Original Article

Analysis of infectious adverse health event costs

Análise dos custos de eventos adversos infecciosos em saúde

Análisis de los costos de eventos adversos infecciosos en salud

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How to cite:
Matta AC, Matsuda LM, Paulino GM, Haddad MC, Ferreira AM, Camillo NR. Analysis of infectious adverse health event costs. Acta Paul Enferm. 2022;35:eAPE01187.

DOI
http://dx.doi.org/10.37689/acta-ape/2022AO011877

Keywords
Patient safety; Cross infection; Medical errors; Costs and cost analysis

Descritores
Segurança do paciente; Infecção hospitalar; Erros médicos; Custo e análise de custo

Descriptores
Seguridad del paciente; Infección hospitalaria; Errores médicos; Costos y análisis de costo

Submitted
May 21, 2020

Accepted
April 12, 2022

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Associate Editor (Peer review process):
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Abstract

Objective: To analyze infectious adverse event (AE) profile and direct costs in the health care process.

Methods: This is a quantitative, analytical, retrospective study, carried out in a public teaching hospital in Paraná, which had a representative sample (n=97) of infectious AE notifications for the first half of 2019. Data were collected from notifications, medical records and reports of inpatient procedures. For the calculation of costs, unit values were assigned to products and services, based on the reference of February 2019.

Results: The sample consisted predominantly of men, aged > 70 years, with a mean hospital stay of 23.5±12.9 days. There was an association between the type of infection and the variables age group, inpatient unit and type of exit (p<0.01 for all), cost groups and types of infection (p<0.05), age group (p<0.05) and type of outcome (p<0.05). When comparing the means of direct and variable costs of patients, victims of infectious AEs and their simulated pairs, laboratory tests and medications stood out.

Conclusion: The occurrence of infectious AEs was associated with the profile of patients and the relevant characteristics of the care process, with an impact on rising costs, especially with medications and laboratory tests.

Resumo

Objetivo: Analisar o perfil e os custos diretos de eventos adversos (EA) infecciosos do processo de cuidado em saúde.

Métodos: Estudo quantitativo, analítico, retrospectivo, realizado em hospital público de ensino do Paraná, que contou com amostra representativa (n=97) das notificações de EA infecciosos referentes ao primeiro semestre de 2019. Os dados foram coletados a partir das notificações, prontuários e relatórios de procedimentos por internação. Para o cálculo dos custos foram atribuídos valores unitários aos produtos e serviços, com base na referência do mês de fevereiro de 2019.

Resultados: A amostra foi composta predominantemente por homens, na faixa etária > 70 anos, com período médio de internação de 23,5±12,9 dias. Constatou-se associação entre o tipo de infecção e as variáveis faixa etária, unidade de internação e tipo de saída (p<0,01 para todas), grupos de custos e tipos de infecção (p<0,05), faixa etária (p<0,05) e tipo de saída (p<0,05). Na comparação das médias de custos diretos variáveis de pacientes, vítimas de EA infecciosos e seus pares simulados, destacaram-se os exames laboratoriais e os medicamentos.

Conclusão: A ocorrência de eventos adversos infecciosos se associou com o perfil dos pacientes e as características relevantes do processo assistencial, com impacto na elevação dos custos, principalmente com medicamentos e exames laboratoriais.

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Conflicts of interest: this study is part of a dissertation entitled *"Eventos adversos em hospital de ensino: análise de custo e causas-raízes em processos de cuidado"*, presented to the Graduate Program in Nursing of the Universidade Estadual de Maringá in 2020.

Resumen

Objetivo: Analizar el perfil y los costos directos de eventos adversos (EA) infecciosos en el proceso de cuidados en salud.

Métodos: Estudio cuantitativo, analítico, retrospectivo, realizado en un hospital público universitario del estado de Paraná, que contó con muestra representativa (n=97) de las notificaciones de EA infecciosos relativos al primer semestre de 2019. Los datos fueron recopilados a partir de las notificaciones, historias clínicas e informes de procedimientos por internación. Para el cálculo de los costos se les atribuyeron valores unitarios a los productos y servicios, con base al referente del mes de febrero de 2019.

