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ORIGINAL ARTICLE

Cost of antimicrobials associated with bacterial infections in hospitalized children and adolescents

Custos de antimicrobianos associados às infecções bacterianas em crianças e adolescente hospitalizados

Costo de antimicrobianos asociados a infecciones bacterianas en niños y adolescentes hospitalizados

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ABSTRACT

Background and Objective: Healthcare-Associated Infections (HAIs) in hospitalized children and adolescents represent a significant challenge due to increasing bacterial resistance and the high costs associated with antimicrobial use. Understanding these factors is essential to optimizing antimicrobial use and reducing clinical and economic impacts. This study aims to describe the costs of antimicrobials associated with bacterial infections in hospitalized children and adolescents. **Methods:** This is an analytical cross-sectional study conducted in two philanthropic hospitals in northern Paraná, Brazil. A total of 234 children and adolescents with HAIs and positive cultures were included between January 2018 and December 2023. Demographic, clinical, and antimicrobial cost data were collected from electronic medical records. For statistical analysis, the Mann-Whitney U test and Spearman's correlation coefficient were used. Multiple linear regression was performed using the enter method. **Results:** Infections caused by resistant microorganisms occurred in 39.3% of cases. Age, length of hospital stay, and antimicrobial susceptibility profile were associated with higher antimicrobial costs. Patients with resistant microorganisms had antimicrobial costs approximately five times higher than those with susceptible microorganisms. Gram-negative bacteria were predominated, with Klebsiella pneumoniae and Pseudomonas aeruginosa being multidrug-resistant species. The most frequently prescribed antimicrobials were aminoglycosides, followed by penicillins combined with beta-lactamase inhibitors, and cephalosporins. **Conclusion:** Age, length of hospital stay, and microbial resistance were significant predictors of antimicrobial costs in hospitalized children and adolescents. Infection control strategies and the rational use of antimicrobials are essential to reducing hospital costs and mitigating bacterial resistance.

Keywords: *Child. Adolescent. Drug Costs. Cross Infection. Microbial Drug Resistance.*

RESUMO

Justificativa e Objetivos: As Infecções Relacionadas à Assistência à Saúde (IRAS) em crianças e adolescentes hospitalizados representam um desafio significativo, devido à crescente resistência bacteriana e aos altos custos associados ao uso de antimicrobianos. Compreender esses fatores é essencial para otimizar o uso desses medicamentos e reduzir impactos clínicos e econômicos. O objetivo deste estudo é descrever os custos de antimicrobianos associados às infecções bacterianas em crianças e adolescentes hospitalizados. **Métodos:** Estudo transversal analítico, realizado em dois hospitais filantrópicos no norte do Paraná, Brasil. Foram incluídos 234 crianças e adolescentes com IRAS e culturas positivas entre janeiro de 2018 e dezembro de 2023. Foram coletados dados demográficos, clínicos e custos diretos dos antimicrobianos dos prontuários eletrônicos. Para análise estatística, foram utilizados os testes U de *Mann-Whitney* e o coeficiente de correlação de *Spearman*. A regressão linear múltipla foi realizada pelo método *enter*. **Resultados:** Infecções por microrganismos resistentes ocorreram em 39,3% da população. Idade, tempo de hospitalização e perfil de sensibilidade se associaram aos maiores custos com antimicrobianos. Aqueles com microrganismos resistentes apresentaram custos com antimicrobianos cerca de cinco vezes maiores em comparação aos com microrganismos sensíveis. Prevaleceram as bactérias Gram-negativas, sendo *Klebsiella pneumoniae* e *Pseudomonas aeruginosa* multirresistentes. Entre os antimicrobianos mais prescritos, os aminoglicosídeos, seguidos pelas penicilinas associadas a inibidores de beta-lactamase e cefalosporinas. **Conclusão:** A idade, tempo de hospitalização e resistência microbiana foram preditores significativos de custos com antimicrobianos em crianças e adolescentes hospitalizados. Estratégias de controle de infecções e uso racional de antimicrobianos são essenciais para reduzir custos hospitalares e mitigar a resistência bacteriana.

