

Antimicrobial resistance in urinary tract infections: Impact on costs and clinical variables

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ABSTRACT

Introduction: Healthcare-associated infections (HAIs) are one of the leading threats to patient health and a challenge for healthcare professionals. Among these, Urinary Tract Infection (UTI) is very common, often caused by antimicrobial-resistant microorganisms (ARMs), leading to longer hospital stays and increased costs.

Objective: To compare clinical variables and the total cost of hospitalization among adult patients hospitalized with positive urine cultures for microorganisms sensitive and resistant to antimicrobials.

Method: Longitudinal, retrospective study conducted between January 2018 and December 2023 at a tertiary-care hospital in southern Brazil. It included patients aged ≥ 18 years who were hospitalized for more than 72 hours and had a positive urine culture. Clinical, microbiological, and financial variables were analyzed. Data were extracted from the *Business Intelligence*® platform and analyzed using SPSS® version 20.

Results: There were 53,452 hospitalizations recorded, with 135 patients presenting positive urine cultures. Of these, 93 (68.9%) had multidrug-resistant organisms and 42 (31.1%) had susceptible organisms. There was a predominance of elderly women (67.4%), hospital stays longer than 15 days (37.8%), and intensive care unit admission (68.9%). Patients with urine cultures positive for resistant organisms incurred significantly higher antimicrobial costs compared with those with cultures positive for susceptible organisms (median R\$ 895.54 vs. R\$ 349.05; $p < 0.001$).

Conclusion: The results of this study demonstrated that hospitalized adult patients with urine cultures positive for antimicrobial-resistant microorganisms experienced greater clinical and economic impact compared with those with susceptible organisms.

Descriptors: Multidrug resistance, Hospital-acquired infection, Healthcare costs, Drug costs, Urinary tract infections.

INTRODUCTION

Urinary Tract Infection (UTI) is one of the most common infections in clinical medicine, characterized as the microbial invasion of any organ of the urinary tract (bladder, urethra, or kidneys). UTIs are typically caused by the human bacterial microbiota itself, which becomes imbalanced with anti-infectious defense mechanisms, or during invasive procedures and contact with nosocomial microorganisms. The main risk factors for this syndrome are related to female sex, advanced age, anatomical abnormalities, and use of urinary catheterization.⁽¹⁾

International studies and systematic reviews indicate that UTIs constitute a significant portion of healthcare-associated infections and the morbidity and mortality associated with urinary tract infections. A high global incidence of UTI is estimated, with greater occurrence in women and elderly individuals, and they are frequently cited among the most common types of healthcare-associated infections.^(2,3,4,5)

In the national scenario, multicenter studies and local studies in Brazil have described a microbiological pattern with predominance of Gram-negative bacilli in urine cultures and progressive increase in resistance rates, which has guided revisions of local empirical therapy guidelines. Institutional studies show regional variation but indicate a trend toward increasing antimicrobial resistance in uropathogens.^(6,7)

Urinary tract infections (UTIs) account for 35% to 45% of Healthcare-Associated Infections (HAIs) in adult patients and become more concerning due to the risk of being caused by Multidrug-Resistant Organisms (MDROs), a growing threat to public health due to their ability to acquire genes that confer antimicrobial resistance, located in transferable genetic elements.⁽⁸⁾

Antimicrobial resistance is recognized as one of the greatest threats to global public health: international studies and reports indicate a continuous increase in infections caused by resistant microorganisms, with significant clinical and population impact, particularly in low- and middle-income countries, where the burden of resistant HAIs is higher.^(9,10)

Antibiotics, although they have revolutionized the treatment of severe bacterial infections, have been showing progressive loss of efficacy. The inappropriate, excessive, and indiscriminate use of these agents in human medicine, veterinary medicine, and agribusiness has significantly contributed to the emergence and spread of resistant microorganisms, increasing the risk of therapeutic failure and imposing a global economic and health impact.^(11,12)

