



The economic impact of healthcare-associated infections in hospitalization in intensive care units

Impacto econômico das infecções associadas à assistência à saúde na internação em unidades de terapia intensiva

El impacto económico de las infecciones asociadas a la salud en la hospitalización en unidades de cuidados intensivos

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ABSTRACT

Objective: To evaluate the economic impact caused by the occurrence of healthcare-associated infections (HAIS) in patients in the Intensive Care Unit (ICU). **Methods:** Integrative literature review, which adopted the PICO strategies – Population: ICU patients, Interest: HAIS, and Outcome: economic impact, Extraction, Conversion, Combination, Construction, and Use (ECUs) and Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) for searching and sampling in the databases that are part of the CAPES Periodicals Portal. **Results:** Twenty-one studies were included, categorized according to author, year, title, location, journal, type of study, and average cost of HAI during ICU admission. In the meantime, the cost of hospitalization of patients with HAI in the ICU is up to four times higher, associated with longer stays, use of antimicrobials and laboratory investigations, especially exacerbated in the detection of multidrug-resistant microorganisms. **Final considerations:** The most common HAI described were respiratory infections, especially Ventilator-Associated Pneumonia and Hospital-Acquired Pneumonia, bloodstream infections, distributed in sepsis, surgical site infection, central venous catheter-associated infection, and urinary tract infection associated with a bladder catheter.

Keywords: Intensive care units, Healthcare-associated infections, Hospital costs.

RESUMO

Objetivo: Avaliar o impacto econômico causado pela ocorrência de infecções relacionadas à assistência à saúde (IRAS) em pacientes internados em Unidade de Terapia Intensiva (UTI). **Métodos:** Revisão integrativa da literatura, que adotou as estratégias PICO – População: pacientes de UTI, Interesse: IRAS e Desfecho: impacto econômico, Extração, Conversão, Combinação, Construção e Uso (UCEs) e Itens de Relato Preferidos para Revisões Sistemáticas e Meta- Análises (PRISMA) para busca e amostragem nas bases de dados que fazem parte do Portal de Periódicos da CAPES. **Resultados:** Foram incluídos 21 estudos, categorizados de acordo com autor, ano, título, local, periódico, tipo de estudo e custo médio de IRAS durante a internação na UTI. Nesse ínterim, o custo de internação de pacientes com IRAS na UTI é até quatro vezes maior, associado a maior tempo de internação, uso de antimicrobianos e investigações laboratoriais, especialmente exacerbadas na detecção de microrganismos multirresistentes. **Considerações finais:** As IRAS mais comuns descritas foram infecções respiratórias, principalmente Pneumonia Associada à Ventilação e Pneumonia Adquirida em Hospital, infecções de corrente sanguínea, distribuídas na sepse, infecção de sítio cirúrgico, infecção associada a cateter venoso central e infecção do trato urinário associada a cateter vesical.

Palavras-chave: Unidades de terapia intensiva, Infecções relacionadas à assistência à saúde, Custos hospitalares.

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RESUMEN

Objetivo: Evaluar el impacto económico causado por la ocurrencia de infecciones asociadas a la atención de la salud (IRAS) en pacientes ingresados en la Unidad de Cuidados Intensivos (UCI). **Métodos:** revisión integrativa de la literatura, que adoptó las estrategias PICO - Población: pacientes de UCI, Interés: HAI y Resultado: impacto económico, Extracción, Conversión, Combinación, Construcción y Uso (ECU) y Elementos de informe preferidos para revisiones sistemáticas y meta - Análisis (PRISMA) para búsqueda y muestreo en las bases de datos que forman parte del Portal de Publicaciones Periódicas de la CAPES. **Resultados:** Se incluyeron 21 estudios, categorizados según autor, año, título, local, revista, tipo de estudio y costo promedio de IRAS durante la estancia en UCI. Mientras tanto, el costo de hospitalización de pacientes con IRAS en UCI es hasta cuatro veces mayor, asociado a mayor estancia hospitalaria, uso de antimicrobianos e investigaciones de laboratorio, especialmente exacerbado en la detección de microorganismos multirresistentes. **Consideraciones finales:** Las IRAS más comunes descritas fueron infecciones respiratorias, principalmente Neumonía Asociada a Ventilación y Neumonía Adquirida en el Hospital, infecciones del torrente sanguíneo, distribuidas en sepsis, infección del sitio quirúrgico, infección asociada a catéter venoso central e infección del tracto urinario asociada a sonda vesical.