Resultados: La muestra estuvo compuesta predominantemente por hombres, del grupo de edad > 70 años, con un período promedio de internación de 23,5±12,9 días. Se verificó la asociación entre el tipo de infección y las variables grupo de edad, unidad de internación y tipo de salida (p<0,01 para todas), grupos de costos y tipos de infección (p<0,05), grupo de edad (p<0,05) y tipo de salida (p<0,05). Al comparar los promedios de los costos directos variables de pacientes, víctimas de EA infecciosos y de sus pares simulados, se destacaron los análisis de laboratorio y los medicamentos.

Conclusión: Los casos de eventos adversos infecciosos se asociaron con el perfil de los pacientes y las características relevantes del proceso de atención, con impacto en la elevación de los costos, principalmente con medicamentos y exámenes de laboratorio.

Introduction

Healthcare-associated infections (HAIs) are defined as those acquired after patient admission and may manifest during hospitalization or after hospital discharge, provided that they are demonstrably related to hospitalization.[1] When considering national and international policies on safe health care promotion, HAIs stand out as the main adverse events (AE) in the health care process.[2,3]

In addition to being associated with high rates of hospital morbidity and mortality,[4] infectious AEs impact the management of health services, as they financially burden care, both by increasing length of hospital stay and costs of materials and services for the management and treatment of damage caused to patients.[5,6]

An example is a study focusing on costs related to infections in hospitals in the last decade, which estimated an incidence of approximately 440,000 cases of HAIs per year among American adult patients, with an annual cost of US$9.8 billion. Of this amount, more than 30% were allocated to the treatment of surgical infections and 25% to the treatment of pneumonia and urinary infections.[7]

A report published by the Canadian Patient Safety Institute, aiming to identify the economic burden of AE in the Canadian health system, showed that most studies on this topic address costs attributed to hospital infections, with values ranging from US$2,027 to US$12,197, per incident.[8]

Health care safety has been highlighted as a topic of discussion among organizations, researchers, managers, health professionals and the general population, who seek quality care, free of errors and/or damages.[9] This is because, according to literature, the financial burden caused by AE influences the adequate distribution of resources within the health system, impairs the production of care, the qualification of care and, consequently, access to health.[6,10,11]

Knowledge of the profile of care AEs, such as HAIs, which have a high incidence and impact on quality of care, represents an important tool for promoting actions aimed at patient safety. Similarly, elucidating the financial aspects related to infectious AEs can contribute to developing institutional strategies focused on resource management, in order to maximize benefits to society.

This study has as a research question: What is the genesis and financial burden of infectious AEs in the context of a highly complex teaching hospital? To answer this question, this study aimed to analyze infectious AE profile and direct and variable costs in the health care process.

Methods

This is a quantitative, analytical, retrospective study carried out at a public teaching hospital in Paraná, with 300 hospitalization beds, being 20 adult Intensive Care Unit (ICU) beds, six burn ICU beds (adult and child), five Pediatric ICU and 17 ICU/Neonatal ICU. Only in 2019, the institution performed more than 180,000 consultations, 13,000 hospitalizations and 10,000 surgeries.[12]

Data were collected from secondary sources (AE notification forms, patient records, input/procedure reports and hospital cost reports issued by Hospital

Statistics and Cost Section sectors, respectively). As a tool to assist in hospital cost management, the institution under study used Agfa Healthcare®, a clinical and hospital management software. The reports provided by the management system allowed identifying direct and variable laboratory and imaging test costs for each Hospitalization Unit, which were obtained by dividing the total monthly cost for each cost unit (electrodiagnosis/endoscopy/radiology and clinical analyses) by the number of patient day-month, resulting in the service unit value for each procedure included in the study. It is noteworthy that laboratory and imaging tests are services specific to the institution under study.

Stratified random sampling was used, based on the total number of reports of infectious AE in the first half of 2019 (N=391) of patients over 18 years old and hospitalized for clinical and/or surgical treatment in Inpatient Units (Male, Female and Communicable Diseases), General ICUs, burn ICUs (Burn Treatment Center) and Emergency Room.

The sample calculation was performed with the aid of a software, G*Power 3 ® - Statistical Power Analyses, considering the effect size =0.25, error probability =0.05 and statistical power =95%. HAI notifications were numbered individually, according to the order they were filed in the Hospital Infection Control Commission (HICC) records. Then, they were randomly selected according to a draw carried out through an online tool, Random.org, which, through algorithms, allows selecting random numbers.

