Revista Prevenção de Infecção e Saúde
The Official Journal of the Human Exposome and Infectious Diseases Network

ORIGINAL ARTICLE DOI: 10.26694/repis.v11in.1.6414

Factors associated with healthcare-associated infections and bacterial resistance in hospitalized children and adolescents

Fatores associados às infecções relacionadas à assistência à saúde e a resistência bacteriana em crianças e adolescentes hospitalizados

Factores asociados a infecciones asociadas a la atención médica y resistencia bacteriana en niños y adolescentes hospitalizados

Susany Franciely Pimenta[1], Nayane Laine Paglione[1], Adriana Valongo Zani[1], Flávia Lopes Gabani[1], Marcela Demitto Furtado[2], Jaqueline Dario Capobiango[3], Rosângela Aparecida Pimenta[1]

How to cite this article:
Pimenta SF, Paglione NL, Zani AV, Gabani FL, Furtado MD, Capobiango, JD, Pimenta RA. Factors associated with healthcare-associated infections and bacterial resistance in hospitalized children and adolescentes.Online Debate on HPV Vaccination in Brazil: A Cross-Sectional Study. Rev Pre Infec e Saúde [Internet]. 2025;11:01. Disponível em: http://periodicos.ufpi.br/index.php/repis/article/view/6414. DOI: https://doi.org/10.26694/repis.v11in.1.6414.

[1] Universidade Estadual de Londrina, Programa de Pós-graduação de Doutorado em Enfermagem, Londrina (PR), Brasil.

[2] Universidade Estadual de Maringá, Programa de Pós-graduação de Doutorado em Enfermagem, Maringá (PR), Brasil.

[3] Universidade Estadual de Londrina, Programa de Pós-graduação de Doutorado em Enfermagem, Londrina (PR), Brasil.

Corresponding Author:
Susany Franciely Pimenta
Address: Avenida Robert Koch, 60, Vila Operária, Londrina (PR), Brasil.
Code: 86038-350
Phone: +55 (43) 99655-5502
E-mail: susany.franciely@uel.br

ABSTRACT

Introduction: Healthcare-Associated Infections (HAIs) increase morbidity, mortality, and hospital costs, favoring the spread of resistant bacteria. Objective: To analyze the factors associated with healthcare-associated infections and bacterial resistance in hospitalized children and adolescents. Method: Case-control study carried out with secondary data extracted from Business Intelligence® (BI) software spreadsheets and notification forms from the Hospital Infection Control Commission (CCIH), from medical records of children and adolescents with Healthcare-Associated Infections (HAIs) and positive microbiological cultures, from 2018 to 2023 from two highly complex philanthropic hospitals in Paraná, Brazil. Demographic and clinical information was collected and analyzed by Chi-square or Fisher's test. Results: Of the 244 children and adolescents, 42.2% had HAIs due to resistant bacteria and 57.8% due to sensitive bacteria. Children < 2 years old accounted for 69.7% of the cases with the highest prevalence of bacterial resistance. The use of invasive devices, such as indwelling urinary catheter (OR: 4.65; 95% CI: 2.53–8.53) and orotracheal intubation (OR: 2.31; 95% CI: 1.31–4.04), may be associated with bacterial resistance, as well as surgical site infections (OR: 3.13; 95% CI: 1.57–6.24), primary bloodstream infection (OR: 1.72; 95% CI: 1.00–2.96), hospitalizations > 30 days and ICU stay > 15 days, and death. Gram-negative bacteria were predominant. Conclusion: The findings highlight the importance of effective infection prevention and control strategies.

DESCRIPTORS

Child. Adolescent. Case-Control Studies. Bacterial Infections. Microbial Drug Resistance.

Submitted: 11/10/2024
Accepted: 19/03/2025
Published: 29/05/2025

INTRODUCTIO

Healthcare-Associated Infections (HAIs) represent a serious threat to the health of hospitalized patients, especially children and adolescents, due to the immaturity of their immune systems and the increased frequency of invasive procedures [1,2]. These infections occur in patients during the provision of healthcare and are acquired after hospital admission, without being present or incubating at the time of admission [3,4]. HAIs can affect any body system, increasing morbidity, mortality, and hospital costs, in addition to promoting the spread of resistant bacteria [3,5,6,7].