Palabras clave: Unidades de cuidados intensivos, Infecciones asociadas a la atención de la salud, Costos hospitalarios.

INTRODUCTION

Health care-associated infections (HAIS) have increasingly become a serious public health problem, as they represent a threat to the safety of hospitalized patients and, in addition, the health professional who provides assistance to the user is also exposed and susceptible to contracting these infections. HAIS are acquired during the provision of health care, considering adverse events associated with health care more frequently and have a high morbidity and mortality with direct repercussions on the safety of the patient and consequently the quality of services (CAVALCANTE EFO, et al., 2019).

Thus, the Intensive Care Units (ICU) are places of high technological complexity, being characterized as a critical area with patient instability, where there is a high risk for the development of HAIS. With this, HAIS are characterized as infections acquired during the care process in a hospital or other care unit, and are considered an important health problem, as they result in high mortality, prolonged hospitalization and favoring the selection and dissemination of multiresistant microorganisms (LEÔNICIO JM, et al., 2019; GARBUIO DC, et al., 2022).

However, patients who acquire these HAIS generate high care costs when compared to those without infection. Several studies show that HAIS represent a crucial health issue and can lead to substantial economic impacts particularly in ICUs. These additional costs are related to the complexity of the treatment and consequently to the additional days of hospitalization. In this way, HAIS have a direct impact on both patient care and increase hospital costs, since they will use many drugs that can be expensive, need a specialized team and a greater number in relation to the number of beds, requires more frequent requests for tests and will consequently result in substantial economic impacts, particularly in ICUs (CAVALCANTE EFO, et al., 2019; MACHADO LG, et al., 2022; OSME SF, et al., 2022). In this sense, for the analysis of costs related to HAI, cohort studies are necessary, or even the use of a database, considering that these involve health institutions, patients and governments. In general, the cost estimation process follows protocols that focus mainly on the direct ones, which are difficult to define, in addition to the use of different methods by hospitals, which can increase the variability and discrepancy of the data (RAMIREZ K, 2018; BENENSON S, et al., 2020; GOMES HMS e GASPARETTO V, 2021).

Thus, Treatment of HAIs, especially antimicrobial therapy, is one of the factors that impact its high cost, especially when related to the treatment of infections caused by agents resistant to antimicrobials. The evaluation of the cost of HAIS is an important step for the implementation of programs capable of mitigating this problem, estimating the benefit-cost ratio in order to prioritize the most effective interventions for the best allocation of resources. It is clear that cost reduction and improvement of services rendered in hospitals should always be under discussion, however, it is clear that these two practices are always on opposite sides, since

logic determines that, for superior service, the funding of processes is necessary. (SALVATIERRA GR, 2003; HUSSEY PS, et al., 2013). To that end, considering essential the evaluation of services and the formulation of indicators to assist managers of hospital pharmacy services in conducting the identification, execution, documentation, control, and monitoring processes (FERREIRA LL, et al., 2019), the objective of the study consisted in the evaluation of the economic impact caused by the occurrence of HAIS in patients in the ICU.

METHODS

This is a comprehensive literature review (CLR), based on the steps proposed by Mendes et al. (2008), which are: 1) Elaboration of the question of the comprehensive review; 2) Establishment of criteria for inclusion and exclusion of parent studies and literature search; 3) Establishing the information to be extracted from the selected studies/categorization of the parent studies; 4) Evaluation of the methodological quality of the included parent studies; 5) Interpretation of the results; and 6) Presentation of the review/synthesis of knowledge.

The acronym PICO (Population, Interest, Comparison and Outcome) was used to construct the research question since it enables the effective search for directing the study according to the proposed objectives (LOCKWOOD C, et al., 2020). Thus, it was established: P - patients in Intensive Care Unit (ICU); I - healthcare-associated infections; C - not applicable, and O - economic impact. Therefore, the following guiding question was formulated: "What is the economic impact caused by the occurrence of HAIS in ICU patients?". To assist in the construction and organization of the search strategy, the model Extraction, Conversion, Combination, Construction, and Use (ARAÚJO WCO, 2020) will be used (**Chart 1**).