Furthermore, infections caused by multidrug-resistant organisms are associated with longer hospital stays and can increase direct hospital care costs up to eightfold when compared to infections caused by susceptible microorganisms.⁽¹³⁾

Systematic reviews on the economic burden of resistance show significant increases in hospital costs, longer length of stay, and higher rates of readmission and mortality associated with resistant infections; macroeconomic estimates also project substantial global financial impact of antimicrobial resistance in the coming decades. This evidence reinforces the need to quantify the local cost of HAIs caused by resistant microorganisms to better guide prevention policies and resource allocation.^(14,15)

In this context, understanding the clinical and economic impact of UTIs caused by multidrug-resistant microorganisms becomes essential, particularly in high-complexity hospital institutions, where the severity of cases, the presence of comorbidities, and the frequent use of invasive procedures may potentiate the occurrence of resistant infections. Estimating the magnitude of the financial impact of this prevalent and potentially preventable condition is particularly useful for measuring cost savings by preventing a case, thereby emphasizing the importance of prevention and the considerable economic consequences of infections caused by resistant microorganisms in the hospital environment, especially UTIs.⁽¹⁶⁾

Thus, the objective of the study was to compare clinical variables and the total cost of hospitalization, including antimicrobial therapy expenses, between hospitalized adult patients with positive urine cultures for antimicrobial-susceptible and antimicrobial-resistant microorganisms, from January 2018 to December 2023.

METHODS

This is a longitudinal, retrospective study with a quantitative approach, conducted from January

2018 to December 2023, a period chosen to encompass six years and allow for the analysis of infection behavior related to HAIs.

The study was conducted at a high-complexity philanthropic hospital located in Southern Brazil, with 274 medical-surgical beds, 48 of which are designated for intensive care, with 28 exclusively dedicated to patients from the Unified Health System (SUS). Approximately 80% of hospital care is provided through SUS.⁽¹⁷⁾ The institution has a clinical and microbiological analysis laboratory operating continuously and has a structured Hospital Infection Prevention and Control Service (SPCIH), composed of a specialized team. Antimicrobial stewardship is computerized and integrated with the electronic medical record. The hospital has been a regional reference center for robotic surgery since 2022, in addition to excelling in the areas of trauma, orthopedics, neurology, and hemodynamic support.

The study population consisted of all patients admitted to the hospital's clinical, surgical, and intensive care units during the period defined for the research. From this population, individuals who met the eligibility criteria were identified, comprising the sample frame. This is a census sampling, consisting of all cases that met the inclusion criteria during the analyzed period, totaling 135 participants. Patients of both sexes, aged 18 years or older, hospitalized for more than 72 hours, who underwent at least one urine culture with a positive result for bacteria, were included.

Patients whose urine cultures showed growth of coagulase-negative *Staphylococcus* were excluded from the analysis, as this bacterium is part of the normal microbiota of human skin and mucous membranes and is frequently isolated as a contaminant in clinical samples, without necessarily indicating an infection.⁽¹⁸⁾ The exclusion of these cases aimed to avoid misinterpretations and ensure greater accuracy in identifying clinically relevant bacterial infections. Additionally, patients with incomplete cost records in their medical charts were also excluded to ensure consistency of the analyzed data.

The clinical variables analyzed included: sex, age, length of hospital stay, intensive care unit (ICU) stay, type of admission (medical or surgical), medical specialty, and clinical outcome (hospital discharge or death). Microbiological variables included identification of bacterial species and their antimicrobial susceptibility profile, obtained from antimicrobial susceptibility testing, which allows verification of whether the microorganism is susceptible or resistant to the different antimicrobial agents tested.