The association between HAIs and Antimicrobial Resistance (AMR) significantly worsens clinical outcomes by limiting therapeutic options and increasing mortality [1,2,3,8,9,10]. According to the World Health Organization (WHO), the prevalence of HAIs is considerably higher in developing countries, with 15.5 cases per 100 patients, compared to 7.6 cases per 100 patients in developed countries. In Brazil, as in other developing countries, this scenario is particularly concerning—especially in the pediatric context, where children and adolescents are more susceptible to HAIs [11,12].

Driven by the inappropriate use of antibiotics and the spread of resistance genes, AMR has become one of the greatest health crises of the 21st century [6,13,14]. A study conducted in a university hospital in southern Brazil revealed that 41.6% of hospitalized children required invasive procedures such as central venous catheterization, urinary catheterization, and mechanical ventilation, and 31% of these developed HAIs [11].

In addition to invasive procedures, factors such as length of hospital stay, use of broad-spectrum antimicrobials, and complexity of hospital care are associated with a higher prevalence of HAIs caused by multidrug-resistant microorganisms [1,2,8,15]. In hospital settings, intrinsic patient-related risk factors—such as comorbidities and surgical procedures—also contribute to the emergence and spread of these pathogens [1,2,5,11].

Identifying and understanding these factors is essential for the adoption of preventive and control measures, especially in the pediatric population, which is more vulnerable to HAIs and bacterial resistance. These actions aim not only to improve the quality of care and reduce adverse events but also to minimize morbidity and mortality associated with these infections and multidrug-resistant pathogens [4,12].

In this context, the present study aimed to analyze the factors associated with healthcare-associated infections and bacterial resistance in hospitalized children and adolescents, seeking to contribute to the development of more effective strategies for combating and preventing these conditions.

METHODS

This was a case-control study conducted in two high-complexity philanthropic hospitals located in the interior of the state of Paraná, Brazil. One of the hospitals is a regional reference center for pediatric cardiac surgery, serving patients from birth to 12 years of age with clinical and surgical conditions. This facility has 50 beds, including 30 in the general ward and 20 in the neonatal and pediatric intensive care unit (ICU), in addition to a pediatric emergency department. The second hospital has 274 beds, including inpatient units and 47 ICU beds for adolescents and young adults over 12 years old, housed in adult care sectors. These facilities serve as the main healthcare entry point for the municipality and surrounding regions.

Inclusion criteria comprised children and adolescents of both sexes, aged between 29 days and under 18 years [16], diagnosed with Healthcare-Associated Infections (HAIs) caused by either antimicrobial-resistant or antimicrobial-sensitive bacteria, as defined by the Hospital Infection Control Committees (HICC) of the participating institutions. Patients who underwent blood cultures, urine cultures, and/or tracheal secretion cultures, and were admitted to hospital wards and/or ICUs between January 1, 2018, and December 31, 2023, were included, totaling 253 patients during the period. Patients with positive cultures for coagulase-negative *Staphylococcus* were excluded due to the inability to rule out colonization by this microorganism, resulting in nine exclusions.

The final convenience sample consisted of 244 children and adolescents. Cases were defined as patients with HAIs caused by antimicrobial-resistant bacteria, while controls were those with HAIs caused by antimicrobial-sensitive bacteria. The dependent variable was the presence of HAIs caused by resistant (cases) or sensitive (controls) bacteria.

Independent variables included: age group (≥29 days to <2 years; 2 to ≤6 years; 7 to ≤11 years; 12 to <18 years); sex (male/female); skin color (white/non-white); place of residence (study municipality/other municipalities); type of hospitalization (clinical/surgical); total length of hospital stay; ICU admission (yes/no) and ICU length of stay in days; use of invasive devices (yes/no) and type of device (central venous catheter [CVC], peripherally inserted central catheter [PICC], indwelling urinary catheter [IUC], and orotracheal intubation [OTI]); type of HAI and number of affected sites (1 site or ≥2 sites); isolated bacteria and antimicrobial susceptibility profile; use of antibiotics (yes/no) and therapeutic class; and clinical outcome (discharge/death).