Descritores: *Criança. Adolescente. Custos de Medicamentos. Infecção Hospitalar. Resistência Microbiana a Medicamentos.*

RESUMEN

Justificación y Objetivo: Las Infecciones Relacionadas con la Atención de la Salud (IRAS) en niños y adolescentes hospitalizados representan un desafío significativo debido a la creciente resistencia bacteriana y a los altos costos asociados con el uso de antimicrobianos. Comprender estos factores es esencial para optimizar el uso de estos medicamentos y reducir los impactos clínicos y económicos. El objetivo de este estudio es describir los costos de los antimicrobianos asociados con las infecciones bacterianas en niños y adolescentes hospitalizados. **Métodos:** Estudio transversal analítico realizado en dos hospitales filantrópicos en el norte de Paraná, Brasil. Se incluyeron 234 niños y adolescentes con IRAS y cultivos positivos entre enero de 2018 y diciembre de 2023. Se recopilaron datos demográficos, clínicos y costos de los antimicrobianos a partir de los registros médicos electrónicos. Para el análisis estadístico se utilizaron la prueba U de Mann-Whitney y el coeficiente de correlación de Spearman. El análisis de regresión lineal múltiple se realizó mediante el método enter. **Resultados:** Las infecciones por microorganismos resistentes ocurrieron en el 39,3% de la población. La edad, el tiempo de hospitalización y el perfil de sensibilidad se asociaron con mayores costos de antimicrobianos. Los pacientes con microorganismos resistentes presentaron costos aproximadamente cinco veces mayores en comparación con aquellos con microorganismos sensibles. Predominaron las bacterias Gram negativas, siendo *Klebsiella pneumoniae* y *Pseudomonas aeruginosa* multirresistentes. Entre los

antimicrobianos más prescritos se encontraron los aminoglucósidos, seguidos pelas penicilinas associadas a inibidores de beta-lactamase y cefalosporinas. **Conclusión:** La edad, el tiempo de hospitalización y la resistencia microbiana fueron predictores significativos de los costos de antimicrobianos en niños y adolescentes hospitalizados. Las estrategias de control de infecciones y el uso racional de antimicrobianos son esenciales para reducir los costos hospitalarios y mitigar la resistencia bacteriana.

Palabras Clave: *Niño. Adolescente. Costos de Medicamentos. Infección Hospitalaria. Resistencia Microbiana a Medicamentos.*

INTRODUCTION

Healthcare-associated infections (HAIs) represent one of the greatest challenges for health systems worldwide.[1,2,3] These infections are acquired by patients during hospitalization or in other health care settings. HAIs are caused by a variety of pathogens, including bacteria, viruses, and fungi, and are associated with significant increases in morbidity and mortality, especially when they occur in more vulnerable populations.[1,3]

Among these populations, hospitalized children and adolescents are particularly susceptible. The fragile immune systems of these age groups, combined with the need for invasive procedures and prolonged use of medical devices, make them particularly vulnerable to infections.[1,4,5] Studies have shown that this prevalence among children is alarming, and its impact on their health and well-being can result in serious complications and, in some cases, death.[3,5,6] Among the main complications is the development and spread of antimicrobial-resistant microorganisms, especially multidrug-resistant bacteria, which make treatment extremely challenging, given that dissemination in hospital settings has been a growing problem related, among other factors, to the excessive and inappropriate use of antibiotics, limiting therapeutic options.[1,2 4,6,8,9,10,11]

Infections caused by multidrug-resistant bacteria are associated with higher rates of morbidity and mortality, as well as high hospital costs.[1,4,7,10] Antimicrobial costs represent a significant portion of hospital expenditures, ranging from 15% to 30%, especially in Treatment of infections caused by resistant microorganisms. This high cost is attributed to the frequent use of broad-spectrum antimicrobials and the need for longer and more complex treatments required for these situations, which directly impacts overall treatment costs.[9] They also compromise the quality of care and hinder the efficient allocation of resources in the healthcare system. Therefore, effective prevention and control strategies are essential to improve clinical outcomes and reduce economic costs.[2,3,9,10,11]

Given the relevance of HAIs, the growing threat of antimicrobial resistance, and the high costs associated with treating these infections, this study aims to describe the antimicrobial costs associated with bacterial infections in hospitalized children and adolescents.

