Implications of Healthcare-Associated Infections in Health Management: Review

Implicações das infeções associadas aos cuidados de saúde na gestão em saúde: revisão

Implicaciones de las infecciones asociadas a la atención de salud en la gestión de la salud: revisión

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Abstract: Objective: Describe the scientific evidence of the implications Healthcare-Associated Infections (HAI) in health management. Method: Systematic review in electronic database using DeCs descriptors. Results: Thirteen articles were analyzed, resulting in ten categories of analysis. HAIs contribute to higher mortality rate and financial costs of hospitalization related to higher: average number of days of hospitalizations; increased spending on antimicrobials, diagnostic and complementary tests and invasive devices or procedures; length of hospital stay in intensive care units (ICU); possibility of readmission and development of other complications. Conclusions: HAIs have direct and indirect repercussions on patients' lives as they represent a threat to the safety and quality of care. Prevention programs and infection control measures are considered effective in reducing the incidence rate of HAIs and consequently in reducing costs.

Keywords: hospital-acquired infections; health management; health care costs.

Resumo: Objetivo: Conhecer a evidência científica sobre as implicações das infeções associadas aos cuidados de saúde (IACS) na gestão em saúde. Metodologia: Revisão sistemática da literatura mediante o uso de descritores DeCS. Resultados: Foram analisados 13 artigos dos quais resultaram dez categorias de análise. As IACS contribuem para o aumento da taxa de mortalidade e dos custos financeiros do internamento hospitalar pelo aumento do número médio de dias de internamento, aumento dos gastos com antimicrobianos, exames complementares de diagnóstico e procedimentos médicos invasivos; aumento do tempo de permanência em unidades de cuidados intensivos (UCI); maior possibilidade de reinternamento e desenvolvimento de outras complicações. Conclusões: As IACS têm repercussões diretas e indiretas na vida dos doentes pois representam uma ameaça à segurança e à qualidade dos cuidados. Os programas de prevenção e medidas de controlo de infeção são considerados eficazes na diminuição da taxa de incidência das IACS e consequentemente na redução dos custos.

Palavras-chave: infecção hospitalar; gestão em saúde; custos de cuidados de saúde.

Resumen: Objetivo: Conocer la evidencia científica sobre las implicaciones de las infecciones asociadas a la atención de la salud (IAAS) en la gestión de la salud. Metodología: Revisión sistemática de la literatura utilizando los descriptores del DeCS. Resultados: Se analizaron trece artículos, que dieron lugar a diez categorías de análisis. Las IAAS contribuyen al aumento de la tasa de mortalidad y a los costes financieros de la estancia hospitalaria, ya que aumentan el número medio de días de hospitalización, el gasto en antimicrobianos, las pruebas diagnósticas complementarias y los procedimientos médicos invasivos; el aumento de la duración de la estancia en las unidades de cuidados intensivos (UCI); la mayor posibilidad de reingreso y el desarrollo de otras complicaciones. Conclusiones: Las IAAS tienen repercusiones directas e indirectas en la vida de los pacientes, ya que representan una amenaza para la seguridad y la calidad de la atención. Los programas de prevención y las medidas de control de la infección se consideran eficaces para reducir la tasa de incidencia de las IAAS y, en consecuencia, los costes.

Palabras claves: infección hospitalaria; gestión en salud; costos de la atención en salud.

