NHS) at £ 2.1 billion with direct costs only. Direct costs are those spent on hospitalization, and indirect costs are the productivity losses for society, due to absenteeism and mortality\(^7\). In the United States, a total of 1.7 million patients diagnosed with HAIs are estimated annually, of which almost 100,000 evolve to death, resulting in costs of more than US 30 billion/year\(^8\).

HAIs are more severe in high-risk populations, such as the elderly, adults admitted to Intensive Care Units (ICUs) and newborns. Incidence rates of HAIs in ICUs in developing countries exceed those of developed countries, mainly due to lack of resources and little knowledge in epidemiology and infection control\(^9\)-\(^10\).

In studies conducted in Brazil, there were a high cost of patients with HAIs admitted to the ICU. In Goiânia-GO, the cost of hospital stay in the ICU of HAI patients was 20.4 times higher compared to patients without HAI. This study evaluated only bloodstream infection\(^11\). In the state of Minas Gerais, the average cost of HAI acquired and related to care in any environment (venous accesses, probes, tubes and others), surgical procedures and infections by multidrug-resistant microorganisms, which currently represent a serious threat to the patient’s health, as they make rehabilitation difficult, especially for patients who are already under intensive care\(^12\).

In the state of Paraná, the cost of hospital stay similar and not superior to the HAI patient.

Data on costs in the ICU are scarce and evaluated, mainly, in large Brazilian centers, being limited/nonexistent the studies in cities in the interior of the states of the Brazilian Midwest Region. Also, there was a scarcity of studies that compared the financial cost between adult HAI patients and without this diagnosis admitted to the ICU.

OBJECTIVES

To evaluate the costs of hospitalization of HAI patients in relation to patients without HAIs in an ICU.

METHODS

Ethical aspects

Ethical principles involving research with human beings were followed, following Resolution no. 466 of 2012 of the National Health Council of the Ministry of Health. Signing the informed consent form was waived by the Research Ethics Committee (CEP – Brazilian acronym), and the study was approved by the CEP of Goiás Federal University.

Design, period, and study setting

This is a retrospective case-control study of patients’ medical records. It was carried out in an ICU consisting of six beds of a medium-sized public hospital in the city of Jataí, located in the southwest region of the state of Goiás, Brazil. For the selection of cases and controls, the medical records of patients hospitalized between January and December of 2015 with a hospital stay longer than 72 hours were evaluated.

The manuscript followed the checklist of items that should be included in the reports of the case-control studies, using the STROBE tool.

Population, inclusion, and exclusion criteria

The present study consisted of adult individuals (aged 18 years or over), of both sexes. Everyone who had a diagnosis of HAI (case group) during 2015 was included. The HAI diagnosis of patients (a group of cases) was made by the Commission for Infection Control Related to Health Care (CICRHC) of the institution, after being admitted to the ICU.

The control group was composed of patients with characteristics similar to the case group. The characteristics evaluated were age group, month and hospitalization period. For each case, two patients were selected as controls. It was constituted as inclusion criteria for patients in the control group: age 18 years or older; the same month of hospitalization of the HAI patient; and hospital stay similar and not superior to the HAI patient.

Study protocol

It was collected variables of interest from the patient's medical record using an instrument developed by the authors, including the following variables: sex (male/female), age (18-40; 40-60 and 60 and over), marital status (single, married or living with a partner, widower), skin color (black, white, brown, yellow, indigenous),
diagnosis of ICU admission (based on the International Classification of Diseases - ICD-10), days of total hospital stay (days), length of stay in the ICU (days), use of antimicrobials (yes/no), topography/type of hospital infection, invasive procedures (yes/no), isolated microorganism, outcome of hospitalization (discharge to another ward, discharge from hospital, transfer to another institution, death), risk factors and comorbidities (yes/no).

For the analysis of hospital costs, the cost of hospitalization was collected. Each patient had a billing form with a description of the procedures performed, but the costs of each procedure were not discriminated or stratified. The costs were described in hospital services and professional, such as physiotherapy assistance, disease treatment, dialysis treatment, daily rates, transfusion medicine, transfusion medicine patient exams, trachea and bronchus, general costs, test performed outside the structure, access to dialysis, hemodialysis, ultrasounds, doctor’s appointments/other, blood products, chest and limb tomography, abdomen and pelvis tomography, chest wall, anesthesia, totaling the cost of hospitalization.