METHODS

This is an analytical cross-sectional study, guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) tool, conducted from January 2018 to December 2023.[12]

The study was conducted in two highly complex philanthropic hospitals, leading the Regional Health Department and other Regional Health Departments covering the state of Paraná and neighboring states. One specializes in the care of children up to 12 years old and has 30 beds, including 10 in the Neonatal ICU and 10 in the Pediatric ICU. The second, a general adult hospital, serves adolescents/young people over 12 years olde and has 274 beds, including 47 in the Intensive Care Unit (ICU). Both hospitals are located in the northern region of the state of Paraná, southern Brazil. The study population consisted of children and adolescents of both genders, aged 30 days up to 18 years old, diagnosed with HAIs, as assessed by the Hospital Infection Control Committee (HICC) of the hospitals, in the clinical, surgical, and/or intensive care units.

It is noteworthy that information on HAI diagnoses was included based on reports of all infections, whether or not associated with the presence of invasive devices, along with laboratory tests and clinical signs characteristic of each type. Those with a new episode of infection associated with invasive devices were considered a new case of infection only after a 14-day interval, with the occurrence of new signs and symptoms, and positive laboratory results.

Those with positive microbiological cultures, who received antimicrobial treatment, and whose total cost of these medications was accounted for during hospitalization were included.

During the study period, 253 children and adolescents who acquired HAIs and presented positive cultures with isolated microorganisms were evaluated. Of these, 10 were excluded for not meeting the antimicrobial cost variable, as they died before treatment began. Nine were excluded due to positive cultures for coagulase-negative Staphylococcus. This microorganism, although frequently identified in cultures, may merely represent colonization—that is, the presence of the agent on body surfaces or

invasive devices without causing an inflammatory or clinical response. Unlike infection, which is characterized by tissue invasion with compatible clinical and laboratory manifestations. Given the impossibility of accurately distinguishing between these cases, exclusion was chosen. Thus, the final sample consisted of 234 children and adolescents.

Regarding blood cultures, urine cultures, and tracheal secretion cultures, the institution has a full-time microbiology laboratory. Microbial growth is detected using an automated method (BD BACTEC™), and positive samples are subsequently analyzed by the Siemens MicroScan® system, which identifies the microbial species.

Regarding the diagnostic criteria for HAIs, institutions adopt the guidelines of the Brazilian National Health Surveillance Agency (ANVISA), annually updated, to confirm infections. Microbiological confirmation is performed through a positive blood culture. Tracheal secretion culture, collected via a suction catheter, with a cutoff point of $\geq 10^6$ CFU/ml, is combined with clinical signs and radiological findings. VAP (Ventilator-Associated Pneumonia) is defined in patients who required mechanical ventilation for more than 48 hours, either by orotracheal intubation or tracheostomy.[10]

PSI (Primary Bloodstream Infection) is diagnosed in patients who had a central venous catheter in place for more than 48 hours and, at the time of infection, were using the device or it had been removed the previous day. The diagnosis was confirmed by clinical signs, laboratory tests, and isolation of the infectious agent in blood cultures. Blood cultures from both the central catheter and peripheral catheters were collected. Common skin contaminants and infections from other sources were not considered.[10]

CAUTI (Catheter-Associated Urinary Tract Infection) was diagnosed in patients with an indwelling urinary catheter for more than 48 hours, with clinical signs and quantitative urinary culture with $\geq 10^5$ CFU/ml, according to the criteria established by ANVISA.[10]

Positive cultures were defined as those that showed microbial growth. Microorganisms were classified according to antimicrobial resistance into two groups: resistant and susceptible.[10] The resistant group was subdivided into multidrug-resistant (MDR) bacteria, including Gram-negative bacilli resistant to 3rd and 4th generation cephalosporins, extended-spectrum β-lactamase (ESBL) producers, and carbapenem-resistant (CR) bacilli, as well as methicillin-resistant Staphylococcus (MRSA). The susceptible group comprised microorganisms that showed susceptibility to the tested antimicrobials.