For analysis purposes, multidrug-resistant microorganisms were considered those classified according to the following criteria: oxacillin-resistant *Staphylococcus* spp, vancomycin-resistant *Enterococcus* spp, and gram-negative bacteria with resistance to at least one class of antimicrobials (carbapenems, polymyxins, cephalosporins, fluoroquinolones, or aminoglycosides), according to the institutional protocol.⁽¹⁹⁾

Data on the number of UTI cases recorded during the study period were obtained from monthly bulletins issued by the Hospital Infection Control Service (SPCIH), prepared according to the updated diagnostic criteria of the Brazilian National Health Surveillance Agency (ANVISA) for Healthcare-Associated Infections (HAIs).⁽²⁰⁾

Urine culture samples were collected by hospital nursing professionals and plated on CLED and *MacConkey* culture media using the streak plate technique to isolate bacterial colonies.^(21,22,23) Microbiological confirmation followed the cutoff point of $\geq 10^5$ colony-forming units per milliliter (CFU/mL).

It should be noted that the data used in this study were secondary, extracted from the hospital information system; the authors did not directly perform the microbiological processing or laboratory analysis of the microorganisms. Sample processing was performed in an automated manner using the BACTEC® system (*bioMérieux* – Brazil), which allows for the detection of microbial growth. Identification of microorganisms and antimicrobial susceptibility profile analysis were conducted using the automated *MicroScan*® system (Siemens).⁽²⁴⁾

Financial data were provided by the hospital's Economic Management sector and are expressed in Brazilian reais (R\$). Total direct costs were considered as expenses directly related to patient care during hospitalization, including laboratory tests, imaging studies, medications, and hospital supplies used. Indirect costs, such as electricity, water, telephone, and building maintenance, were not included

in the calculation, as they represent general estimates that are difficult to attribute individually to patients, nor were costs related to medical-hospital supplies used in antimicrobial administration (syringes, diluents, and infusion sets) and the time spent by the nursing staff.

The specific costs of antimicrobials were extracted from the total direct cost and calculated based on the unit price paid by the hospital to the supplier, already including possible discounts and charges. The administered quantity was obtained through medical records and hospital pharmacy records, considering the prescribed dose, treatment duration, and the number of patients who received the antimicrobial during the analyzed period.

To calculate the mean direct cost of antimicrobials, the following formula was used: Mean Direct Cost = $\sum(\text{Cost of Antimicrobial per Patient}) / \text{Total Number of Treated Patients}$.⁽²⁵⁾ Data extraction and integration were performed using the *Business Intelligence*® (BI) platform, a tool that consolidates information from multiple sources, such as electronic medical records and administrative databases, enabling predictive analyses, pattern identification, and resource optimization. BI also provided access to previously parameterized cost calculations, ensuring standardization, speed, and reliability in financial analysis. The information was exported to *Microsoft Excel*® spreadsheets and subsequently analyzed statistically using *IBM SPSS Statistics*® software, version 20.

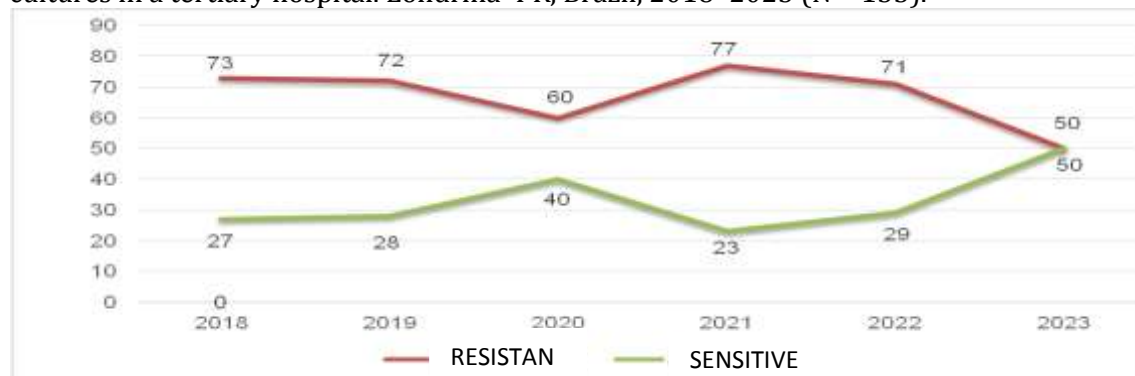
For classification of the bacterial resistance profile, microorganisms were categorized into two groups, susceptible and resistant, according to the criteria established by the *Brazilian Committee on Antimicrobial Susceptibility Testing*.⁽²⁶⁾ The comparison of antimicrobial costs between groups was performed using the non-parametric *Mann-Whitney U* test, since data normality was rejected at the 5% significance level. To verify the association between the resistance profile and qualitative variables (sex, age group, length of hospital stay, ICU stay, reason for hospitalization, and clinical outcome), Pearson's chi-square test or Fisher's exact test was used, according to data appropriateness.