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Introduction

Healthcare-Associated Infections (HAIs) are a public health concern on a global scale, [1] described by the European Center for Disease Prevention and Control (ECDC) as an infection acquired during health care provision in a hospital or other health institution. [2] This type of infections has direct and indirect costs in societies, associated not only with healthcare costs, but also by the increasing of the patient's dependency after discharge. [3] The ECDC [4] recognizes the existence of high charges for European countries associated with HAIs, particularly about the patient security. According to the Centers for Disease Control and Prevention (CDC) in 2015 in the USA, more than 687.000 HAIs occurred in hospitalized patients and 72.000 of these having died during these infections. [5] The ECDC estimates that daily, in the ICU of the European hospitals, are approximately 81.089 patients with HAIs. [4] In 2017, the prevalence of HAIs in Portugal was 7.8 % and several health institutions recognize the existence of associated financial, economic, social, and individual costs. [6, 7] This issue has a direct influence on health management, making it urgent to understand its dimensions as well as the measures to prevent it. [8] Lorenzetti et al. [9] define health management as the knowledge applied to the planning of health organizations, involving the management of health networks to guarantee universal, total, and equitable assistance to the needs of populations.

The central importance of understanding how the prevalence of HAIs limits health management on the high financial and safety impact that these infections imply for health systems, making it mandatory to adopt preventive measures by the entities of health for their prevention. [10]

Prior studies to the current systemic review already have found a direct association between HAIs and the impact of health management. Barros concluded that patients with HAIs had twice of the financial cost during hospitalization compared to those who did not develop any infection. [11]

Given these statements, this article aims to describe the scientific evidence of the implications of HAIs in health management and its dimensions.

Methods

A systemic review was performed following the PRISMA 2009 Checklist protocol, containing a 27-item checklist and a four-step flowchart whose objective is to help authors to improve the reporting of systematic reviews. [12] The process began with the elaboration of the research question according to the PICo format: "What are the implications for Health Management (I) attributable to Healthcare Associated Infections Associated (P)?"

The review considered studies written in Portuguese, English and Spanish, published between 2009 and 2019, full text presentation, free access with peer review and at least 2 descriptors. Other systematic reviews and studies with more than 10 years, repeated, in other languages, without free access or with population younger than 18 years were excluded. In addition, studies that did not correspond to the topic based on titles/abstracts were excluded.

The research was carried out in June 2019 using the EBSCOhost platform CINAHL with full text and Medline with full text), SciELO and PubMed. The following descriptors (DeCS) were used in a Boolean logic: "cross infection" (S1) AND "cost and cos analysis" (S2) AND "health management" (S3). Figure 1 depicts the methodological approach that was employed.