For data collection, Microsoft Excel 2013® spreadsheets were provided by the institutions, containing information from electronic medical records extracted from the Business Intelligence® program. HAI diagnoses were obtained through individual forms, with HAI notifications completed by the Hospital Infection Control Committee (HICC) team, which evaluates patients with infectious diseases, in accordance with revised diagnostic criteria established by ANVISA.

Data were tabulated in Microsoft Excel® 2013 spreadsheets from February to April 2024. Demographic variables were categorized as follows: gender (female and male), age (≥30 days to ≤1 year, 2 to 6 years, 7 to 12 years, and 13 to <18 years), race (White and Black), and resident in the Health Region and other regions. Clinical variables included total hospitalization time (in days), ICU stay (yes or no), ICU length of stay (in days), reason for hospitalization (medical or surgical), presence of two or more HAIs, microbiological culture results, isolated microorganism, antimicrobial susceptibility profile (sensitive or resistant microorganism), antimicrobial therapy, days of antibiotic therapy, and clinical outcome (discharge and death).

For the antimicrobial cost variable, values were calculated individually, considering the cost of the unit dose of each drug formulation and the period of use, according to records provided by the institution's financial department. The cost of antimicrobial therapy was presented as the average direct cost of antimicrobials, expressed in Brazilian *Reais* (R$). The analysis included exclusively the direct costs of antimicrobials used in the treatment of HAIs with positive cultures, after diagnostic confirmation according to the HICC criteria, regardless of the route of administration and including dosage variations. Antimicrobials used for prophylaxis were not included in the analysis. The values were subsequently converted to US dollars (USD) based on the exchange rate in effect on November 8, 2024, assuming a rate of R$5.76 per dollar.

The collected data were subjected to descriptive statistical analysis, with presentation of absolute and relative frequencies for categorical variables, and measures of central tendency (median) and dispersion (quartiles and Interquartile Range [IQR]; minimum and maximum) for continuous variables.

The distribution of quantitative variables was assessed using the Shapiro-Wilk normality test, which indicated that none of the variables were normally distributed. To compare continuous variables, such as total hospitalization time (in days), ICU stay (in days), and antimicrobial costs, according to the antimicrobial susceptibility profile (sensitive and resistant), the nonparametric Mann-Whitney U test for independent

samples was used. Spearman's correlation coefficient was used to estimate bivariate correlations.

Effect size interpretations close to 0.10 were considered to indicate weak correlations, up to 0.30 moderate, and 0.50 strong.[13]

The models were evaluated using the Adjusted Coefficient of Determination (adjusted R^2), expressed as a percentage, to measure the correlation between the variables. To identify discrepancies in the observed distributions, the standardized adjusted residuals were analyzed. The model's multicollinearity was assessed using the Variance Inflation Factor (VIF), considering variables with scores greater than 10 as problematic. To detect outliers, Cook's D was used, considering scores >2 as a highly influential factor, indicating the presence of outliers. Bootstrapping procedures (BCA with 95% CI) were used to correct for possible deviations from the normality of the residuals.

After performing the multiple linear regression analysis, the enter method was used, in which all independent variables were entered simultaneously into the model, without prior selection or exclusion based on statistical criteria. This method was used to test the association between predictor variables (age in months, length of hospitalization (in days), length of ICU stay (in days), sensitivity profile (sensitive and resistant), and outcome (discharge and death)) and the response variable (antimicrobial costs). This model presented the regression coefficient estimates, their respective confidence intervals, and p-values. Furthermore, we considered unstandardized coefficients (β), which reflect the direct impact of each variable on antimicrobial costs, and standardized coefficients (βeta), which allow relative comparisons between the model variables. All analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 20.0, with a significance level of 5%.

This study is an excerpt from the research project entitled "Clinical and Economic Impact of Antimicrobial Resistance on Hospital Costs," approved by the Health Research Ethics Committee of the proposing institution, under No. 5,632,608, with Certificate of Approval for Ethical Assessment (CAAE) No. 24711718.8.0000.0099.

RESULTS

The study sample included 234 children and adolescents diagnosed with HAIs and positive microbial cultures, of which 142 (60.7%) were susceptible to microorganisms and 92 (39.3%) were resistant. Ages ranged from 29 days to 17 years, with a median of 12.5 months. They were also mostly females, ages 29 days to 1 year old, who were white (Table 1).