This research is part of the project entitled "Clinical and economic impact of antimicrobial resistance on hospital costs," approved by the Research Ethics Committee Involving Human Subjects of Irmandade Santa Casa de Londrina, through an amendment (Opinion No. 5.632.608), registered under the Certificate of Presentation for Ethical Appreciation (CAAE) No. 24711718.8.0000.0099.

RESULTS

Between 2018 and 2023, 53,452 hospitalizations were recorded. Among hospitalized patients, 135 presented positive urine cultures during the hospitalization period. Of these, 68.9% (n = 93) presented at least one urine culture with isolation of multidrug-resistant microorganisms, while 31.1% (n = 42) had urine cultures with antimicrobial-susceptible microorganisms. Throughout the years analyzed, variation in the frequency of urine cultures with resistant microorganisms was observed. In 2021 and 2018, the highest proportions of bacterial isolates with antimicrobial resistance profiles were recorded (Figure 1).

Figure 1. Percentage distribution of antimicrobial-resistant and antimicrobial-susceptible urine cultures in a tertiary hospital. Londrina-PR, Brazil, 2018–2023 (N = 135).



Legend: RESISTANT - Microbiological urine culture resistant*; SENSITIVE - Microbiological urine culture sensitive**

Source: Prepared by the authors, 2025.

Among the analyzed patients, the majority were female and elderly, with a mean length of hospital stay exceeding 15 days and a high frequency of intensive care unit (ICU) admissions. Statistical analysis did not identify significant differences between these clinical variables and the occurrence of multidrug-resistant microorganisms (Table 1).

Table 1. Distribution of clinical-demographic variables and microbial susceptibility profile in urine cultures from hospitalized patients. Londrina-PR, Brazil, 2018 to 2023 (N=135).

Variables	Total N (135)	Patients UMR n= 93 (%)	Patients UMS n= 42 (%)	p-value
Gender				
Masculine	63 (46,7%)	48 (51,6%)	15 (35,7%)	0,086
Feminine	72 (53,3%)	45 (48,4%)	27 (64,3%)	
Age range				
>18 a <30 years	3 (2,2%)	3 (3,2%)	-	0,108
≥30 a ≤59 years	41 (30,4%)	29 (31,2%)	12 (28,6%)	
≥60 years	91 (67,4%)	61 (65,6%)	30 (71,4%)	
Hospitalization period				
≤7 days	4 (3,0%)	2 (2,2%)	2 (4,8%)	0,224
8 a 14 days	41 (30,4%)	25 (26,9%)	16 (38,1%)	
15 a 29 days	51 (37,8%)	33 (35,5%)	18 (42,9%)	
≥ 30 days	39 (28,9%)	33 (35,5%)	6 (14,3%)	
Stay in ICU				
Yes	93 (68,9 %)	63(67,7%)	30 (71,4%)	0,668
No	42 (31,1 %)	30 (32,3%)	12 (28,6%)	
Days in ICU				
It wasn't necessary	42 (31,1 %)	30 (32,3%)	12 (28,6%)	0,233
Up to 6 days	40 (29,6 %)	25 (26,9%)	15 (35,7%)	
7 to 14 days	24 (17,8 %)	14 (15,0%)	10 (23,8%)	
15 to 29 days	24 (17,8 %)	19 (20,4%)	5 (11,9%)	
≥ 30 days	5 (3,7 %)	5 (5,4%)	-	
Reason for hospitalization				
Clinical	69 (51,1 %)	46 (49,5%)	23 (54,8%)	0,568
Surgical	66 (48,9 %)	47 (50,5%)	19 (45,2%)	
Clinical outcome				
Hospital discharge	82(60,7 %)	54 (58,1%)	30 (66,7%)	0,343
Death	53 (39,3 %)	39 (41,9%)	14 (33,3%)	

Legend: RMU-Resistant microbiological urine culture*; SMU-Susceptible microbiological urine culture**; 1 p-value refers to the Chi-square test.