Data collection was performed using an instrument composed of three parts: Part I - Items for patient sociodemographic and clinical characterization; Part II - Incident characterization and damage classification (mild, moderate or severe); Part III – Survey of medical and hospital supplies and diagnostic and/or therapeutic procedures related to AE.

To ensure reliability in the description of resources related to incidents, a report with a summary of procedures per hospitalization for each patient was requested from the Statistics Section of the institution under study, containing items classified as direct and variable costs. The reports contained a description of products and services provided to each patient, including medications, laboratory and imaging tests.

All data collected about the resources used in the care process related to AE were listed, with the help of a data collection instrument (prepared by the author) and then compared with the descriptive reports of products and services, made available by the Statistics Section. Then, detailed data on input and service consumption, as well as the unit values of products and services, according to the reference of February 2019 and presented in *reais* (R$, Brazilian currency), were tabulated in Microsoft Excel® spreadsheets.

To compare the mean direct and variable costs of hospital treatment between patients who were victims and non-victims of infectious AE, simulated pairs were created for each individual diagnosed with HAIs and included in the study sample. The parameters for comparison were based on the mean daily cost of inpatient units (with medications, laboratory and imaging tests) and on the movement of patients who were victims of infectious AE through inpatient units. Subsequently, the subtotals related to direct and variable medications, laboratory and imaging test costs were calculated and transferred to the final database.

For this study, direct and variable costs were classified according to the Cost Accounting theoretical framework, under the Absorption Costing model, which classifies costs as expenses directly linked to the production process of a good or service. In this sense, direct costs are considered as those that can be directly appropriated to the product/service, through a consumption measure, being classified as variables when they depend directly on the volume of production or services provided.[13]

The descriptive and inferential statistical analyses of this study were performed in SPSS 2.0 (Statistical Package for the Social Sciences), version 21. For qualitative variables, a chi-square test was used to verify associations. Additionally, a binary logistic regression test was applied to identify the relationship between the outcome death and the predictor variable type of infection. To verify differences in length of stay between the different types of infection, the Levene test was initially applied to verify data homogeneity, followed by the one-factor ANOVA. To compare costs according to independent variables, the Kruskal-Wallis test or Mann-Whitney test was applied. When necessary, Dunn's post-hoc test was also applied, and the Cox & Snell test was applied to assess the risk of death related to the type of infection.

Data normality was verified using the Shapiro-Wilk test. Due to the non-parametric distribution, the Mann-Whitney test was performed to detect differences in cost between patients who developed and did not develop infectious AEs. The level of significance adopted for all inferences was p<0.05.

Considering the nature of the data sources, the Research Ethics Committee of the university to which this study is linked was requested to waive the Informed Consent Form (ICF) (Opinion 3.401.589). The project is registered on *Plataforma Brasil*, with CAAE (*Certificado de Apresentação para Apreciação Ética* - Certificate of Presentation for Ethical Consideration) 10303919.0.0000.0104.

Results

The sample consisted of 93 patients, with a mean age of 61.3±18.7 years and a mean hospital stay of 23.5 ± 12.9 days. Table 1 shows the characterization data of the studied sample.

Characterization of infectious adverse events

To complement the characterization of infectious AEs, an association analysis was performed between type of infection and age group, type of infection and hospitalization unit and type of infection and type of exit (p<0.01 for all). Regarding age group, there was a higher prevalence of ventilator-associated pneumonia (VAP) among patients aged >70 years (38.5%), followed by patients aged 51 to 70 years (30.8%). A higher prevalence of non-ventilator-associated pneumonia (NVAP) (61.8%) and urinary tract infection (UTI) (55.6%) was observed in individuals older than 70 years. Regarding the type of infection, surgical site infections (SSI) and primary bloodstream infection (PBSI) and those classified as other, which include skin infections (54.5%), soft tissues (66.7%) and osteomyelitis (42.9%), showed a higher prevalence in the age group between 51 and 70 years. Regarding the association between type of infection and hospitalization unit, there was a higher prevalence of VAP in the Emergency Room (50%) followed by ICU/BICU (46.2%). The Emergency Room was also the unit with the highest prevalence of NVAP (38.2%). Regarding UTI, these occurred in equal proportions in the Male Unit and in the Emergency Room (both with 44.4%). In the operating room, there were 90.9% of SSI. The same proportion of PBSI occurrence was found for the Male Unit and ICU/BICU (33.3% for both) and for the BTC and Emergency Room (16.7% for both). For the other types of infection, the highest frequency occurred in the Female Unit (42.9%). The same frequency was observed for the Male Unit and ICU/BICU (both with 28.6%). It was also possible to observe a significant association between clinical outcome death and type of infection (p<0.01), and for VAP and NVAP infections (19; 73.1%), and 21 (61.8%) patients, respectively, evolved to death (Table 1).