**Analysis of results and statistics**

The collected data were analyzed using descriptive statistics, with frequency distribution in absolute numbers and percentage for categorical variables and average and standard deviation for continuous variables. To check the difference between the variables, the chi-square test was applied ($\chi^2$) for categorical variables and Student’s T-test for continuous variables. To estimate the associations of the variables, were calculated Odds Ratio (OR) association measures. There was an association between hospital cost and the presence or absence of HAI by means of linear regression, and the model was adjusted by the number of days of hospital stay, age, sex, ethnicity, and marital status. These variables were selected because they are the socioeconomic and demographic information collected from the patients’ medical records, as they are important variables to assess the profile of individuals most likely to develop HAI. One hypothesis is that patients living in a domestic partnership may have a healthier life and, consequently, a better state of health and less risk of developing HAI. The results of the statistical tests were considered significant for $p<0.05$. The data were analyzed using Epi Info software version 7.0 and Stata version 12.0.

**RESULTS**

The total sample in the present study was 63 patients, 21 cases and 42 controls. Of the cases of HAI, 52.4% were female; 76.2% were non-white (66.7% brown and 9.5% black); and 71.4% did not live with a partner. Regarding age, 57.1% of HAI patients and 59.5% of those without HAI had from 18 to 60 years old. There was no significant difference between sociodemographic characteristics and the presence or absence of HAI (Table 1).

The hospitalization cost for HAI patients was four times higher than those without HAIs; on average, R$ 16,132.21 compared to R$ 4,014.26 for the control patient ($p<0.001$). Hospital stay and ICU stay were statistically significant in HAI patients. The average (standard deviation - SD) of total days of hospital stay was 35.0 (23.5) for HAI patients, while in the control it reached 12.9 (7.8) days. In the ICU, the average hospital stay was 26.5 (19.4) days for cases and 6.9 (3.9) days for controls ($p<0.001$). When stratified, it was found that 38.1% of HAI patients remained more than 30 days. Among patients without HAI, there was no stay longer than 30 days (Table 1).

The average cost in Real (R$) of all cases was approximately R$ 10,000.00. The cost ranging from R$ 1,000.00 to 10,000.00 was observed in 38.1% in cases versus 95.2% in controls. The costs related to the control case subjects (2.4%) ranged from R$ 10,000.00 to 20,000.00. Concerning the other individuals with HAI, 28.6% had a cost of R$ 10,000.00 to 20,000.00; 19% from R$ 20,000.00 to 30,000.00; and 14.3% from R$ 30,000.00 to 40,000.00. The hospital cost and length of stay were higher among HAI individuals compared to those without HAIs (Figure 1).

The main diseases that led to ICU admission, according to the International Classification of Diseases (ICD-10), were grouped into: respiratory diseases; circulatory system diseases; digestive tract diseases; diseases of the urinary tract; infectious and parasitic diseases; neurological diseases and trauma. The most frequent risk factors present at admission were: Systemic Arterial Hypertension, Cardiac Insufficiency and Diabetes Mellitus. There was no significant association between the clinical conditions of patients at admission and the presence or not of HAI. However, there was a borderline association for the HAI onset among patients admitted with infectious and parasitic diseases ($p=0.07$), and, among those admitted due to trauma, HAI was not observed ($p=0.09$) (Table 2).

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**Table 1 - Sociodemographic characteristics according to the presence or absence of Health Care-Associated Infections of patients admitted to an Intensive Care Unit, Jataí, Goiás, Brazil, 2015**

| Categorical variables | HAI* Patients | Patients without HAI* | p value* |
|-----------------------|--------------|----------------------|----------|
| **Sex**               |              |                      | 1.000    |
| Female                | 11 (52.4)    | 22 (52.4)            |          |
| Male                  | 10 (47.6)    | 20 (47.6)            |          |
| **Skin color**        |              |                      | 0.109    |
| White                 | 5 (23.8)     | 15 (35.7)            |          |
| Non-white (brown and black) | 16 (76.2) | 22 (52.4) |          |
| Uninformed            | 0 (0.0)      | 5 (11.9)             |          |
| **Marital situation** |              |                      | 0.180    |
| Live with partner     | 6 (28.6)     | 21 (50)              |          |
| Do not live with partner | 15 (71.4) | 20 (47.6) |          |
| Not informed          | 0 (0.0)      | 1 (2.4)              |          |
| **Age (years)**       |              |                      | 0.856    |
| 18 |- 60                | 12 (57.1)     | 25 (59.5)            |          |
| 60 or more            | 9 (42.9)     | 17 (40.5)            |          |
| **ICU stay**          |              |                      | $<0.001$ |
| <5 days               | 2 (9.5)      | 19 (45.2)            |          |
| 6 to 30 days          | 11 (52.4)    | 23 (54.8)            |          |
| > 30 days             | 8 (38.1)     | 0 (0.0)              |          |
| **Continuous variables** |          |                      |          |
| Hospitalization Cost (R$) | 16,132.2 (11,232.08) | 4,014.3 (2,492.28) | $<0.001$ |
| Total days of hospital stay | 35.0 (23.5) | 12.9 (7.8) | $<0.001$ |
| Total days in ICU*    | 26.5 (19.4) | 6.9 (3.9)           | $<0.001$ |