Source: Prepared by the authors, 2025.

The main medical specialties affected by urinary tract infections were: internal medicine (25.2%), neurosurgery (20.1%), nephrology (10.5%), neurology (9.6%), and orthopedics (7.4%), data not available in table.

Among patients with positive urine cultures and identification of resistant microorganisms, prevalences of 18.5% for multidrug-resistant (MDR) microorganisms, 40.7% for carbapenem-resistant (CR), and 8.1% for polymyxin-resistant (PR) were observed. The majority of these infections (92.2%) were caused by gram-negative bacteria, while only 7.8% were attributed to gram-positive bacteria.

The most frequently identified microorganisms in urine cultures were *Klebsiella pneumoniae* (36.3%), *Escherichia coli* (17.0%), *Pseudomonas aeruginosa* (10.4%), *Acinetobacter baumannii* (6.7%), and *Staphylococcus aureus* (4.4%). Other less prevalent pathogens included *Enterococcus faecalis*, *Serratia marcescens*, *Enterobacter cloacae*, *Proteus mirabilis*, *Morganella morganii*, among others, totaling 100% of the analyzed samples.

Table 2. Mann-Whitney test analysis of antimicrobial costs and total direct costs (in Brazilian reais R\$), according to the susceptibility profile of microorganisms isolated in urine cultures, in a tertiary hospital. Londrina-PR, Brazil, 2018 to 2023 (N=135).

	Median	IIC	Mann-Whitney
Cost of antimicrobials			
UMR	895,54	R\$256,00 – 1.929,93	0,001
UMS	349,05	R\$85,52 – 781,97	
Total direct cost			
UMR	7.618,59	R\$3.916,66-15.454,80	0,062
UMS	5.496,59	R\$2.194,95-11.341,17	

Legend: UMR-Resistant microbiological urine culture*; UMS-Susceptible microbiological urine culture**; IQR – interquartile range; Financial values expressed in Brazilian reais (R\$).

Source: Prepared by the authors, 2025.

In the cost analysis in Brazilian reais (R\$), patients with positive urine cultures for resistant microorganisms (UMR) had significantly higher antimicrobial costs compared to those with susceptible urine cultures (UMS) (median R\$ 895.54; IQR: R\$ 256.00–1,929.93 vs. R\$ 349.05; IQR: R\$ 85.52–781.97; $p = 0.001$). Regarding the total direct cost of hospitalization, although patients with UMR presented higher median values (R\$ 7,618.59; IQR: R\$ 3,916.66–15,454.80) compared to patients with UMS (R\$ 5,496.59; IQR: R\$ 2,194.95–11,341.17), this difference did not reach statistical significance ($p = 0.062$).

DISCUSSION

The objective of this study was to compare clinical variables and hospitalization costs, including antimicrobial therapy expenses, between patients with urinary tract infection caused by antimicrobial-susceptible and antimicrobial-resistant microorganisms.

Overall, a high prevalence of resistant microorganisms was observed among the evaluated patients, with a predominance of cases in women over 60 years of age. Although no statistical significance was found, this finding is consistent with the literature, which indicates greater female susceptibility due to anatomical factors that favor bacterial ascension, such as a shorter urethra and proximity to the anal region.⁽²⁷⁾ Additionally, the increased incidence of UTI in elderly individuals is widely recognized.^(28,29,30)

The greater vulnerability of the elderly to UTI is related to immunosenescence, accumulation of comorbidities, and frequent use of antimicrobials and invasive devices, factors that increase the risk of recurrence and infections by resistant strains.^(31,32,33) The presence of biofilm-producing microorganisms in these patients additionally contributes to greater bacterial persistence and therapeutic failure.⁽³³⁾