Considering this association, the logistic regression model was applied to verify the relationship between the variables mentioned. It was observed that the type of infection can explain 24% of the types of hospital outcomes (death or discharge), according to the Cox & Snell test. Based on the model employed, it was found that patients who develop NVAP or UTI have a lower chance of death when compared to patients diagnosed with VAP (p<0.05 for both). For the other types of infection, no significant relationships were observed. The correlation between patients' types of infection and hospitalization period was also verified, highlighting the infections included in the other types group, with a mean of 36.5 days (± 11.7) of hospitalization. The other types group included cases of skin infections and osteomyelitis. There was also emphasis on the mean length of stay for PBSI (26.1 days ± 11.7) and VAP (24.8 days ± 14.9). However, one-way analysis of variance (ANOVA) showed no significant difference for this variable, according to the type of infection (p= 0.07).

Table 1. Clinical and demographic characterization of patients, victims of healthcare-associated infections (n=93)

Characteristic/Incident	n(%)
Age	
≤ 30 years	8(8.6)
31 to 50 years	17(18.3)
51 to 70 years	31(33.3)
>70 years	37(39.8)
Sex	
Male	61(65.6)
Female	32(34.4)
Inpatient unit*	
Male	16(17.2)
Female	9(9.7)
ICU/BICU	24(25.8)
BTC	2(2.2)
Emergency Room	32(34.4)
Operating room	10(10.8)
Hospital stay period	
≥ 15 days	32(34.4)
16 to 30 days	40(43.0)
> 30 days	21(22.6)
Type of outcome	
Discharge	46(49.5)
Death	46(49.5)
Transfer	1(1.1)
Type of infection**	
VAP	26(28.0)
NVAP	34(36.6)
UTI	9(9.7)
SSI	11(11.8)
PBSI	6(6.5)
Other types	7(7.5)
Mean age (SD)	61.3±18.7
Length of stay	23.5 ± 12.9
Time to infection	7.17±5.7

*Inpatient unit: ICU/BICU – Intensive Care Unit/Burn Intensive Care Unit; BTC – Burn Treatment Center; **Type of infection: VAP – ventilator-associated pneumonia; NVAP – non-ventilator-associated pneumonia; UTI – urinary tract infection; SSI – surgical site infection; PBSI – primary bloodstream infection.

Direct and variable cost analysis derived from infectious adverse events

Data related to direct and variable costs of AE did not present a normal distribution, given the amplitude of variation in values related to the general and specific costs for managing AE. Thus, the results are presented in the form of median and minimum/maximum. Regarding general direct and variable costs of infectious AEs, there were more expressive values for the class of laboratory tests, followed by medications, with a median value (minimum and maximum) of cost equal to R$4,484.50 (R$61.20-R$28,133.50) and R$2,407.30 (R$273.40-R$30,274.50), respectively. Imaging test costs ranged from R$35.70 to R$16,863.00. Specific antimicrobial costs ranged between R$9.00 and R$13,705.90 (Table 2).

Table 2 highlights the values of direct and variable costs, detailed by groups, according to type of infection, age group, type of exit, as well as its association with laboratory test, imaging test, medication and antimicrobial costs. All associations between the type of infection and variable costs were statistically significant. Thus, it was decided to apply Dunn's post-hoc test for comparison between pairs for different types of infection. Regarding laboratory test costs, patients with SSI had lower costs compared to patients who developed VAP (p=0.001). Similarly, this relationship was observed for imaging test costs (p=0.02).

Patients who developed VAP also had higher imaging test costs compared to patients with other types of infections (p=0.01). Regarding medication costs, those who developed other types of infections had a higher cost compared to those with UTI (p=0.02). Medication costs were higher for patients with other types of infections when compared to patients who developed UTI (p=0.008) and PNAV (p=0.03).