*Note: HAI* – Health Care-Associated Infections; ICU* – Intensive Care Unit; SD* – Standard Deviation; “n” – number, “p-value refers to the chi-square test; “p-value refers to Student’s t-test.”
patients admitted to an Intensive Care Unit, Jataí, Goiás, Brazil, 2015

Table 2 - Clinical conditions of the patient on admission according to the presence or absence of Health Care-Associated Infections between patients admitted to an Intensive Care Unit, Jataí, Goiás, Brazil, 2015

| Disease                          | HAI* patients n (%) | Patients without HAI* n (%) | ρ value |
|----------------------------------|---------------------|-----------------------------|---------|
| Respiratory diseases             |                     |                             | 0.13    |
| Yes                              | 7 (33.3)            | 7 (16.7)                    |         |
| No                               | 14 (67.7)           | 35 (83.3)                   |         |
| Circulatory system diseases      |                     |                             | 0.85    |
| Yes                              | 7 (33.3)            | 15 (35.7)                   |         |
| No                               | 14 (67.7)           | 27 (64.3)                   |         |
| Digestive tract diseases         |                     |                             | 0.78    |
| Yes                              | 3 (14.3)            | 5 (11.9)                    |         |
| No                               | 18 (85.7)           | 37 (88.1)                   |         |
| Infectious and parasitic diseases|                     |                             | 0.07    |
| Yes                              | 4 (19)              | 2 (4.8)                     |         |
| No                               | 17 (81)             | 39 (95.2)                   |         |
| Diseases of the urinary tract    |                     |                             | 0.14    |
| Yes                              | 0                   | 4 (9.5)                     |         |
| No                               | 21 (100)            | 38 (90.5)                   |         |
| Neurological diseases            |                     |                             | 0.14    |
| Yes                              | 0                   | 4 (9.5)                     |         |
| No                               | 21 (100)            | 38 (90.5)                   |         |
| Traumas                          |                     |                             | 0.09    |
| Yes                              | 0                   | 5 (11.9)                    |         |
| No                               | 21 (100)            | 37 (88.1)                   |         |
| Risk factors                     |                     |                             | 0.82    |
| Yes                              | 17 (81)             | 33 (78.6)                   |         |
| No                               | 4 (19)              | 9 (21.4)                    |         |

Note: HAI* – Health Care-Associated Infections; “n” – number, “p-value” refers to the chi-square test.

Table 3 - Hospital outcome according to the presence or absence of Health Care-Associated Infections of patients admitted to an Intensive Care Unit, Jataí, Goiás, Brazil, 2015

| Outcome          | HAI* n (%) | Patients without HAI* n (%) | OR 1 | CI 95% 2 | ρ value |
|------------------|------------|----------------------------|------|----------|---------|
| Death            | 12 (66.7)  | 6 (14.3)                   | 2.953; 51.003 | <0.001 |
| Discharge to ward| 0.27       | 0.0727; 0.946              | 0.021 |
| Hospital discharge| 0.0044     | 1.532                      | 0.088 |
| Transfer to another institution | 0.18       | 0.0044; 1.532              |       |

Note: HAI* – Health Care-Associated Infections; “n” – number, “OR” – Odds Ratio; “CI” – Confidence Interval.

Table 4 - Linear regression for the association between the cost and the presence of Health Care-Associated Infections among patients admitted to an Intensive Care Unit, Jataí, Goiás, Brazil, 2015

| | Hospital Cost | CI 95% 1 | ρ value |
|-------------------|--------------|----------|---------|
| HAI* (without/with) | 4370.3       | 1225.1; 7515.4 | 0.007 |
| Days of Hospital stay | 352.7       | 272.7; 432.7 | <0.001 |
| Age (years) | 741.3       | -1777.5; 3260.2 | 0.557 |
| Sex (male/female) | -2646.9     | -5093.0; -200.8 | 0.035 |
| Ethnicity (white/non-white) | -2002.5  | -4601.9; 596.9 | 0.128 |
| Marital status (live/does not live with a partner) | -495.2     | -2832.2; 1841.8 | 0.672 |

Note: HAI* – Health Care-Associated Infections; “CI” – Confidence Interval.

DISCUSSION

The hospital cost and length of hospital stay for HAI patients were higher compared to patients who did not have HAI. Also, the most prevalent age group was of adult patients (less than 60 years) and the sex distribution was proportional. The most frequent topography was infections related to the respiratory system. Death was the most frequent outcome in cases of HAI and may have been a consequence of infections.