In this study, a higher proportion of resistant microorganisms was observed in patients with longer hospital stays and in intensive care units, although without statistical association. This pattern is described in the literature because the critical hospital environment favors antimicrobial selective pressure, in addition to greater exposure to invasive procedures, conditions that facilitate the dissemination of resistant strains.^(34,35)

Regarding clinical outcomes, it was found that more than half of hospitalized patients with UTI progressed to medical discharge. On the other hand, among those who died, the majority had urine cultures with resistant microorganisms. Although this difference is substantial from a numerical standpoint, no statistically significant association was observed between antimicrobial resistance and mortality. This absence of direct correlation is discussed in previous studies, which, although reporting higher mortality in infections by resistant microorganisms, especially in hospital settings and ICUs, also highlight that variables such as clinical stability and time to initiation of appropriate treatment may mitigate this impact.^(36,37,38,39,40)

Regarding the microbiological profile, most infections were caused by gram-negative bacteria, particularly *Klebsiella pneumoniae* and *Escherichia coli*, both belonging to the Enterobacteriaceae

family. These bacteria, natural inhabitants of the intestinal microbiota, are recognized as important etiological agents of UTI and other nosocomial infections, such as pneumonia, bacteremia, and intra-abdominal infections.⁽⁴¹⁾ Their predominance in urinary infections is related to their intestinal origin and ability to colonize the urinary tract. Furthermore, these species demonstrate a high capacity to develop resistance through plasmids and cellular modifications, which explains the high prevalence of infections by multidrug-resistant microorganisms.⁽⁴²⁾

From an economic perspective, the present study identified a significant impact of bacterial resistance on treatment costs. It was observed that antimicrobial costs were higher among patients with infections by resistant microorganisms compared to susceptible ones, indicating an important economic impact associated with antimicrobial resistance. Although the total cost of hospitalization did not show a significant difference between groups, an increase in total direct costs was observed among patients with infections by resistant microorganisms.

These findings are reinforced by a Brazilian study conducted in a public hospital, which also demonstrated a relevant impact of nosocomial infections on direct costs. In that study, the median antimicrobial cost reached R\$ 309.40 among patients with resistant microorganisms, a value lower than that found in the present study. Differences such as severity of cases treated, institutional profile, and use of broad-spectrum antimicrobials may explain this disparity. Moreover, while the comparative study identified a median of R\$ 6,129.50 for other direct costs, in the present study the total direct cost of hospitalization was higher, both for patients with infections by resistant microorganisms and for those with susceptible microorganisms, reinforcing the magnitude of the economic impact associated with antimicrobial resistance in our setting.⁽⁴³⁾

The financial impact of UTI becomes even more significant when there is progression to sepsis. In a study conducted at a Brazilian university hospital, it was observed that patients with severe sepsis or septic shock generated, in one year, a total cost of R\$ 3,692,421.00 (approximately US\$ 1,649,138.00), evidencing the high economic burden associated with these conditions. The main infectious sources were pneumonia and UTI, with pulmonary sepsis being the most costly (R\$ 2,908,378.00), followed by urinary sepsis (R\$ 723,328.00).⁽⁴¹⁾ These data complement the findings of the present study by demonstrating that, in addition to the direct costs of antimicrobial-resistant UTI, its progression to sepsis represents an even more costly burden for the healthcare system.