For the relationship between costs and the variable age group, there was no difference between characterization and laboratory and imaging test costs (p>0.05 for both comparisons). For medication costs, patients aged >70 years had a lower cost compared to the other three categories (p≤0.02 for all comparisons).

Regarding antimicrobial costs, the only difference occurred between the age groups >70 years and 31 to 50 years. Younger patients had a higher cost compared to those over 70 years of age (p=0.026).

It is noted that a patient leaving by transfer had a cost of R$6,973.60 with laboratory tests, R$2,773.10 with imaging tests, R$2,620.80 with medications and R$1,744.20 with antibiotics. Significant differences were found only for laboratory and imaging test costs, and for both cases, patients who were discharged due to death had a higher cost compared to patients who were discharged (p≤0.01 for both comparisons).

It was also found that 47 patients (50.5%) had an antimicrobial cost lower than 50% of the total

Table 2. Laboratory test, imaging test, medication and antimicrobial costs for patients with healthcare-associated infections (n=93), according to the type of infection, age group and type of outcome (discharge or death)†

	Laboratory tests		Imaging tests		Medications		Antimicrobials	
	Median (min – max) (R$)	p- value	Median (min – max) (R$)	p- value	Median (min – max) (R$)	p- value	Median (min – max) (R$)	p- value
Type of infection								
VAP	5,950.55 (3,586.80– 28,133.50)	0.002*	3.214.35 (425.80 – 5,398.80)	0.002*	3.590.75 (611.50 – 21.554.80)	0.002*	1.473.90 (48.20 – 13.705.90)	0.009*
NVAP	4,323.75 (905.50 – 10,889.80)		2,583.70 (35.70 – 5,320.60)		1.497.45 (325.50 – 15.375.40)		757.45 (150.60 – 12.384.80)	
UTI	3,136.00 (678.20 – 8,878.80)		1,798.00 (58.60 – 3,327.00)		1.195.50 (273.40 – 2.893.50)		309.40 (9.00 – 2.274.70)	
SSI	1,967.80 (61.20 – 7,694.70)*		951.00 (61.20 – 4,171.40)*		2.108.40 (477.10 – 12.298.50)		707.30 (141.70 – 4.502.10)	
PBSI	3,502.55 (1,646.40 – 16,789.40)		726.25 (102.00 – 16,863.00)		4,959.50 (717.70 – 30,274.50)		1,770.65 (411.20 – 8,210.50)	
Others	2,383.40 (1,223.00 – 10,047.00)		338.20 (96.90 – 2,900.00)**		6,681.10 (2,648.40 – 10,761.10)		3,132.10 (1,506.00 – 8,273.30)**	
Age group								
≤30 years	4,627.55 (61.20 – 10,047.00)	0.940*	1,039.00 (107.10 – 4,654.70)	0.527*	3,467.40 (2,108.40 – 12,517.90)***	0.001*	1,915.10 (227.40 – 8,801.20)	0.008*
31 to 50 years	5,217.50 (313.60 – 28,133.50)		2.576.20 (265.20 – 5,398.80)		4,262.90 (500.50 – 21.554.80)***		2,446.40 (141.70 – 13,705.90)***	
51 to 70 years	4,245.40 (439.00 – 9,788.90)		1,504.50 (58.60 – 5,237.60)		2,901.40 (477.10 – 30,274.50)***		1,135.70 (9.00 – 7,127.00)	
>70 years	4,163.00 (905.50 – 16,789.40)		2,111.00 (35.70 – 16,863.00)		1,250.10 (273.40 – 12,974.80)		626.90 (49.70 – 6,909.80)	
Type of outcome								
Discharge	3,563.30 (61.20 – 2,8133.5)	0.005**	1,425.70 (58.60 – 16,863.00)	0.001**	2,733.80 (273.40 – 30,274.50)	0.953**	1,232.25 (9.00 – 13,705.90)	0.726**
Death	5,507.60 (905.5 – 11,242.60)*		2,669.05 (35.70 – 5,320.60)††		2,046.75 (325.50 – 15,375.40)		822.40 (48.20 – 12,384.80)	