HAI diagnoses were previously established by the HICC of the institutions and included: Primary bloodstream infection (PBSI); pneumonia; ventilator-associated pneumonia (VAP); urinary tract infection (UTI); catheter-associated urinary tract infection (CAUTI); and surgical site infection (SSI). HAI reports were considered based on the documentation of all infections, regardless of the presence of invasive devices, and confirmed through laboratory tests and clinical signs specific to each infection type. To ensure accurate identification of distinct infection episodes, a minimum 14-day interval was adopted between device-associated infections. This criterion, along with the appearance of new signs and symptoms and laboratory confirmation, aligns with the guidelines of the Brazilian Health Regulatory Agency (ANVISA), which recommend distinguishing between continuous and new infectious episodes to avoid duplicate records and ensure standardization of surveillance data [17].

Blood culture collection followed institutional protocols and was performed by nurses. Blood samples were immediately delivered to lab assistants and technicians for inoculation into BD BACTEC™ culture medium vials. The cultures were processed using the BACTEC® automated system (models FX, 9000 series), which detects microbial growth.

Urine cultures were also collected by nurses and sent to the laboratory by assistants and technicians. In the lab, samples were plated on CLED and MacConkey agar media. The streaking technique was used to isolate colonies, followed by incubation and microbiological analysis of the colonies.

Tracheal secretion samples were obtained by nurses or physiotherapists through aspiration or bronchoscopy using sterile catheters. The collected secretion was plated on culture media such as blood agar and subjected to streaking to facilitate the isolation of colonies.

Identification of microorganisms and determination of their antimicrobial susceptibility profiles in blood, urine, and tracheal secretion cultures were performed using the automated MicroScan® system (Siemens). All samples were collected prior to the research and strictly followed institutional protocols.

The institutions followed diagnostic criteria for HAIs in accordance with the annually updated guidelines of ANVISA. Microbiological confirmation of tracheal secretion cultures obtained by aspiration considered a threshold of $\geq 10^6$ CFU/mL, combined with clinical signs and radiographic findings. VAP was defined as pneumonia in patients who had been mechanically ventilated for more than 48 hours via orotracheal intubation or tracheostomy [17].

PBSI was defined in patients with a central venous catheter in place for more than 48 hours and who were either using the catheter or had it removed the day prior to infection onset. Diagnosis required clinical signs and laboratory tests confirming microorganism isolation in blood culture, with paired blood samples collected from both the central catheter and peripheral blood. Microorganisms typically associated with skin contamination or another infection source were not considered [17].

CAUTI was defined as occurring in patients with an indwelling urinary catheter in place for more than 48 hours, presenting clinical signs and a quantitative urine culture $\geq 10^5$ CFU/mL, in accordance with ANVISA classification [17].

Bacterial isolates were categorized into two groups according to their antimicrobial resistance profile: sensitive and resistant. The resistant group was subdivided into multidrug-resistant (MDR) strains, including Gram-negative bacilli resistant to third- and fourth-generation cephalosporins, extended-spectrum ß-lactamase (ESBL) producers, and carbapenem-resistant (CR) bacilli, as well as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). Sensitive microorganisms demonstrated susceptibility to the tested antimicrobials [17].

Secondary data were extracted from spreadsheets provided by the institutions, generated using Business Intelligence® (BI) software, and from individual HAI notification forms provided by the HICC, in accordance with ANVISA's definitions and diagnostic criteria. The data were organized in Microsoft Excel

2013® and later exported for analysis using the Statistical Package for the Social Sciences (SPSS)®, version 20.0.

Descriptive analyses were performed using absolute and relative frequencies for categorical variables. The association between resistant and sensitive groups and exposure variables was evaluated using Pearson's Chi-square test or Fisher's exact test, as appropriate. Associations were estimated using the odds ratio (OR) with corresponding 95% confidence intervals (95% CI). For numerical variables, the Shapiro-Wilk normality test was applied. As the data did not follow a normal distribution, results were expressed as medians and interquartile ranges (IQR). A significance level of $p < 0.05$ was adopted.

To ensure methodological quality, the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) checklist was used [18].

This study is a subset of the research project titled "Clinical and Economic Impact of Antimicrobial Resistance on Hospital Costs." Ethical principles for research involving human beings were respected, in accordance with Resolution No. 466/2012 of the National Health Council of the Brazilian Ministry of Health. The study was approved by the Research Ethics Committee of the proposing institution (CEP/ISCAL), under opinion number 5.632.608 and Certificate of Ethical Appreciation (CAAE) number 24711718.8.0000.0099.