Chart 1 - Comprehensive review search strategy.

Question	What is the economic impact caused by the occurrence of HAIS in ICU patients?		
Strategy	P (Population)	I (Interest)	O (Outcome)
Extraction	ICU Patients	HAIS	Economic impact
Conversion	Intensive Care Units	Cross infection	Economics
Combination	"Intensive care units"	"Cross infection", "Health-associated infections", "Pneumonia", "Pneumonia, ventilator-associated" "Sepsis", "Urinary tract infections", "Surgical wound infection"	"Economics", "Hospital costs", "Health care costs"
Construction	"Intensive care units"	"Cross infection" OR "Health-associated infections" OR "Pneumonia" OR "Pneumonia, ventilator-associated" OR "Sepsis" OR "Urinary tract infections" OR "Surgical wound infection"	"Economics" OR "Hospital costs" OR "Health care costs"
Usage	#1 "Intensive care units" AND "Cross infection" OR "Health-associated infections" OR "Pneumonia" OR "Pneumonia, ventilator-associated" OR "Sepsis" OR "Urinary tract infections" OR "Surgical wound infection" AND "Economics" OR "Hospital costs" OR "Healthcare costs" #2 "Intensive care units" AND "Cross infection" AND "Hospital costs"		

Source: Barroso LKD, et al., 2023.

The terms were identified after consultation with the Health Sciences Descriptors of the Virtual Health Library and Medical Subject Headings (MeSH/PubMed). To the equation, the uncontrolled vocabulary "health-associated infections" was included to obtain a targeted search strategy and broaden the findings. The Boolean operators AND and OR were used to cross-reference controlled and uncontrolled vocabulary. Studies that answered the research question, published in Portuguese, English, and Spanish, and available electronically in full and without a time framework were included.

The exclusion criteria were: studies to evaluate costs related to drug testing and surgical procedures; letters, editorials, reflective studies, experience reports, review reports, course final papers, dissertations, and thesis. The search for studies occurred in September 2022, between the 7th and the 16th, through the Portal of Periodicals of CAPES, by access to the Brazilian Federated Academic Community (CAFe), with the compilation from the higher education institution and registration at the State University of Ceará. The electronic databases consulted were: Medical Literature Analysis and Retrieval System Online (MEDLINE),