Regarding the reason for hospitalization, 65.4% of patients were admitted for surgical procedures, of which 70.5% were cardiac surgeries. This reflects the reality of one of the hospitals studied, a reference in pediatric cardiac surgeries.

It was found that 68.2% were from other municipalities and Regional Health Departments. Among the 54 deaths, 48.1% presented antimicrobial resistance.

Outcomes related to length of hospital stay and ICU stay were significantly higher among those with antimicrobial-resistant pathogens (Table 1).

Table 1. Comparison of antimicrobial sensitivity profiles among children and adolescents with sensitive and resistant microorganisms in high-complexity hospitals from 2018 to 2023. Paraná, Brazil

Categorical variables	Infection by Sensitive Microorganisms* N (%)	Infection by Resistant Microorganisms** N (%)	Total N (%)
Total	**142 (60.7)**	**92 (39.3)**	**234 (100.0)**
Gender			
Female	76 (58.9)	53 (41.1)	129 (55.1)
Male	66 (62.9)	39 (37.1)	105 (44.9)
Age range			
1 month to 1 year	101 (60.8)	65 (39.2)	166 (71.0)
2 to 6 years	23 (62.2)	14 (37.8)	37 (15.8)
7 to 11 years	13 (68.4)	63 (1.6)	19 (8.1)
12 to ≤18 years	54 (1.7)	75 (8.3)	12 (5.1)
Race			
White	115 (62.2)	70 (37.8)	185 (79.1)
Black	27 (55.1)	22 (44.9)	49 (20.9)
Specialty			
Clinic	54 (66.7)	27 (33.3)	81 (34.6)
Surgery	88 (57.5)	65 (42.5)	153 (65.4)
Origin			
RS† residence	45 (62.5)	27 (37.5)	72 (31.0)
Other regions	97 (59.9)	65 (40.1)	162 (68.0)
Outcome			
Discharge	114 (63.3)	66 (36.7)	180 (76.9)
Death	28 (51.9)	26 (48.1)	54 (23.1)

Abbreviation: *Antimicrobial-sensitive microorganisms; **Antimicrobial-resistant microorganisms; †Regional Health.

Furthermore, antimicrobial costs were significantly higher for patients with resistant microorganisms, being approximately five times higher than the costs associated with sensitive microorganisms (Table 2). For the sensitive group, the 1st quartile cost

R$43.19 (US$7.49) and the 3rd quartile cost R$1,277.03 (US$221.52), while for the resistant group, the 1st quartile cost R$441.49 (US$76.58) and the 3rd quartile cost R$4,899.37 (US$849.87).

Table 2. Comparison of clinical variables and antimicrobial costs among children and adolescents with infections caused by sensitive and resistant microorganisms in highly complex hospitals from 2018 to 2023. Paraná, Brazil

Continuous variables	Infection by Sensitive Microorganisms *	Infection by Resistant Microorganisms **	Total
	Median (IQR) ‡	Median (IQR) ‡	*p-value*[1]
ICU stay (in days)	16 (29.00)	26 (35.00)	**< 0.001**
Hospitalization time (in days)	27 (30.00)	36 (44.00)	**< 0.001**
Antimicrobial cost #	265,18 (1,242.02)	1.347,71 (4,523.67)	**< 0.001**
	45,99 (215.44)##	233,68 (784.70)##	

Abbreviation: *Antimicrobial-sensitive microorganisms; **Antimicrobial-resistant microorganisms; ‡IQR-Interquartile range; [1] p-value refers to the Mann-Whitney test; # Costs in *Reais* (R$); ## Costs in US dollars (US$).

When analyzing the sensitivity profile of the microorganisms, 328 bacterial strains were identified, of which 268 (81.7%) were Gram-negative. The most prevalent bacteria were Klebsiella pneumoniae (24.6%), Pseudomonas aeruginosa (23.8%), and Escherichia coli (12.6%). Among the Gram-positive bacteria, the most frequent was Staphylococcus aureus (70%), followed by Enterococcus spp. (28.3%).