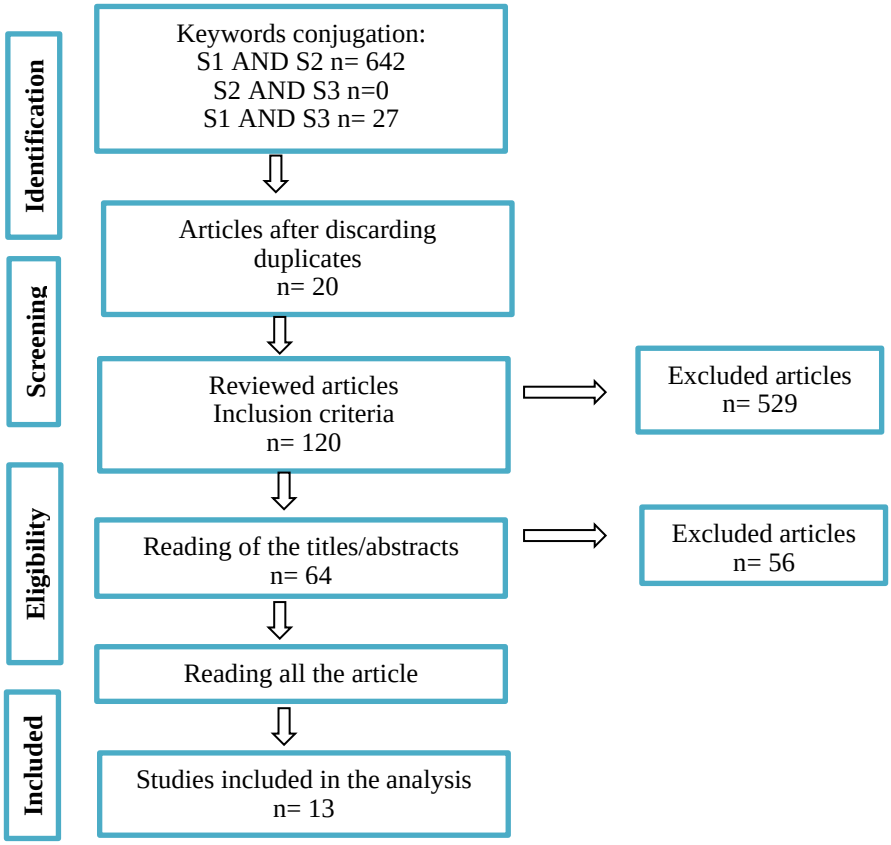

Figure 1. Study selection process. Adaption of PRISMA 2009

Results

Thirteen studies published between 2009 and 2017 were analyzed. These studies are predominantly retrospective with comparison and analysis between groups. The privileged data treatment was the statistical analysis. These studies are from several countries on different continents, which enrich the cultural diversity of this review. Most of the articles were written in English. Study participants were hospitalized patients divided into two groups: patients with HAIs and patients without HAIs. The objective was to compare the costs associated with the presence of HAIs and their implications. The articles that made up the corpus of analysis are shown in Table 1.

It should be noted that the analysis of the articles was carried out by double review, having resorted to a third reviewer in case of doubt and/or disagreement.

Table 1. Articles selected for analysis

Title Year of publication Authors	Study location	Type of study Objective	Results
Nosocomial infections impact in a hospital in Bogota (Colombia): effects on mortality and hospital costs (2015) Saavedra et al. [13]	University Hospital of level 4: inpatient services and ICU´s. Colombia.	Case-control. Comparison of the costs and mortality rates associated with HAIs between 2 groups of inpatients – patients with HAIs and patients without HAIs.	- Increased costs of hospitalization in patients with HAIs; - Higher mortality rate in patients with HAIs; - Increased length of hospital stay in patients with HAIs; - The service of surgical specialties was the service with more HAIs. - Most common HAIs: Pneumonia, surgical site infection, sepsis, UTI; - Most common microorganisms: Gram negative and Gram positive bacteria; - Increased costs of antimicrobials in patients with HAIs. The higher cost was associated with the bacteremia secondary at catheter. - Some patients had more than one HAIs and more than one microorganism in the same hospital stay.
Hospital costs of nosocomial multi-drug resistant *Pseudomonas aeruginosa* acquisition (2012) Morales et al. [14]	Hospital in Barcelona, Spain (level not evidenced)	Retrospective study. Comparison of the cost associated with Pseudomonas aeruginosa infection	- Increased costs of hospitalization in patients with resistance to *P. aeruginosa*; - Patients with resistance and multidrug resistance underwent a greater number of invasive procedures (e.g., mechanical ventilation, hemodialysis, bronchoscopy); - Increased length of hospital stay in patients with resistance and multidrug resistance; - Higher mortality rate in patients with drug resistance.
Financial impact of nosocomial infections in the intensive care units of a charitable hospital in Minas Gerais, Brazil (2012) Nangino et al. [15]	Hospital in Brazil, ICU (level not evidenced)	Retrospective study. Analysis of the economic impact of HAIs on ICU.	- Increased costs per day of hospitalization in patients with HAIs; - Increased length of hospital stay in patients with HAIs; - Most common HAIs: ventilator-associated pneumonia; bloodstream infection; UTI; site infection; surgical site infection. - The HAIs associated with more costs were ventilator-associated pneumonia and bloodstream infection. - Patients with surgical site infection and bloodstream infection have more costs in ICU.
Economic burden of methicillin-resistant Staphylococcus aureus bacteremia in critical care patients in hospitals in Bogotá (2014) Barrero et al. [16]	9 hospitals of level 3/4 Colombia	Multicenter cohort study. Description of the costs associated with bacteremia caused by *S. Aureus* in hospital units.	- Increased costs and length of hospital stay in patients with bacteremia by MRSA; - Higher mortality rate in patients with MRSA; - Increased costs in patients with MRSA associated to diagnostic tests, antibiotic therapy, invasive procedures and respiratory physiotherapy.