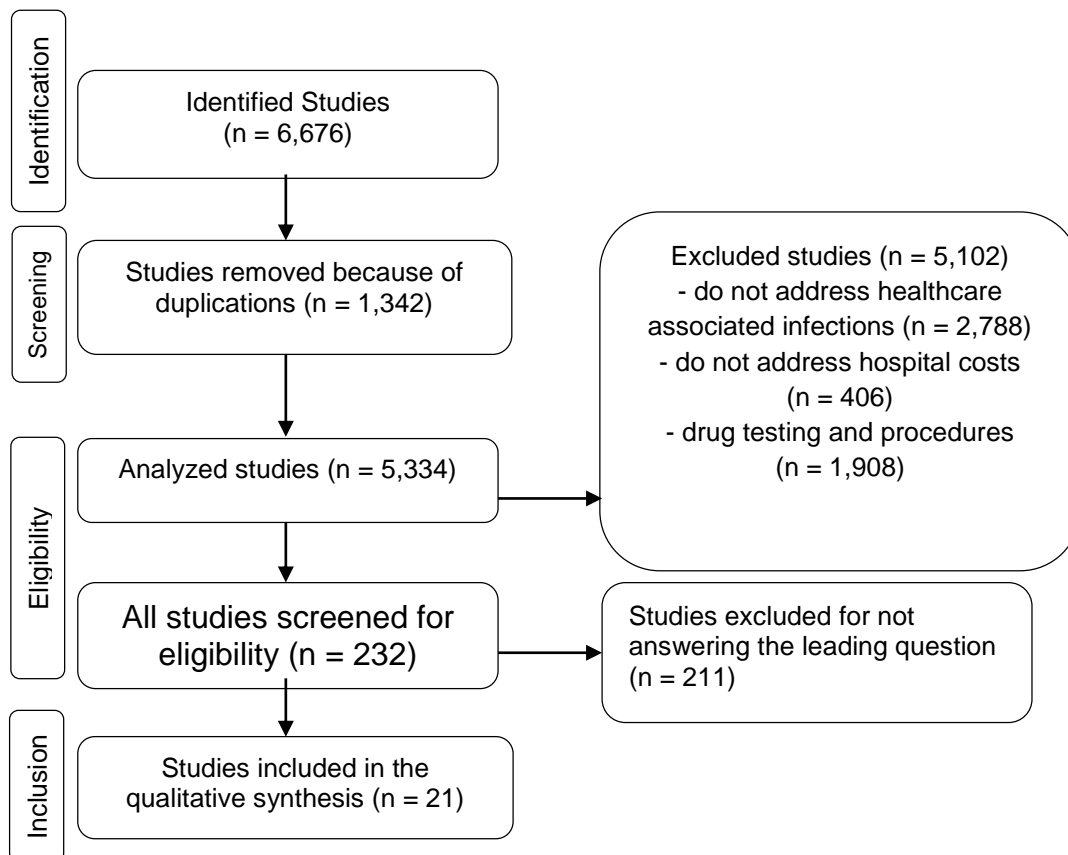
via the National Library of Medicine (PubMed); Science Direct, Web of Science; Scientific Electronic Library Online (SciELO); Latin American and Caribbean Literature on Health Sciences (LILACS), and Índice Bibliográfico Español en Ciencias de la Salud, via BVS. To guarantee the quality of the search, compilation of studies, and removal of duplicates, the recommendations of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) group (MOHER D, et al., 2009) were followed, with the support of Mendeley, a software for reference management.

The search was conducted by two researchers, independently and simultaneously, and, in case of discrepancies, a third researcher was consulted. Initially, titles and abstracts were read; those related to the theme were read in full. Once selected, the following information was extracted: year, country, and journal of publication; professional category of the authors; objectives; method, and main results. For the extraction of information, a Microsoft Excel tool was drafted. The analysis and integration of results were based on the data reduction method, through critical reading. The results were presented in the form of a synoptic summary and in a descriptive manner, in order to promote the incorporation of evidence and the identification of gaps in knowledge.

RESULTS

According to the search, 6,676 articles were initially found in the selected databases. Thus, duplicate studies were then removed (n=1342) and 5334 were analyzed. Therefore, studies that did not address HAIS, hospital costs, and costs related to drug testing and surgical procedures were excluded (n = 5099). Thus, 235 studies were read in full to assess eligibility. In the end, 21 were compiled as a sample, as shown in **Figure 1**.

Figure 1 – Flowchart of the comprehensive review article compilation process.



Source: Barroso LKD, et al., 2023.

Table 1, below, provides the characterization of the sample as to author, year, title, place, journal, type of study, and an average cost of HAIS in the ICU.

Table 1- List of selected studies.