Out of the identified microorganisms, 161 (49%) presented some resistance mechanism. Of these, 65.2% were MDR, 21.7% CR, and 5.6% MRSA. Regarding antimicrobial classes, aminoglycosides were the most commonly used, accounting for 207 (21.6%), followed by penicillins combined with beta-lactamase inhibitors, with 188 (19.6%), and cephalosporins, with 134 (14%). The most commonly prescribed individual antimicrobials were amikacin, with 155 (16.2%); the piperacycline+tazobactam combination, with 127 (13.2%); and vancomycin, with 101 (10.5%). Almost all children and adolescents, 220 (94%), used more than one antibiotic, accounting for 957 antimicrobial cycles.

The results demonstrate that all variables in the multiple linear regression model, with an adjusted R^2, explain 44% of the variance in antimicrobial costs.

Age, length of hospital stay, and sensitivity profile demonstrated a statistically significant and positive association with antimicrobial costs (Table 3). However, length of ICU stay and outcome (discharge and death) did not show a significant association with antimicrobial costs.

Table 3. Multiple regression of demographic and clinical variables as predictors of antimicrobial costs for children and adolescents in high-complexity hospitals from 2018 to 2023. Paraná, Brazil.

Predictor variables	β*	Standardized βeta** coefficients	Antimicrobial Costs # CI 95% [1]	p-value
Age	16.5	0.176	7.20;25.8	**< 0,001**
Length of stay in the ICU	29.1	0.190	-13.4;71.7	0,180
Length of hospital stay	57.2	0.441	22.3;92.1	**< 0,001**
Sensitivity profile‡	539.5	0.119	171.6;1921.1	**0,019**
Outcome†	135.5	0.073	-349.0;1843.4	0,181

Abbreviation: ‡Sensitivity profile (Sensitive or resistant); †Outcome (discharge or death);
β* Non-standardized coefficient; βeta Standardized coefficient; **CI[1] 95% confidence interval; # Costs in *Reais* (R$) and p-value refers to the multiple linear regression test.

DISCUSSION

The results of the study of children and adolescents with HAIs, confirmed by microbiological tests involving the isolation and identification of microorganisms in blood cultures, urine cultures, and/or respiratory secretion cultures, reveal several important nuances regarding the impacts of antimicrobial-resistant microorganisms compared to sensitive microorganisms. The main predictors of increased antimicrobial costs were age, length of hospital stay, and the sensitivity profile of the microorganisms. In contrast, length of ICU stay and the outcome of death did not show a statistically significant association with these costs.

It is noteworthy that, among children and adolescents with culture-positive HAIs, the distribution between the groups with resistant and sensitive microorganisms was relatively similar regarding demographic variables, with the majority of patients in the 1-month to 1-year age range, a predominance of females and White race, and a significant positive correlation between age and antimicrobial costs. Studies indicate that, in this age group, their still-developing immune systems may make them more susceptible to acquiring HAIs.[14,15,16,17] Furthermore, as children and adolescents age, treatment costs tend to increase. The importance of individualized management strategies to optimize treatment and reduce the costs associated with caring for patients with HAIs is highlighted, especially in more vulnerable age groups.[17,18]

In the present study, it was observed that most children and adolescents had prolonged hospital stays. In particular, those with resistant microorganisms had significantly longer ICU stays and total hospitalization days. This is similar to other studies, which strongly demonstrate the relationship between resistant microorganisms and increased hospital stays, therapeutic costs, and mortality. It is noteworthy, however, that other clinical conditions, such as congenital heart disease requiring surgical

correction and other underlying comorbidities, may also have contributed to prolonged hospital stays.[17,18,20,21]

An epidemiological study conducted in a pediatric intensive care unit in China revealed that the prevalence of hospital-acquired infections in the PICU ranged from 10% to 25%. Furthermore, a series of risk factors were identified that could potentially be modified to reduce additional complications and minimize the need for more complex therapeutic interventions.[16]

Regarding the study results, there was no statistically significant association between the length of ICU stay and antimicrobial costs. Although several studies indicate that the transmission of multidrug-resistant microorganisms is most frequently reported in critical care units, such as ICUs, it is observed that all hospital sectors are impacted by the selection and spread of these microorganisms, consequently increasing costs.[16,17,18,22]