Assessing the burden of pneumonia using administrative data from Malaysia, Indonesia, and the Philippines (2016) Azmi et al. [17]	Hospitals in Indonesia (42), Malaysia (2) e Philippines (18) (levels not evidenced)	Comparative study. Description of the incidence, mortality rate, hospital stay rate and costs associated with community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) in 3 Asian countries.	- For every 100.000 patients there was: Malaysia (4205 CAP/2187 HAP); Philippines (14245 PAC/5615 HAP); Indonesia (988 CAP (538 HAP); - Higher mortality rate in HAP than in CAP in three countries; - The comorbidities most associated with HAP were chronic lung disease and hearth disease; - Increased costs per day of hospitalization in patients with HAP; - Increased length of hospital stay in the HAP than in the CAP.
Cost and characterization of hospital infection among the elderly (2013) Izaias et al. [18]	Hospital in Brazil (with inpatient and surgery units)	Cross-sectional and quantitative study. Characterization of the profile and costs associated with nosocomial infection in the elderly.	- Most common HAIs: respiratory tract, urinary tract and surgical site infection; - Increased costs and length of hospital stay in patients with HAIs; - Hospital services with higher HAIs rates: Urgency, ICU and Medicine; - Some patients had more than one HAI; - Diagnosis of HAI was making after 8 days of hospitalization.
An economic evaluation of *Clostridium difficile* infection management in an Italian hospital environment (2012) Magalini et al. [19]	Hospital in Rome, Italy. (level not evidenced)	Retrospective study. Description of the costs associated with *Clostridium difficcile* infection.	- Increased length of hospital stay in patients with infection with *Clostridium difficcile*; - Increased use and costs associated with antimicrobials; - Extra costs of 13957 euros per patient with infection of *Clostridium difficcile;* - ICU hospitalization with higher costs in patients with *Clostridium difficcile* infection; - Increased costs associated to: need of isolation measures, complications (surgery for stoma placement) and diagnostic tests.
The cost of resistance: incremental cost of methicillin-resistant *Staphylococcus aureus* (MRSA) in German hospitals (2009) Resch et al. [20]	2 University hospitals of level 4; 2 Hospitals of basic care. 2 specialized hospitals and 5 hospitals multipurpose. Germany	Retrospective and comparative study. Analysis of the impact associated with MRSA infection in hospitals in Germany.	- Increased length of hospital stay in patients with MRSA infection; - Higher mortality rate in patients with MRSA infection; - Increased costs associated with patients with MRSA infections; - MRSA patients have worse clinical conditions; - Patients with infection by MRSA needed more invasive procedures.
Attributed costs of health care-associated infections in a Colombian hospital, 2011-2015 (2019) Ortiz-Mayorga et al. [21]	Hospital of level 4 in Bogotá, Colombia	Case-control. Determination of the factors associated with the increase in HAIs costs in a health institution in Bogotá.	- The costs with antibiotic therapy represented 41 % of the total cost of hospitalization in patients with HAIs; - Complementary diagnostic tests and laboratory tests represented the 2nd highest costs of hospitalization (13.5 %); - Increased length of hospital stay for patients with HAIs (average plus 7 days); - Ventilator-associated pneumonia was the HAIs with higher cost.