VAP – ventilator-associated pneumonia; NVAP – ventilator-non-associated pneumonia; UTI - urinary tract infection; SSI – surgical site infection; PBSI – primary bloodstream infection; SD – standard deviation; Min – minimum; Max – maximum. *p<0.05 vs. VAP. * * p<0.05 vs. UTI and p<0.05 vs. NVAP. * **p<0.05 vs.> 70 years. † Only one patient was identified with exit by transference, thus a non-parametric statistical inference was performed, so because there was no variation, the value was omitted from descriptive data. †† †p<0.05 vs. discharge. *Kruskal-Wallis test; **Mann-Whitney test

medication costs and 46 (49.5%) had a cost higher than 50% with antibiotics. Thus, there is a similarity for this condition in patients who had infection. When comparing antimicrobial costs in relation to the total medication costs between the different types of infections (VAP, NVAP, UTI, SSI, PBSI and other types), no significant associations were observed (p=0.22).

Figure 1 shows the data from the comparison of means of direct and variable laboratory, imaging test and medication costs, performed between patients-victims of infectious AE and simulated pairs, who did not develop infection. Patients without infection had lower costs for laboratory and imaging tests (p≤0.01 for both). On the other hand, the cost of medication was higher for patients without infection (p=0.01).

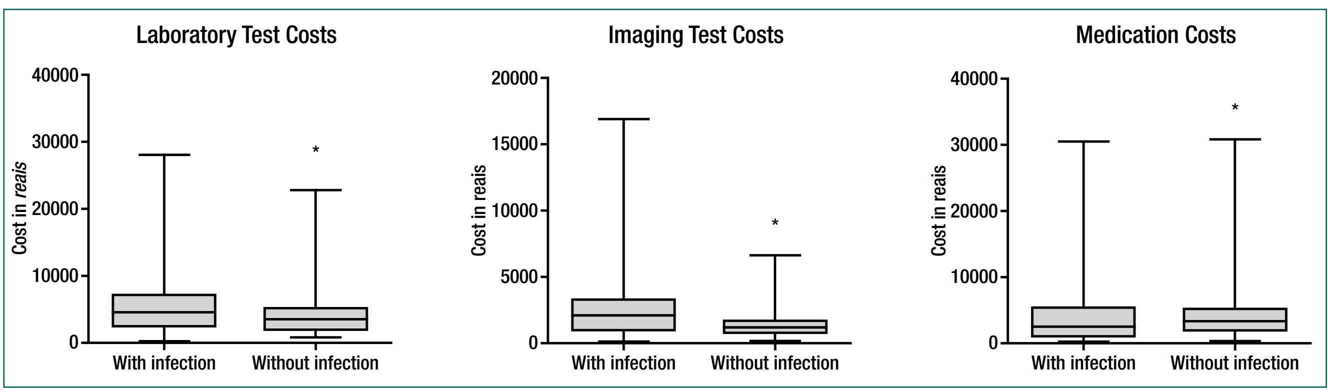

Figure 1. Comparison of laboratory, imaging test and medication costs between patients with and without healthcare-associated infections (n=93) *p<0.05

Discussion

There is a predominance of male individuals, aged over 70 years, with a mean age of 61.3 years (±18.7). This finding is similar to other studies focusing on the epidemiological profile of HAIs, which indicate a higher incidence of this type of care AE in elderly patients.[14,15] There is no evidence in literature that relates sex with predictive factor of infectious AE. However, with regard to older adults, it is known that the immunosenescence process, associated with chronic-degenerative diseases, is a risk factor for infectious complications and an increase in the recovery period.[16]

In the care context of this study, in which infections occur, the high incidence of AE in the Emergency Room unit stands out. This data differs from literature[17] and standards already established by health authorities in Brazil,[18] which highlight the prevalence of HAIs in the intensive care environment. This fact may be related to the profile of patients treated at the institution investigated because it is a public teaching hospital, which acts as a reference for highly complex care, for an extensive area of coverage in its regional health.