RESULTS

The sample consisted of 244 children and adolescents diagnosed with healthcare-associated infections (HAIs) and positive bacterial cultures, with 103 (42.2%) infected by resistant bacteria and 141 (57.8%) by sensitive bacteria. The median age was 12 months, with an interquartile range of 30 months.

As presented in Table 1, the majority of participants with either resistant or sensitive bacteria were under two years of age. There was no statistically significant difference between the groups (p = 0.160).

The proportion of resistance was higher among females compared to males. No significant differences were observed between the groups regarding skin color or place of origin (Table 1).

Table 1 – Analysis of factors associated with healthcare-associated infections caused by resistant and sensitive bacteria in hospitalized children and adolescents in two high-complexity hospitals from 2018 to 2023. Londrina, Paraná, Brazil

Variables	Total n=244	Resistent	Sensitive			
		n= 103	n=141			
	n %	n %	n %	OR*	95% CI †	*p*-value‡
Age group						
≥ 29 days to < 2 years	170 (69.7)	77 (45.3)	93 (54.7)	1.52	0.86-2.68	0.160
2 to ≤ 6 years	36 (14.8)	12 (33.3)	24 (66.7)	0.64	0.30-1.35	0.276
7 to ≤ 11 years	23 (9.4)	5 (21.7)	18 (78.3)	0.34	0.12-0.97	0.045
12 to < 18 years	15 (6.1)	9 (60.0)	6 (40.0)	2.15	0.74-6.25	0.181
Sex						
Male	110 (45.1)	44 (40.0)	66 (60.0)			
Female	134 (54.9)	59 (44.0)	75 (56.0)	1.18	0.70-1.96	0.603
Skin color						
White	57 (23.4)	24 (42.1)	33 (57.9)			
Non-white	187 (76.6)	79 (42.2)	108 (57.8)	1.00	0.55-1.83	1.000
Place of origin						
Study municipality	73 (29.9)	33 (45.2)	40 (54.8)			
Other municipalities	171 (70.1)	70 (40.9)	101 (59.1)	0.84	0.48-1.46	0.573

Source: Prepared by the author.
Note: The group '29 days to < 2 years' was used as the reference category. *OR: Odds Ratio; †CI: Confidence Interval; ‡p-value: Pearson's Chi-square test; significance level.

Children and adolescents hospitalized for surgical reasons had a higher odds ratio for bacterial resistance (OR: 1.95; 95% CI: 1.11–3.40). The use of invasive devices, such as urinary indwelling catheters (CVC) (OR: 4.65; 95% CI: 2.53–8.53) and endotracheal intubation (ETI) (OR: 2.31; 95% CI: 1.31–4.04), was significantly associated with bacterial resistance (Table 2).

Table 2 – Association between clinical variables and bacterial resistance in hospitalized children and adolescents in two high-complexity hospitals from 2018 to 2023. Londrina, Paraná, Brazil