Rising United States Hospital Admissions for Acute Bacterial Skin and Skin Structure Infections: Recent Trends and Economic Impact (2015) Kaye KS et al. [22]	Urban and Rural Hospitals USA	Comparative retrospective analysis. Determination of the resources and variations in hospital costs associated with skin infections and surgical site infections.	- Increased length of hospital stay in patients with surgical local infection; - Increased hospital costs in patients with surgical local infection.
Associated with Health Care-Associated Infections in Cardiac Surgery (2015) Greco G et al. [23]	9 Cardiothora-cic surgery units EUA.	Prospective study. Determination of the cost associated with the most frequent HAIs in the 2 months after the surgery.	- Increased length of hospital stay in patients with HAIs (including ICU); - Costs associated with initial hospitalization was higher in patients with HAIs; - Most common HAIs: Pneumonia (48 %), Sepsis (20 %), *Clostridium difficille* infection (18 %) and surgical site infection; - Patients who developed HAIs during the hospitalization had a higher risk of readmission.
Enterococcal bacteraemia: factors influencing mortality, length of stay and costs hospitalization (2103) Cheah ALY et al. [24]	2 hospitals of level 3. Australia.	Retrospective comparative study. Identification of the factors associated with mortality, length of stay and hospital costs in patients with VRE and VSE	- Increased length of stay and higher costs in patients with VRE bacteremia; - Linezolid-treated patients with lower mortality rate; - Length of hospital stay and cost was not related to the time of antibiotic used; - In patients with VSE bacteremia, the correct use of antimicrobials was decisive in terms of costs, mortality rate and length of hospital stay; - Mortality rate did not increase in the patients with VRE bacteremia.
The Risk Factors, Costs, and Survival Analysis of Invasive VRE Infections at a Medical Center in Eastern Taiwan (2017) Jiang HL et al. [25]	Taiwan Medical Center of level 4: ICU and inpatients units. China.	Comparative study. Comparison of the costs and mortality rates between patients with VRE and patients with VSE; Analysis of risk factors for VRE infection.	- Higher mortality rate for patients with VRE infection; - Costs three times higher with antimicrobials for patients with VRE; - Higher rates of HAIs per VRE in ICU; - Causes of VRE infection: central venous catheter (81.3 %) ventilator use (52.1 %) and septic shock (43.8 %); - Higher use of antimicrobials was associated with higher risk of having VRE infection.

Source: Own elaboration (2019)

After filling in the table, we formulated categories of results considering the distribution of data by frequencies, that is, the number of studies in which a certain result is mentioned.

From the analysis of the 13 articles, ten categories of results were obtained (Table 2).

Table 2. Results categories

Results Categories	Studies	Main conclusion
Increased financial costs associated with length of hospital stay	13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24	Patients with HAIs were 2 to 9 times more costs by day in hospital admissions.
Increased length of hospital stays	13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24	Patients with HAIs had, on average, 2 to 20 more days of hospitalization.
Increased costs with the use of antimicrobials	13, 14, 15, 16, 18, 19, 21, 23, 24, 25	Patients with HAIs had 28 times higher costs by day.
Increased mortality rate	13, 14, 16, 17, 20, 24, 25	Mortality rate in patients with HAIs ranged from 7 %-64.6 %.
Increased length of hospital stays of patients in ICU/greater number of patients with ICU need	13, 14, 15, 16, 21, 23, 24	On average, 5 more days of hospitalization in the ICU, which implies twice the costs.
Increased monetary expenses with complementary diagnostic tests	14, 16, 19, 21, 23	It may correspond to 13.5 % of the total amount of hospitalization.
Higher number of invasive medical procedures	14, 16, 20,25	Patients with HAIs were subject to 7 % more procedures.
Higher probability of developing complications	13, 16, 19, 25	Sepsis, surgeries, need for invasive ventilation, increased degree of dependence.
Development of a second HAI	13, 18	22.9 % of patients had more than one HAI.
Higher probability of readmission	23	33 % of patients were readmitted.