The limitation of the number of ICU beds, a general problem within the Unified Health System (SUS – *Sistema Único de Saúde*) and a reality in the institution under study, can contribute to prolonged stay of critically ill patients with high demands for care in emergency care and hospitalization units, which do not have the physical-functional structure to meet the demands of critically ill patients. Studies that focus on estimates of access to ICU beds indicate that demands for ICU beds are highly dynamic, a fact that makes it difficult to plan the resources needed for adequate care and favors the formation of waiting lines that overwhelm units classified as gateways and support for ICUs.[19,20]

When analyzing the association between the type of infectious AE and hospitalization unit, the Emergency Room also stood out for concentrating 50% of cases of VAP, 44.4% of UTI and 38.2% of NVAP, unlike the evidence present in literature, which consecrate the ICU as an environment with the highest risk and with the highest proportion of infections, due to the non-passive process characteristics.[21]

Considering the mean length of stay, a mean of 23.5 days (±12.9) of hospitalization was obtained for patients included in the sample. Of these, the majority (43.0%) remained hospitalized between 16 and 30 days. In the analysis of variations in length of stay, the profile of patients treated, as well as the level of care complexity, should be taken into account. In this regard, a study carried out in a high complexity university hospital in the city of Rio de Janeiro showed a median value of ICU stay, significantly higher among patients who were victims of AE (34 days).[17]

Another study focusing on the clinical profile of patients with infectious AE showed a lower mean length of stay when compared to the results of this study, with a mean length of stay of 18 days. This data reinforces the perception about the variability related to the characteristics of the population studied and the institution in which the study was conducted.[22] Still regarding length of hospitalization, a study conducted in Sweden points out that the presence of HAIs contributed to an increase of 14.2% in the total hospitalization period, when compared to patients who were not victims of this type of AE.[23]

Regarding the type of infection, there was a predominance of infectious respiratory diseases, with 36.6% and 28.0% of NVAP and VAP respectively, followed by SSI, which had an incidence of 11.8%. These results are consistent with the national and international literature, which point to respiratory infections as the most incident in the health care context.[14,24]

Respiratory infections, associated with mechanical ventilation, stand out among AEs related to invasive procedures in health care and directly impact mortality rates of patients that are victims of HAIs.[25,26] Thus, to avoid them, scientific literature indicates the use of prevention protocols such as high decubitus maintenance (30 to 45º), daily "awakening" of sedation conditions, supraglottic secretion aspiration, periodic exchange of respirator circuits and humidifiers, cuff pressure monitoring, post-pyloric positioning of enteral tube, among others.[27]

Regarding infectious AEs costs, those related to laboratory tests and medications stood out. These items were associated with type of infection, age group and type of outcome (discharge or death).

For direct laboratory test and medication costs, medians of R$4,484.50 and R$2,407.30 were obtained, respectively. However, there was a significant variation between values, both for laboratory test (R$61.20 to R$28,133.50) and medication costs (R$273.40 to R$30,274.50). These data may be related to the diversity of clinical diagnoses observed among the sample components (Table 2).

A recent study on HAI costs in a Brazilian teaching hospital, focusing on treatment of infectious AEs in older adults, showed similar variability to the present study, when analyzing direct costs of antibiotic therapy, as it found that the mean cost was R$1,336.90, with a standard deviation of R$2,422.80, minimum cost of R$0.24 and maximum of R$14,866.26.[16] This same study detected significance in the comparison between costs and respiratory and urinary infections.

In the context of intensive care assistance, other researchers obtained similar results when analyzing medication costs for HAI treatment, with total the antimicrobial cost ranging between US$3.28 and US$117,865.52.[21] In the present investigation, medication costs for infection treatment were significantly higher for cases of SSI and other types of infections such as skin/soft tissue infections and osteomyelitis, when compared, respectively, with VAP (p=0.001) and UTI (p=0.02) (Table 2).

A literature review research conducted by Brazilian authors in national and international databases on the financial burden caused by SSI to health systems pointed out that the costs of this type of infection can reachUS$10,000.00 per day, depending on the type of microorganisms causing the infectious process, its resistance profile and type of surgery.[28] However, the authors reinforce the need to pay attention to discrepancies in values, resulting from deficiencies in the records and management of HAI hospital costs.

Corroborating the results of this study on UTI, a study conducted in a tertiary hospital in Barcelona, Spain, classified UTI as the most frequent primary focus of bacteremia, with an incidence greater than 20%.[29]

It is important to emphasize that, in the context of this study, laboratory and imaging tests are not classified as therapeutic measures for infectious AEs. Nevertheless, they represent essential data for diagnosis and treatment, since they allow the health team to obtain parameters regarding patients' clinical evolution.