No.	AUTHOR AND YEAR	STUDY OBJECTIVES	COUNTRY	JOURNAL	TYPE OF STUDY	AVERAGE COST
A1	Wang YC, et al. (2020)	To estimate the clinical and economic impact of intensive care unit-acquired bloodstream infections in Taiwan.	Taiwan	BMJ Open	Prospective cohort study	US\$ 16,038
A2	Laupland KB, et al. (2006)	The objective of this study was to quantify the excess length of stay, mortality and cost attributable to ICU-acquired BSI.	Canadá	J Hosp Infect	Cohort study	US\$ 25,155
A3	Brunelli SM, et al. (2016)	Purpose: Bloodstream infections (BSIs) complicate the management of intensive care unit (ICU) patients. We assessed the clinical and economic impact of BSI among patients of a managed care provider group who had a central venous catheter (CVC) placed in the ICU.	USA	J Crit Care	Desk study	US\$ 129,000
A4	Osme SF, et al. (2022)	To estimate direct costs associated with the most significant HAIS in 50 teaching hospitals in Brazil, affiliated to the unified health system (Sistema Único de Saúde: SUS).	Brazil	Braz J Infect Dis	Methodological study	US\$ 112,924,421
A5	Silva PLN, et al. (2017)	Identificar a relação de custo-benefício na prevenção e no controle das infecções hospitalares em uma unidade de terapia intensiva neonatal.	Brazil	J. Health Biol Sci	Desk study	US\$ 1,668.81
A6	Leal MA e Vilela AAF (2021)	Avaliar custos de internação hospitalar de pacientes com e sem Infecção Relacionada à Assistência em Saúde em uma Unidade de Terapia Intensiva.	Brazil	Rev. Bras. Enferm.	Retrospective case-control study	US\$ 2,981.92
A7	Nangino GO, et al. (2012)	As infecções nas unidades de terapia intensiva estão associadas a elevada morbidade e mortalidade, além de alto custo. A análise desses aspectos pode contribuir para a otimização de recursos financeiros relacionados.	Brazil	Rev Bras Ter Intensiva	Retrospective cohort study	US\$ 1,257.53

No.	AUTHOR AND YEAR	STUDY OBJECTIVES	COUNTRY	JOURNAL	TYPE OF STUDY	AVERAGE COST
A8	Dramowaski A, et al(2016)	This article investigates burden, spectrum, risk factors, and impact of pediatric HCAI measured by prospective clinical surveillance at a South African referral hospital.	South Africa	J Hosp Infect	Cohort study	US\$ 371,887
A9	Anderson DJ, et al. (2013)	The main goal of this subcommittee was to calculate the direct costs of selected HAI for acute care hospitals in NC and, subsequently, the state of NC.	USA	Am J Infect Control	Retrospective cohort study	US\$ 985,000 to 2.7 million/ year
A10	Kaye KS, et al. (2014)	To quantify the effect of nosocomial bloodstream infection (BSI) on older adults, including mortality, length of stay (LOS), and costs attributed to BSI.	Israel	J Am Geriatr Soc	Retrospective cohort study	US\$ 102,276/ case
A11	Baier C, et al. (2020)	This study therefore provides data on the incidence of primary nosocomial CLABSI in hematologic and oncologic patients, as well as on contributing risk factors and the financial burden of CLABSI.	Germany	PloS one	Retrospective cohort study	EUR 8,810/ case
A12	Su LH, et al. (2020)	Our study aimed to evaluate the negative impacts of MRDB-HAIS versus HAIS due to non-MDRB (non-MRDB-HAIS).	USA	PLoS one	Retrospective case-control study	
A13	Niederman MS (2001)	Conduct a survey of factors that contribute to increased costs in the management of ventilator-associated pneumonia.	USA	Crit Care	Retrospective cohort study	US\$ 20,000
A14	Chen Y, et al. (2005)	Economic evaluation has become increasingly important in healthcare and infection control. This study evaluated the impact of nosocomial infections on cost of illness and length of stay (LOS) in intensive care units (ICUs).	China	Infect Control Hosp Epidemiol	Retrospective cohort study	US\$ 10,354 to US\$ 3,985
A15	Kollef MH, et al. (2012)	To evaluate the economic impact of ventilator-associated pneumonia (VAP) on length of stay and hospital costs.	USA	Infect Control Hosp Epidemiol	Retrospective cohort study	US\$ 39,828 to US\$ 99,598