Variáveis	Total n=244	Resistente n= 103	Sensível n= 141	OR*	95%† CI	*p*-value‡
	n %	n %	n %			
Reason for hospitalization						
Surgical	162 (66.4)	77 (47.5)	85 (52.5)	1.95	1.11-3.40	0.020
Clinical	82 (33.6)	26 (31.7)	56 (68.3)			
Invasive devices						
CVC	169 (69.3)	76 (44.9)	93 (55.0)	1.45	0.82-2.54	0.208
PICC	153 (62.7)	58 (37.9)	95 (62.1)	0.62	0.36-1.05	0.083
CVD	156 (63.9)	85 (54.5)	71 (45.5)	4.65	2.53-8.53	**0.001**
IOT	159 (65.2)	78 (76.0)	81 (57.5)	2.31	1.31-4.04	**0.004**
Topography of HAIs						
SSI	43 (17.6)	28 (65.1)	15 (34.9)	3.13	1.57-6.24	**0.001**
BSI	78 (32.0)	40 (51.3)	38 (48.7)	1.72	1.00-2.96	**0.053**
ITU-AC	62 (25.4)	32 (51.6)	30 (48.4)	1.66	0.93-2.97	0.101
ITU	33 (13.5)	14 (42.4)	19 (57.6)	1.01	0.48-2.12	1.000
PNEUMONIA	25 (10.2)	12 (48.0)	13 (52.0)	1.29	0.56-2.97	0.531
PAV	88 (36.1)	43 (49.9)	45 (51.1)	1.52	0.90-2.59	0.138
Number of HAIs						
1 infection	155 (75.8)	61 (33.0)	124 (67.0)			
≥ 2 infections	59 (24.2)	42 (71.2)	17 (28.8)	5.02	2.64-9.53	**<0.001**
Length of hospital stay						
3 to < 30 days	117 (48.0)	34 (29.1)	83 (70.9)			
≥ 30 days	127 (52.0)	69 (54.3)	58 (45.7)	2.90	1.70-4.93	**<0.001**
ICU stay						
Yes	212 (86.9)	99 (46.7)	113 (53.3)	6.13	2.07-18.0	**<0.001**
No	32 (13.1)	4 (3.9) ‡‡	28 (87.5)			
ICU length of stay						
< 14 days	57 (26.9)	15 (26.3)	42 (73.7)			
≥ 15 days	155 (73.1)	84 (54.2)	71 (45.8)	3.31	1.69-6.46	**<0.001**
Clinical outcome						
Discharge	180 (73.8)	69 (38.3)	111 (78.4)			
Death	64 (26.2)	34 (53.1)	30 (46.9)	1.82	1.02-3.24	**0.055**

Source: Prepared by the author.
OR*: Odds Ratio; †CI: Confidence Interval; ‡Pearson's Chi-square test; ‡‡Fisher's Exact test. CVC: Central Venous Catheter; PICC: Peripherally Inserted Central Catheter; CVD: Indwelling Urinary Catheter; IOT: Orotracheal Intubation; PAV: Ventilator-Associated Pneumonia; IPCS: Primary Bloodstream Infection; ISC: Surgical Site Infection; ITU-AC: Catheter-Associated Urinary Tract Infection; ITU: Urinary Tract Infection.

Regarding the topography of healthcare-associated infections (HAIs), both groups showed a higher prevalence of ventilator-associated pneumonia (VAP), primary bloodstream infections (PBSI), and catheter-associated urinary tract infections (CA-UTI). Although these sites had high odds ratio (OR) values, surgical site infections (SSI) showed a statistically significant association with bacterial resistance, with an OR of

3.13 (95% CI: 1.57–6.24), and PBSI also showed a borderline association (OR: 1.72; 95% CI: 1.00–2.96) for infections caused by resistant microorganisms.

Children and adolescents with two or more HAIs had a significantly higher risk of bacterial resistance (OR: 5.02; 95% CI: 2.64–9.53).

Hospital stays longer than 30 days and intensive care unit (ICU) stays of 15 days or more were also associated with resistance. Children and adolescents in the sensitive group had a median length of stay of 15 days (IQR: 25), while the resistant group had a median of 32 days (IQR: 40). Patients admitted to the ICU had higher odds of developing bacterial resistance, with additional increased odds associated with ICU stays of 15 days or more.

The present study identified a statistically significant association between bacterial resistance and death (p = 0.055) (OR: 1.82; 95% CI: 1.02–3.24).

In total, 343 bacteria were identified, of which 176 (51%) were resistant and 167 (49%) were sensitive. Among fermenting Gram-negative bacteria, *Klebsiella pneumoniae* was the most prevalent, with 53 isolates, of which 38 were multidrug-resistant. Among non-fermenters, *Pseudomonas aeruginosa* stood out, with 44 strains, including 25 classified as multidrug-resistant (Table 3).

Among Gram-positive bacteria, *Staphylococcus aureus* was the most frequent, accounting for 17 of the total isolates, 14 of which were methicillin-resistant (MRSA). *Enterococcus faecium* and *Enterococcus faecalis* were less prevalent, with two isolates resistant to vancomycin (VRE) (Table 3).