Source: Own elaboration (2019)

The overall HAIs rate in the studies analyzed ranged from 1.8 % [13] to 17 %. [18]. In turn, the most frequent HAIs reported was respiratory tract infections,[13-15, 17, 18, 23, 25] bloodstream infections,[13, 15, 23, 25] urinary tract infections (UTI),[13-15,18] gastrointestinal infections,[23] skin and soft tissue[14] and other locations.[13] Regarding the microorganisms described in the studies were found: vancomycin-resistant enterococci (VRE),[24, 25] Pseudomonas aeruginosa,[14] Clostridium difficile (CD),[19, 23] methicillin-resistant aureus (MRSA),[16, 20] Gram negative bacilli[13] and fungi.[13]

Pneumonia [15, 21, 23] and bloodstream infection [15] were associated with higher financial costs. The ICU units had the highest incidence of HAIs and was the service with higher financial costs associated. [14-16, 18, 19, 25] The other services with high number of HAIs occurrences were the surgical service, [13, 19] medicine service [18, 19] and emergency service. [18]

Discussion

HAIs are an important public health concern that arises from adverse effects of care, contributing to higher mortality/morbidity and monetary costs, mainly due to the increased length of hospital days, increased costs with antimicrobials, increased complications and the degree of dependence of the patient after discharge,[13, 15-21, 25, 26] also inflating the costs at a socioeconomic and family level.[27] Furthermore, the life quality of patients and their families is also affected.[28, 29]

The **increased financial costs associated with higher length of hospital stay** in patients with HAIs were reported in 12 of the 13 studies analyzed. In a study by Nangino et al. [15] it was observed that infected patients had expenses 9 times higher per day (R$1,093.94 vs. R$9,763.78 [Brazilian real]), with ventilator-associated pneumonia (VAP) and bloodstream infection associated with higher costs/day. These results are similar to those found in the article by Pina et al. [30] where they report that VAP can represent an additional cost of 40.000 dollars per episode. In addition, the need of isolation precautions in most patients with HAIs also contributes to the increase in hospitalization costs, namely expenses with personal protective equipment. [19]

The **increased length of hospital stay in several days** was also reported in 12 studies. [13-24] In the studies, the increase was, on average, from 2[17] to 20[14] more days. In a study by Izaias et al [18] the elderly with HAIs had an average of 24 days of hospitalization, which resulted in an average increase of 15 days compared to the elderly without HAIs, and subsequent increased in costs with medication, exams, and other procedures.

The **increased costs related to the use and acquisition of antimicrobials** were reported in 10 studies. [13-16, 18, 19, 21, 23-25] In a study by Saavedra et al. [13] the median cost of using antimicrobials in infected patients was 28 times higher than the daily value of patients without HAIs (US$132.5 vs. US$4.7 [US dollar]). In addition, the excessive use of antimicrobials promotes multidrug resistance. [14, 31, 32] According to epidemiological surveillance data from the European Antimicrobial Resistance Surveillance Network, [33] Portugal has a high rate of antimicrobial resistance (AMR), being among the European countries with the highest rate of MRSA, *Enterococcus faecium* resistant to vancomycin and *Acinetobacter* with combined antimicrobial resistance. The more antimicrobials are previously used, the probability of HAIs occurrence is higher, namely infections by VRE[25] or CD.[19] Patients with infections caused by resistant microorganisms have a higher number of co-morbidities or more several clinical conditions, earlier mortality, longer hospital stays and a high consumption of health resources.[6, 16] The ECDC reported 33.000 deaths in Europe annually and €1 billion in annual health expenditures, which highlights the critical need to ensure that antimicrobials are used with prudence and that infection prevention and control measures are implemented.[34] Thus, it is essential to understand the problem of multi-resistance to antimicrobials, since they have a strong impact on the economy.[14]

For this, it is necessary to improve the knowledge of HAIs and AMR, promote good practices and the training of health professionals [36-39] to reduce HAIs and AMRs and strengthen the local, regional, and national structures of the Infection Prevention and Control Program and AMR [1, 7]

An **increased mortality rate** was reported in 7 studies. [13, 14, 16, 17, 20, 24, 25] The mortality rate varied between 7 % [20] and 64.6 % in the study by Jiang et al. [25], which compared patients with VRE and patients with vancomycin-sensitive *enterococci* (VSE) (39.4 %). In the study by Saavedra et al.[13] the mortality rate in patients with HAIs was