The causes of hospitalization of the studied patients were similar to the national evidence(13). Moreover, the reasons for hospitalization depends on the hospital profile(14). As for the risk factors presented in the patients’ admission, the clinical conditions were similar and did not influence the diagnosis of HAI.
As for the distribution of HAI topographies of patients hospitalized in the ICU, the similarity was observed with other evidence, in which the infection related to the respiratory system was the most frequent\(^\text{17}\). The worldwide rate of pulmonary infection in the ICU was reported in 64% and, in the groups of Brazilians, was shown the frequency of 71.2% of respiratory infection as the most frequent type of HAI in the ICUs, with gram-negative ones responsible for 72% of microorganisms isolated in infections, and as the main agent Pseudomonas, followed by Klebsiella\(^\text{14,16}\).

As for the microbiological exams to identify the agents that cause infection in ICU patients, one study showed a low identification of these microorganisms (37.5%)\(^\text{17}\) and another, similar to the present study, slightly higher (50.7%)\(^\text{16}\). Laboratory diagnosis and appropriate microbiological identification of the causing agent of the disease are essential conduits to ensure control of the spread of infection-causing bacteria through the rational prescription of antibiotics and the use of clinical protocols, controlling bacterial resistance, morbidity and mortality\(^\text{18}\). The cost of antimicrobials in the ICU is high, and must be controlled and rationalized\(^\text{19}\). Through the implementation of an antimicrobial use monitoring program, it was possible to reduce the use of these drugs\(^\text{20}\) and, consequently, the costs. Epidemiological surveillance of multidrug-resistant microorganisms is one of the strategies for the control of HAIs, and the effectiveness of public health actions should also be assessed, as well as the capacity and quality of microbiology laboratories, with the aim of providing the safety of health services in Brazil\(^\text{21}\).

In cases of HAI, the most frequent outcome was death, with high lethality in pneumonia. Due to the high number of deaths among patients with HAIs, we raised the hypothesis that it was a consequence of infections. Other studies showed a mortality rate of 34.6%\(^\text{17}\), 57.6%\(^\text{22}\) and 65.4%\(^\text{14}\), lower data than those presented in the present study, indicating a possible relationship between infection and mortality\(^\text{16}\).

The cost of hospitalization was very high among HAI patients. In other studies, the costs of hospitalization for patients with HAIs were, on average, 2 to 3 times higher than the costs for treating patients without HAIs\(^\text{7,10,12,23}\). This evidence did not compare all types of HAIs, so there may be an even greater difference in costs between patients with and without HAIs.

Regarding hospital stay, in total days of hospital stay, the average of the present study was high compared to another study, which showed an average stay of 15 days for HAI patients and three days for patients without HAI\(^\text{11}\). However, the data in the present study were similar to the findings of Tiburcio\(^\text{22}\) study, which identified an average hospital stay of 26.4 days for patients who acquired HAI in the ICU and 6.4 days for those without this diagnosis. They also converge to the results obtained by Pereira and collaborators\(^\text{16}\), who verified an average in ICU stay of 21.2 days for patients with HAIs. The relative risk of acquiring HAI among patients who remain in the ICU for more than 30 days is 6.94 times greater than those who stay less than 5 days\(^\text{24}\).

There was no difference between the groups regarding invasive procedures and the use of antimicrobials. In another study, 100% of patients were submitted to invasive\(^\text{16}\) procedures. ICU patients are susceptible to infections due to critical condition and frequent invasive procedures, which create a gateway for HAI agents\(^\text{24}\). Furthermore, good practice strategies, such as professional training and improvements in working conditions, can increase patient safety within the ICU\(^\text{25}\).

It is necessary to adopt cost management that supports decision making and highlights the quality of spending. Currently, these expenses are being made with resolutions, treatments, hospitalizations or prevention of these HAIs\(^\text{26}\). HAIs prevention control in critically ill patients and avoided HAI incurs a lower cost\(^\text{27}\).

**Limitations of the study**

This study had limitations regarding the small number of articles about the HAI costs and case-control studies for comparison between patients with and without HAI to discuss the subject. The costs of hospitalizations were researched using a billing form that did not specify the spending on daily ICU, medication, and procedures. The indirect costs of hospitalization were also not evaluated. Thus, the HAI costs in the evaluated hospital may be even higher than those presented in this study, which highlights the need to calculate the costs of HAI for better allocation of financial resources.

**Contributions to health**

The accounting for infection costs makes it possible to review the prevention strategies that are being used to control HAIs, promoting greater reflection among managers on the allocation of these resources to HAI prevention practices. Furthermore, it assists in decision making to increase the quality of health care, enabling a safer hospital stay for the patient. Also, the present study can contribute to increasing the knowledge of the scientific community regarding the economic impact of HAI in the ICU.

**CONCLUSIONS**

This study presented the characteristics of HAI in the institution under study and showed high financial costs of hospitalization of patients with diagnoses of infection compared to patients without a diagnosis of HAI. The survey of financial costs in the health system can favor economic management and the appropriate spending of resources for health promotion and prevention programs.
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