The presence of resistant infections increases the challenge for healthcare professionals, who must adopt rigorous infection control measures and consider therapeutic alternatives that are often limited due to antimicrobial resistance.[16,17] Therefore, it is crucial to implement effective hospital infection prevention and control strategies to mitigate these adverse impacts on pediatric health.[16,19]

It is noteworthy that results from national and international studies are similar in identifying the increasing difficulty in treating infections due to pathogen resistance to conventional antibiotics, highlighting the urgent need to develop new therapeutic strategies and prevent the irrational use of antimicrobials.[8,16,17,18,21 ,23,24,25]

The present study demonstrated that the susceptibility profile of microorganisms showed a statistically significant association with antimicrobial costs. Sensitive microorganisms tend to be associated with lower costs, while resistant microorganisms tend to be associated with higher costs. These findings corroborate the results of previous studies, which indicated that treatments for resistant infections generate substantially higher costs due to the need for more expensive antimicrobials and the prolonged treatment period.[18]

Regarding the microorganisms isolated in the cultures, Gram-negative bacteria predominated, with Klebsiella pneumonia being the most common, followed by Pseudomonas aeruginosa. Both showed a high prevalence of resistance to multiple antibiotics, indicating the need for rigorous infection control measures and continuous monitoring for resistance. Studies have identified Klebsiella pneumoniae as an

opportunistic pathogen that frequently causes serious infections in hospital settings, especially in patients with compromised immune systems.[26]

A case-control study conducted in the Central-West region of Brazil found similar results, with a predominance of Gram-negative bacteria. However, in this study, Pseudomonas was the most common, followed by Klebsiella pneumonia in HAI cases. Furthermore, infections were associated with significantly high hospital costs, longer hospital stays, and higher ICU mortality.[24]

A systematic review of the implementation and outcomes of antimicrobial stewardship programs in pediatrics globally identified that antimicrobials are frequently prescribed to children, and that, of these children, the high prescription rate raised concerns about their appropriateness and necessity, as it indicated that 20% to 50% of antimicrobials could be dispensable.[14]

The irrational use of this medication exposes children to antimicrobial resistance, significantly increasing the chances of complications, mortality, and associated healthcare costs.[6,14]

Mortality was 54 cases (23.1%), and the presence of resistant microorganisms correlated with greater disease severity, reflected in high death rates. The importance of controlling antimicrobial resistance to improve outcomes is highlighted.[10,18]

Direct antimicrobial costs varied considerably, being up to five times higher for resistant microorganisms compared to sensitive ones. This reflects the need for more complex and prolonged treatments to combat resistant infections. Therefore, understanding direct costs is crucial for hospitals, as it allows for efficient resource allocation, improved quality of care, and maintenance of the institution's financial viability, as argued by other authors.[24]

Authors highlight that the implementation of antimicrobial stewardship programs in pediatric hospitals has been shown to significantly reduce the costs associated with antimicrobial use. These programs focus on optimizing antimicrobial prescribing, avoiding inappropriate and excessive use, which are common contributors to increased healthcare costs.[14]

Consistent with other authors, this study highlights the importance of global cooperation, effective policies, and rigorous surveillance to mitigate the effects of antimicrobial resistance, emphasizing the need for a coordinated effort between governments, healthcare professionals, and the scientific community.[6,23] To mitigate these problems, it is essential to adopt strategies that promote the rational use of

antimicrobials for this population and in various related areas.[6,14,23,25,26] These results reinforce the need for improvements in antimicrobial stewardship programs, especially in healthcare services, and investment in further research in this area.

This study highlights the need for rigorous infection control and rational antimicrobial prescribing to contain bacterial resistance and optimize costs. Measures such as epidemiological surveillance and rational use policies are essential to minimize the clinical and economic impacts associated with treating infections in hospitalized children and adolescents.

Although the multiple linear regression model explained 44% of the variance in antimicrobial costs, the results indicate potential limitations related to the influence of other predictor variables not included in the model. Factors such as individual characteristics of children and adolescents, institutional prescribing patterns, and unmeasured clinical variables may impact observed costs. Future studies should explore these aspects to deepen understanding of the determinants of antimicrobial costs and improve management strategies.

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