No.	AUTHOR AND YEAR	STUDY OBJECTIVES	COUNTRY	JOURNAL	TYPE OF STUDY	AVERAGE COST
A16	Saleh SS, et al. (2010)	To investigate the cost impact of hospital-acquired complications (HACs).	USA	Medical Care	Prospective cohort study	US\$ 700 to US\$ 90,000
A17	Sodhi J, et al. (2016)	The current study was undertaken to evaluate the impact of HAIS on length of stay and costs of health care in children admitted to Paediatric Intensive Care Unit (PICU) of a tertiary care hospital in north India.	India	Indian J Med Res	Prospective cohort study	US\$ 3,413 to US\$ 56,587
A18	Kyaw MH, et al. (2015)	This study assesses the impact of <i>S. aureus</i> or <i>P. aeruginosa</i> pneumonia in ICU patients on healthcare costs, utilization, and mortality both during hospitalization and subsequent to discharge from the hospital.	USA	BMC Health Serv Res	Observational retrospective cohort	US\$ 81.7 billion
A19	Neves LE, et al. (2021)	To verify the economic viability and effectiveness of Surfic® in relation to the use of other disinfectant products in the reduction of HAIs in a medium-sized private hospital in the city of Goiânia.	Brazil	RRS-FESGO	Cross-sectional study	US\$ 2,009.86 To US\$ 1,726.43
A20	Leôncio JM, et al. (2019)	To assess the impact of Healthcare-associated Infections on the cost of hospitalization for children.	Brazil	Rev Esc Enferm USP	Coorte Prospective cohort study	US\$ 1,497.92 to 8,561.12
A21	Hung TM, et al. (2022)	This study aims to investigate the direct medical cost (defined as costs directly related to medical services) in the context of critical care for key infectious diseases (tetanus, sepsis, and dengue) in a referral hospital in HCMC, Vietnam, explore how the costs and cost drivers can vary and investigate the patients' out-of-pocket costs in the context of the national health insurance program.	Vietnam	Frontiers in Public Health	Cross-sectional study	US\$ 2,590 to US\$ 4,250

Source: Barroso LKD, et al., 2023.

DISCUSSÃO

Patients who are hospitalized in the ICU, it is more common to acquire hospital infection, because these patients usually present a clinical picture/severity that leaves them more susceptible to infections, due to being exposed to procedures considered invasive, also due to the suppression of their immune system and prolonging hospitalization, with this, they have a high risk of acquiring HAIS. However, as much as patients admitted to these units benefit from quality and technological multidisciplinary assistance, they run the risk of acquire infection between five and ten times higher than in other units, even if represent 5% to 10% of hospital beds (BAPTISTA KCC, et al., 2020; CONTREIRO KS, et al., 2021).

By and large, the literature postulates that the costs of ICU admissions accounted for 86.5 to 91.2% of total hospital admission costs (HUNG TM, et al., 2022). In this context, HAIS amass annual costs between US\$ 124.1 to US\$ 347.8 million (ANDERSON DJ, et al., 2013). Thus, it is estimated that the cost of hospitalization of patients with HAI is up to four times higher compared to patients without HAI during their ICU stay (p-value < 0.001). Additionally, these were found to be associated with higher mortality (p-value < 0.001), longer hospital stays (p-value=0.021), and higher hospital costs (p-value=0.007) (LEÔNICIO JM, et al., 2019; LEAL MA e VILELA AAF, 2021).

It is worth mentioning that for the determination of costs, direct, indirect and preventive. The first, direct, is related to the costs of diagnosis and treatment, such as exams, period of hospitalization, antimicrobials, among others. Already the second, indirect, involves secondary social costs, such as a certificate for absence from work, changes in family routine, death and others that are difficult to measure. Lastly, the preventive measures associated with the control of these complications, such as the standardization of protocols and conduct, remuneration of specialized professionals and the maintenance of programs (RODRIGUES ALL, 2007).

In a hypothetical scenario without HAIS, Osme SF et al. (2022) propose the direct annual cost of hospital care for 26,649 patients admitted to adult ICUs from 50 hospitals was US\$ 112,924,421. There was an increase of approximately US\$56 million in a 29.1% scenario, and an increase of US\$147 million in a 61.6% scenario. The impact on direct cost becomes significant from a 10% HAIS prevalence, where US\$2,824,817 is added for each 1% increase in prevalence.

For example, in a survey conducted in India, the average total costs for patients with and without HAIS were US\$ 3,413 and US\$ 943, respectively (SODHI J, et al., 2016). Allied with this, authors report that patients with HAI had their ICU admissions prolonged by 11.4 days compared to patients without infection. When it comes to the average cost per hospitalization, this represented an additional expense of US\$ 978. That is, a study carried out in Belo Horizonte, Brazil, found a substantial difference between an average of 21.43 days for infectious cases and 14 days for non-infectious ones. Showing an average length of stay of 38.2 days for patients with HAIS, costs were R\$1.5 million compared to R\$250,000. (SILVA PLN, et al., 2017).