Similar results have been observed internationally. In Lebanon, a comparative study between patients with UTI caused by resistant and susceptible *E. coli* showed a 29% increase in total costs in resistant cases, with mean length of stay also being longer.⁽⁴⁴⁾

In European countries and Turkey, the average cost per hospitalization for complicated UTI was € 5,700, with the presence of multidrug-resistant bacteria being one of the main factors for increased expenditure. Emergency admissions, infections resulting from indwelling urinary catheterization resulting in septic shock or severe sepsis, in patients with comorbidities and presenting multidrug resistance (MDR), were associated with higher costs. The authors suggest that better knowledge of the reasons for variations in length of hospital stays could facilitate better standardization of quality of care for patients with complicated UTI and allow more efficient allocation of healthcare resources.⁽⁴⁵⁾ In Japan, although the healthcare system is highly structured and recognized for its efficiency, the median medical costs per hospitalization due to UTI reached US\$4,250, demonstrating that even in contexts with high organizational care, UTIs represent a significant economic impact.⁽⁴⁶⁾

Corroborating these findings, a recent international systematic review analyzed the economic impact of community-acquired UTIs, especially those caused by resistant bacteria. All included studies reported significant increases in hospital costs in resistant cases, with emphasis on infections by carbapenemase-producing Enterobacteriaceae, associated with higher mortality rates and length of stay.⁽⁴⁷⁾

Finally, in the North American context, a systematic review indicated that catheter-associated urinary tract infections generate additional costs ranging from US\$876 to more than US\$10,000, depending on clinical severity, type of hospital unit, and patient profile. Even in systems with rigorous prevention protocols, these infections continue to represent an important source of preventable expenses.⁽⁴⁸⁾

Thus, by integrating the findings of this study with the national and international panorama, it is

observed that antimicrobial resistance in UTI represents not only a clinical challenge but also an economic one, due to increased antimicrobial use, prolonged hospitalizations, and greater therapeutic complexity. These results reinforce the importance of consistent institutional strategies for antimicrobial stewardship, continuous microbiological surveillance, and actions to reduce the use of invasive devices, especially in higher-risk patients.

Although this study provided relevant information about clinical factors associated with antimicrobial resistance in patients with urinary tract infection, some limitations must be acknowledged. As this was a study conducted in a single hospital, the results may not reflect the reality of other institutions, which may present different microbiological profiles and resistance patterns.

Furthermore, the retrospective design and use of secondary data may be subject to incomplete records, variability in information quality, and absence of some variables of interest, which may limit the accuracy of the analyses. Another point to consider is that the definition of multidrug-resistant microorganisms was based on institutional classification, which may diverge from updated national and international criteria, making direct comparisons with other studies difficult. Finally, the economic analysis contemplated only direct hospital costs, without including indirect costs, such as impact on quality of life, readmissions, and loss of productivity, indicating the need for future investigations with a more comprehensive approach.

CONCLUSIONS

The results of this study demonstrated that hospitalized adult patients with positive urine cultures for antimicrobial-resistant microorganisms had a greater clinical and economic impact compared to those with susceptible microorganisms. A predominance of infections was observed in elderly women and a prevalence of gram-negative bacteria, especially *Klebsiella pneumoniae* and *Escherichia coli*, associated with prolonged hospital stays and intensive care unit admissions. Antimicrobial resistance was related to increased direct hospitalization costs, particularly antimicrobial therapy expenses, reinforcing the importance of continuous surveillance, rational use of antibiotics, and implementation of institutional protocols that contribute to better clinical outcomes and optimization of healthcare resources.

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Study conception and design and/or data collection: Sidnei Dias Silva and Nayane Laine Paglione Dias. Data analysis and interpretation: Susany Franciely Pimenta. Drafting of the manuscript and/or critical revision for important intellectual content and/or final approval of the version to be published: Sidnei Dias Silva, Caio Ferreira de Oliveira, Nayane Laine Paglione Dias, Angela Maffi Paiva, Marcio Aram Vacamoreno Paiva Maffi.

RESEARCH ETHICS COMMITTEE APPROVAL

Approved by the Research Ethics Committee of Irmandade Santa Casa de Londrina, opinion no. 5.632.608, Certificate of Presentation for Ethical Appraisal (CAAE) 24711718.8.0000.0099.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE FOR CONTENT GENERATION

The authors used ChatGPT during the preparation of this work to assist with writing, textual revision, and improvement of the clarity of the scientific content. After using the tool, the authors reviewed and edited the content as needed and take full responsibility for the published material.