31.6 % compared to 5.1 % in patients without HAIs; in patients resistant and with multidrug resistance to antimicrobials caused by *Pseudomonas aeruginosa*, the mortality rate was approximately twice as compared to patients without resistance (24.6 % vs. 12.8 %);[14] in a comparative study among patients with MRSA/*methicillin-sensitive staphylococcus aureus* (MSSA), the mortality rates were respectively, 60.7 % and 45.1 %.[16] It should be noted that in this last study, 53% of the individuals have died during hospitalization. In a similar study of Resch et al. [20] patients with MRSA had an average of 7 % higher mortality (18.3 % vs. 10.9 %). Only in the study by Cheah et al. [24] there was no increase in mortality in patients with VRE bacteremia compared to patients with VSE bacteremia.

Other implication of HAIs was the **increased length of hospital stay of patients in ICU or the greater number of patients with ICU need,** reported in 7 studies. [13-16, 21, 23, 24] In the study by Saavedra et al. [13] 54.5 % of infected patients required hospitalization in ICU with an increase of 5 days of hospitalization compared to patients without HAIs who also required ICU. Greco et al. [23] found a mean increase in a length of stay in patients with HAIs of 14 days, with 47 % of that time being due to the need for ICU admission. In 2013, the ECDC estimated that, daily, in the ICU of European hospitals there were 81.089 patients with HAIs. The annual case numbers of HAIs are around 3.2 million people. [40] Nangino et al. [15] referred to the impact on public health that patients with HAIs represents, since, by increasing the number of days of hospitalization, they will restrict the access of other patients, namely to ICU units. [41] In turn, the increase in the length of stay in the ICU leads to an increase in expenditure/day. In the study of Nangino et al. [15] this value was approximately 1.7 times higher. This amount includes the **increase in monetary expenses with complementary diagnostic tests**. [14, 16, 19, 21, 23] In the study by Barrero et al. [16] the amount spent on laboratory tests and diagnostic images in patients with MRSA was 1.6 times higher than the amount spent compared to patients with MSSA. Ortiz-Mayorga et al. [21] concluded that exams and laboratory tests performed on patients with HAIs represented the second highest cost associated with hospitalization – 13.5 % of the total value. In the study by Magali et al. [19] 2.28 % of the total cost of hospitalization was spent on laboratory tests associated with the diagnosis of CD.

In most studies, patients with HAIs or AMRs showed increased disease severity and clinical instability, requiring **invasive medical procedures** as invasive mechanical ventilation, hemodialysis, bronchoscopy, digestive endoscopy, central venous catheter (CVC) or surgery. [14, 16, 20, 25] In the study by Resch et al. [20] patients with MRSA were 7 % more likely to require invasive mechanical ventilation.

Four of the studies analyzed reported a **higher probability of developing other complications**. [13, 16, 19, 25] Barrero et al. [16] reported that patients with infections caused by resistant microorganisms may present a greater number of co-morbidities or more severe clinical conditions, progressing, in this case, to septic shock. In the study by Magali et al. [19] 17.3 % of the patients developed serious complications of CD infection (organ failure, hypotension, anemia requiring blood transfusions) and 4.5 % of them required surgical interventions (colectomy total, ileostomy, and colostomy).

The **development of a secondary HAI** in the same hospitalization was mentioned in two studies. [13, 18] In the study by Saavedra et al. [13] 19.1 % of the patients had more than one HAI during the same period of hospitalization, while Martins et al. [26] mentioned slightly higher values (38.89 % of patients presented two HAIs).