In another scenario, costs differed by about US\$ 7,000 ($P < 0.05$), with an increase of 18.2 days of hospitalization ($P < 0.001$) and US\$ 353 for each additional day in the ICU ($P < 0.001$) (CHEN Y, et al., 2005). In pediatric units, HAIS accounted for a direct cost of USD 371,887 and an additional 2,275 days of hospitalization, 2,365 antimicrobial days, and 3,575 laboratory investigations (DRAMOWSKI A, et al., 2016).

Accordingly, Brazilian results show a comparison between patients with and without infection, unveiling a longer stay (15 [11-25] versus 3 [2-6] days; $p < 0.01$), higher spending per patient in the intensive care unit (an average of US\$ 1804.62 [US\$ 1006.47-3328.47] versus US\$ 202.03 [76.89-509.24]; $p < 0.01$) and higher spending per day of intensive care unit stay (US\$ 114.23 [75.23-154.90] versus US\$ 66.36 [32.16-132.92]; $p < 0.01$) (NANGINO GO, et al, 2012). Specifically, the mean total ICU cost was US\$ 675 (interquartile range (IQR) US\$ 550, US\$ 990), US\$ 273 (IQR US\$ 168, US\$ 503), and US\$ 64.4 (IQR US\$ 55.3, US\$ 95.9) for patients with sepsis, tetanus, and dengue fever, respectively (HUNG TM, et al., 2022).

Likewise, the average cost was significantly higher (US\$ 126,399.5) ($p < 0.001$) among patients who underwent some invasive procedure during hospitalization compared to those who did not undergo procedures or surgeries (US\$ 1302,88) (DRAMOWSKI A, et al., 2016).

In the meantime, respiratory infections, especially Ventilator-associated and Hospital Pneumonia, bloodstream infections, distributed in sepsis, surgical site infection, infection associated with a central venous catheter, and infection of the urinary tract associated with bladder catheter (SALEH SS, et al., 2010; LEAL MA e VILELA AAF, 2021).

HAI were significantly associated with length of ICU stay, malnutrition, HIV infection, comorbidities, indwelling devices, blood transfusion, and hospital transfer (DRAMOWSKI A, et al., 2016). The most frequently identified biological agents were *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant *Enterococcus* (LEAL MA e VILELA AAF, 2021).

Therefore, the considerable expense is justified due to the need for high-cost medications, substitutive and supportive therapies related to organ dysfunction, and laboratory tests (CONDE KA, et al., 2013). In hospital institutions, especially in ICUs, antimicrobial costs represent *"from 30% to 50% of the total spent on medications, and at least 50% of patients use antibiotics at some point during hospitalization"* (OLIVEIRA AC e PAULA AO, 2012). In HAI, antibiotic costs are considerably higher, with an average of US\$ 172 (IQR US\$ 155, US\$ 233) (HUNG TM, et al., 2022).

A survey applied in inpatient units of a hospital center in Europe found that patients who acquired HAI had overall antimicrobial costs 2.5 times higher compared to those who did not, with incremental costs amounting to € 1,389.40. Thus, it is observed that the costs with HAI outweigh the benefits for both the institution and the patient, as well as the increase in invasive procedures, as a result of antibiotic therapy. (MARTINS MITM, et al., 2007).

Regarding the issue, Su LH, et al. (2020) state that among a group affected by multidrug-resistant agent HAI, significant differences were found in overall hospital expenses, costs for medical and nursing services, drugs, rooms/beds, and ICU length of stay compared to the non-resistant group, the average overall hospital costs increased by 26%, with an average length of stay 13% higher.

Patients with *S. aureus* or *P. aeruginosa* pneumonia had a longer average length of stay (37.9 or 55.4 vs 7.2 days, $P < 0.001$) and ICU stay (6.9 or 14.8 vs 1.1 days, $P < 0.001$), higher rate of mechanical ventilation (62.6% or 62.3% vs 7.4%, $P < 0.001$), higher mortality (16.0% or 20.2% vs 3.1%, $P < 0.001$), and higher average total hospitalization costs (US\$ 146,978 or US\$ 213,104 vs US\$ 33,851, $P < 0.001$) (KYAW MH, et al, 2015).