Imaging test costs also showed a high range of variation (R$35.70 to R$13,705.90) and stood out for the group diagnosed with VAP when compared to other types of infections. This finding is consistent, since radiological parameters are essential for clinical management in patients with respiratory tract infections. Despite the importance of imaging tests, scientific literature[30] warns that it is necessary to consider the consequences of frequent patient exposure to radiation sources and also the financial impact on the indiscriminate use of this type of diagnostic resource.

A study conducted in a hospital in Portugal, aiming at quantifying and qualifying imaging tests performed unnecessarily in an urgency and emergency service, showed high rates of cancellation, with emphasis on causes related to errors in scheduling and duplicate requests.[30] In this investigation, the authors reinforce the need for greater control over the request for imaging tests, in order to avoid exposing patients to unnecessary risks, to reduce costs and maximize the resources available in health services.

In general, cost analysis studies address values attributed to HAI treatment from an institutional perspective. However, due to difficulties of conducting this type of study, there is a predominance of methods based on estimates, due to comparative analyzes and patient follow-ups.[31]

As an alternative to research based on estimated data to survey the costs of care AE, there are matched cohort studies. However, studies of this type are predisposed to biases related mainly to individual characteristics, which are difficult to control, such as initial diagnoses and comorbidities, which favor the occurrence of complications and increase in the mean length of hospital stay.[32]

Finally, when comparing costs attributed to the care of those who presented infectious AE with their simulated pairs, it was observed that patients without infection had lower costs for laboratory and imaging tests ($p \leq 0.01$ for both). However, medication costs were higher for these patients ($p=0.01$).

In Figure 1, it is also possible to notice the amplitude of variation of the values attributed to both groups, possibly due to diagnostic variability between the sample components. In this study, patients were not paired with individuals with diagnostic compatibility, which represented a limitation for the comparison of hospital cost means.

Although it was not the focus of this study, when analyzing medication costs, a significantly higher median was found for the group of simulated pairs (R$3,472.10, ranging from R$700.80 to R$22,789.50) when compared to patients with infectious AE (R$4,484.50, ranging from R$61.20 to R$28,133.50). It was also noticed an inconstancy in medication protocols, with diversity in the prescription of antimicrobials in relation to the type of infection.

It is important to emphasize that the standardization and rational use of medications, with emphasis on the class of antimicrobials, is a recommendation widely publicized by national and international health organizations that work in the area of HAI control, such as the Brazilian National Health Regulatory Agency (ANVISA - *Agência Nacional de Vigilância Sanitária*) and World Health Organization (WHO). This is because the indiscriminate use of medications is responsible for a series of consequences that affect the population, such as the increase in health costs.[27]

As a limitation of this study, it is indicated the impossibility of pairing AE patients with other patients, with regard to diagnostic compatibility, a circumstance that made it difficult to compare the means of hospital costs.

The characteristics of the institution in which this study was carried out are also noteworthy, as it is a general teaching hospital, with multiple inpatient units, diversified care profiles, and constant displacement of patients based mainly on the availability of beds. Unlike other cost analysis studies, mostly carried out in a single inpatient unit, focused on a specific patient profile, the present study included clinical and surgical patients from different medical specialties, who were displaced in different inpatient units, exposed to different care protocols and professional groups.

With regard to costs related to essential human resources for health care, it is noteworthy that these were not included in the analyses of this study, considering that these in most cases are classified as fixed direct costs for public health institutions.

It is suggested that further studies focusing on the economic burden of infectious AEs be carried out in order to elucidate the standards of treatment for infectious AEs within the scope of SUS and, therefore, to assess more assertively the financial impact of this type of incident and its consequences.

Conclusion

In conclusion, infectious AEs are frequent in the care context studied, being responsible for the increase in direct and variable costs related to hospitalization. AEs were associated with relevant aspects of the profile of patients and care characteristics, such as hospitalization unit, influence in HAI incidence. Also, with regard to the costs of managing infectious AE, there was wide variability between cost groups (medications, laboratory tests, imaging tests).

Acknowlegdments

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001 (Process number: 88881.595318/2020-01).

Collaborations

Paulino GME contributed to study conception, data analysis and interpretation, article writing.

Matta ACG, Ferreira AMD and Camillo NRS contributed to data interpretation, and article analysis and writing. Matsuda LM and Haddad MCL contributed with relevant critical review of the intellectual content and final approval ofthe version to be published.

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