Table 3 – Bacterial resistance profile and distribution of isolated bacteria in children and adolescents hospitalized in two high-complexity hospitals from 2018 to 2023. Londrina, Paraná, Brazil

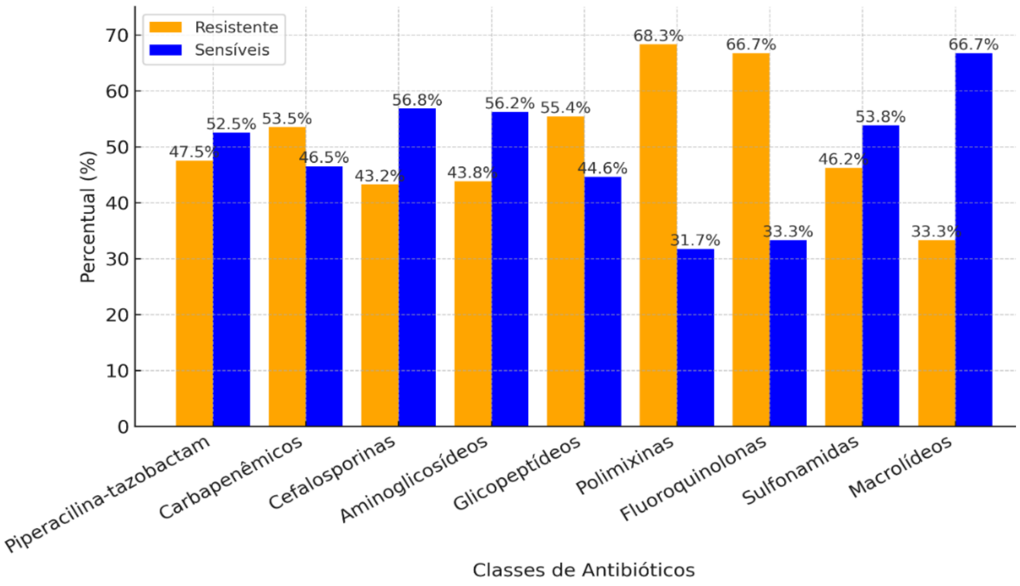
Bacterial Sensitivity Profile	**Resistant**					**Sensitive**	
	CR	**MR**	**MRSA**	**PR**	**VRE**	**Sensitive**	**Total**
	n= 11	n= 105	n= 14	n= 5	n= 2	n= 206	n= 343
Fermenters							
Klebsiella pneumoniae	12 (24.0)	38 (36.1)		3 (60)		26 (37.6)	69 (20.1)
Escherichia coli	1 (2.0)	4 (4.0)				29 (85.2)	34 (9.9)
Enterobacter spp	11(22.0)	12 (11.4)			1 (50.0)	18 (58.0)	31 (9.0)
Others	3 (6.0)	3 (3.0)				26 (81.2)	32 (9.3)
Non-fermenters							
Pseudomonas aeruginosa	17 (34.0)	25 (24.0)		2 (40.0)		36 (53.7)	67 (19.5)
Acinetobacter baumannii	5 10.0)	8 (7.6)				12 (60.0)	20 (5.8)
Stenotrophomonas spp		4 (4.0)				6 (60.0)	10 (2.9)
Others	1 (2.0)	7 (6.6)				3 (27.2)	11 (3.2)
Gram-positive bacteria							
Staphylococcus aureus		3 (2.8)	14 (100)			30 (63.8)	47(13.7)
Enterococcus spp		1 (0.9)			1 (50.0)	15 (88.2)	17 (4.9)
Others						5 (100)	5 (1.4)

Source: Prepared by the author.

Carbapenem-Resistant (CR), Multidrug-Resistant (MR), Methicillin-Resistant Staphylococcus aureus (MRSA), Polymyxin-Resistant (PR), Vancomycin-Resistant Enterococci (VRE), and bacteria sensitive to the tested antibiotics (Sensitive).

The use of antibiotics varied significantly between the groups. Piperacillin-tazobactam was the most used antimicrobial in both groups, while carbapenems were more prevalent in cases of infections caused by resistant bacteria (53.5% vs. 46.5%). Children and adolescents with infections by resistant microorganisms showed a higher frequency of polymyxin use (68.3% vs. 31.7%), fluoroquinolones (66.7% vs. 33.3%), and glycopeptides (55.4% vs. 44.6%). In contrast, antibiotics such as beta-lactams (cephalosporins) (56.8% vs. 43.2%) and macrolides (66.7% vs. 33.3%) were more frequently used in the treatment of infections caused by sensitive bacteria (Figure 1).