With regards to Ventilator-Associated Pneumonia (VAP), the incidence rate reached 1.27 per 1,000 ventilator days, inferring longer average durations of mechanical ventilation (21.8 vs 10.3 days), ICU stay (20.5 vs 11.6 days), and hospitalization (32.6 vs 19.5 days). The average hospitalization expenses were US\$ 99,598 for patients with VAP and US\$ 59,770 for patients without VAP, representing an absolute difference of US\$39,828 (KOLLEF MH, et al., 2012).

In Central Venous Catheter associated (CVC) bloodstream infections, the incidence rate was 10.6 cases per 1,000 CVC days. The use of more than one CVC per case, CVC insertion for conditioning for stem cell transplantation, acute myeloid leukemia, leukocytopenia ($\leq 1000/\mu\text{L}$), carbapenem therapy, and pulmonary diseases were independent risk factors for HAI. In the meantime, the directly attributable hospital expenses were € 8,810 per case. These additional costs result in an attributable median loss of 8,171 € per case as costs exceeded reimbursements. This data on the clinical and economic impact underline the need for proper adherence to appropriate and recommended infection control measures (BAIER C, et al., 2020).

Similarly, the development of bloodstream infection was associated with a longer hospital stay (+18 days), a more than 3-fold increase in the risk of in-hospital death, and an additional cost of US\$ 129,000 for the index hospitalization ($p < 0.001$) (LAUPLAND KB, et al., 2006; BRUNELLI SM, et al., 2016; WANG YC, et al., 2020). The mortality rate of cases was 49.4% compared to 33.2% for controls (OR = 2.1, $P < 0.001$) (KAYE KS, et al., 2014).

Moreover, the analysis of the impact of sanitizing agents on HAIS revealed that solutions with alkylbenzyl ammonium chloride - benzalkonium chloride 5.2% and polyhexamethylene biguanide - PHMB 3.5% infer a decrease in cases of primary bloodstream infection (BSI), urinary tract infection (UTI), and ventilator-associated pneumonia (VAP), in comparison with solutions of alkyldimethylbenzyl ammonium chloride, nonionic surfactant, glucoprotamine, solvent, complexing agent, anticorrosive agent, and water or alcohol 70°. In the meantime, it is found that prudent implementation of surface disinfection regimes is effective in preventing or minimizing adverse effects (NEVES LE, et al., 2021).

Based on this, it is implied that understanding the burden of the cost of HAIS in the ICU is essential, since the direct costs and increased length of stay have an impact on public health, as an important limiting factor of access. In this way, the tackling of the whole question is encouraged in order to build subsidies with strong evidence to support decision-making by healthcare professionals and managers, impacting on the formulation of policies and implementation of cost-effective interventions. Focusing not only on cost reduction, but in providing safe care, with impacts on reducing mortality associated with HAIS in the ICU.

FINAL CONSIDERATIONS

This study focused on appraising the economic impact generated by HAIS in ICU admissions through a comprehensive literature review, which resulted in a sample of 21 articles. In the meantime, the hospitalization expenses in patients with HAIS in the ICU was up to four times higher compared to patients without HAIS, related to longer stays, use of antimicrobials, and laboratory investigations, especially exacerbated in multidrug-resistant HAIS, showing that HAI has a significant financial impact on the health system and contributes to a longer stay of hospitalized patients. The most common HAIS described were respiratory infections, especially ventilator-associated (VAP) and hospital-acquired pneumonia (HAP), and bloodstream infections (BSI), divided into sepsis, surgical site infection, central venous catheter-associated infection, and urinary tract infection associated with a urinary catheter. The limitations of the study are related to the study design adopted, which suggests the further development of the theme by conducting population studies that investigate the scenario of practices in the various Brazilian scenarios in order to support the construction of subsidies for healthcare professionals and managers, directed at policy formulation and implementation of cost-effective interventions. This data can be used to support further investment in HAIS reduction efforts in the country.

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