At last, the **higher probability of readmission** [23] reported by Greco et al. [23] show that patients who developed HAIs in the first hospitalization had a higher rate of readmission (33 %). In Oliveira et al. [42], the surgical site infection was the main cause of hospital readmission (in 13.2 % of cases). About 48 % of readmissions associated with HAIs could be avoided and are associated with indicators of low-quality care. [43]

In the analyzed studies, the overall rate of HAIs varied between 1.8 % [13] and 17 %. [18] Data from the Portuguese Health Systems Observatory [7] reported that the prevalence rate of HAIs in a hospital context in Portugal was 7.8 %, in 2017.

The ECDC in its HAIs and AMR prevalence study reported that 5.9 % of patients developed an HAIs. [34] The prevalence and typology of HAIs are variable, denoting differences worldwide. In the USA, the most common infections are UTI and VAP. In Europe, the most prevalent HAIs are respiratory tract infection (pneumonia in 21.45 % of episodes), UTI (18.9 %) and bloodstream infections (10.8 %). [44]

In several studies [30, 45-47], the authors refer to surgical procedures, the use of invasive devices, the use of antimicrobials and the length of hospital stay as the main risk factors for the acquisition of HAIs, as well as the infections by multidrug-resistant microorganisms, which currently represent a significant threat due to the therapeutic impasse they cause. In the USA, in a 2011 study, [7] 25.6 % of HAIs occurred in association with the use of a medical device. Several authors [27, 40, 45, 48-50] have corroborated the relationship between the development of HAIs and the presence of invasive devices, namely ventilator-associated pneumonia, CVC-associated bloodstream infection and catheter-associated UTI. More than half of these infections are preventable based on the implementation of preventive strategies, given the scientific evidence. [51, 52] Thus, it is essential to reduce the use of invasive devices to prevent infection and minimize cross-transmission. [53]

Patients with co-morbidities such as lung and heart disease, [17, 19, 23, 54-56] changes in kidney and liver function, [19, 42, 54] diabetes, [19, 22, 42, 54-56] hemodialysis, [55] chemotherapy [25,56] and immunosuppression [19, 21, 57] may have predisposition to HAIs.

International and national studies show that the prevalence of HAIs is higher in patients admitted to ICUs where, on average, 19.5 % of patients have at least one HAI, while in all other units the average is 5.2 %. [40] The problem of antimicrobial resistance is also higher in ICUs, mostly associated with the severity of the patients' clinical situation, the frequent use of antibiotics and the heterogeneity in the implementation of HAIs prevention and control measures. [58]

Effective treatments for certain multidrug-resistant microorganisms caused by HAIs, such as MRSA, VRE and Gram-negative producers of extended-spectrum beta-lactamase (ESBL), are becoming scarce. [27, 59, 60] In 2017, the most frequent microorganisms isolated in Portugal were *Pseudomonas Aeruginosa*, *Klebsiella pneumoniae* and *Staphylococcus aureus*. [61]

As already mentioned, HAIs entail high financial costs. It is estimated that the total annual cost to the Portuguese National Health Service of additional days of hospital stay due to IACS is approximately 280 million euros. Most of this savings would be available as soon as infection rates are reduced. [62]

Conclusion

In addition to the clinical burden that HAIs entail, there are also economic and social consequences, such as abstention from work, disability, reduced quality of life, etc.

The main limitation of this systematic review is contemplating articles from different countries and continents, with illustrating different realities in different health care services. In addition, data were presented differently in each article (frequencies, percentages, and different currency units), as well as the categories of results, which made comparisons difficult. Other limitation is the fact that the studies were carried out only in the hospital setting. No data were found regarding social implications and the degree of dependence after discharge.

It is concluded that HAIs significantly increase the financial costs of hospitalization and have direct and indirect repercussions on the lives of patients, compromising the safety and quality of care provided. [28, 63] The reduction of hospitalization days and the rational use of antimicrobials are mentioned as major factors to minimize the implications with these infections. Prevention programs and proper infection control measures, as well as the implementation of automated surveillance systems, are considered effective strategies to reduce the incidence of HAIs and the subsequent costs associated with these infections. [1, 52, 61, 62, 64-66]

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