Figure 1 – Percentage distribution of antimicrobial use in children and adolescents with healthcare-associated infections caused by resistant and sensitive bacteria in two high-complexity hospitals from 2018 to 2023. Londrina, Paraná, Brazil



DISCUSSION

The analysis of factors associated with bacterial resistance in hospitalized children and adolescents revealed that children under two years of age were more vulnerable to infections caused by resistant bacteria. This finding is consistent with previous studies that highlight the increased risk in this age group, attributable to immunological immaturity, greater exposure to antimicrobials, and dependence on invasive procedures[3,13,19].

Moreover, these data are in line with the findings of Raoofi et al. (2023), who identified a higher prevalence of nosocomial infections in children aged zero to five years. The authors also demonstrated that the prevalence of healthcare-associated infections (HAIs) progressively decreased with increasing age, with an estimated reduction of 0.04 for each additional year of life [20].

Antibiotic-resistant infections often result in prolonged illness, increased risk of hospitalization, and a greater likelihood of complications. In children, who are already vulnerable due to their developing immune systems, these complications can be especially severe. Bacterial resistance turns common bacterial infections into potentially life-threatening conditions, impacting overall quality of life and possibly leading to long-term health consequences [14,21].

Surgical cases were more prevalent among children and adolescents with antimicrobial-resistant infections compared to those hospitalized for clinical treatment. Previous studies indicate that surgical procedures, especially those of high complexity, constitute risk factors for hospital-acquired infections caused by multidrug-resistant microorganisms, due to prolonged exposure, use of invasive devices, and extended hospital stays[9,22-25].

Additionally, the fact that one of the studied institutions is a reference center for pediatric cardiac surgeries may have contributed to the high proportion of hospitalizations related to surgical procedures. This context highlights the importance of infection prevention strategies and the judicious use of antimicrobials, especially in pediatric populations undergoing complex surgical interventions [9,22-25].

It is estimated that between 3% and 20% of surgical procedures present complications related to surgical site infections (SSI), which are responsible for up to one-third of the mortality associated with surgical interventions. In the national context, SSIs rank third among healthcare-associated infections (HAIs), accounting for up to 31% of hospital occurrences. Furthermore, the SSI incidence rate is widely recognized as an indicator of the quality of care provided in healthcare services[26].

In the present study, invasive devices were associated with increased odds of bacterial resistance.

The use of indwelling urinary catheters (CVD) was associated with increased odds of infection by resistant bacteria. Likewise, orotracheal intubation (IOT) showed increased odds of infection by resistant microorganisms. These findings are consistent with the literature, which highlights biofilm formation and prolonged exposure as critical factors for this condition(14,25,27).

A study conducted in a pediatric intensive care unit (PICU) in Japan found that catheterization lasting more than 10 days was associated with odds ratios ranging from 2.76 to 3.44 for the development of urinary tract infections (UTIs). Moreover, catheter-associated urinary tract infection (CAUTI) is widely recognized as one of the most prevalent infections in PICUs, with urinary catheter use being the main risk factor for severe and complicated UTIs. These findings support the results of the present study, emphasizing the relevance of proper management of invasive devices to reduce the risk of bacterial resistance(22,28).

Although the association between other invasive devices and bacterial resistance did not reach statistical significance, national and international epidemiological studies show that HAIs caused by resistant bacteria can be triggered by different invasive devices (3,9,25,29). These studies report a higher frequency of occurrence in intensive care units (ICUs), due to the clinical severity and health status of the patients (22-25).

Surgical site infections (SSI) showed increased odds of bacterial resistance. The literature emphasizes that the vulnerability of pediatric patients to SSIs is intensified by the need for surgical interventions, which expose the body to additional risk factors, as well as prolonged exposure to invasive devices and broad-spectrum antimicrobials(24,25).

Primary bloodstream infections (IPCS) were associated with increased odds of infection by resistant bacteria. This finding reinforces the importance of effective strategies for the insertion and maintenance of catheters, as improper handling may favor colonization by multidrug-resistant pathogens(25).

Although pneumonia, ventilator-associated pneumonia (VAP), and urinary tract infections (UTIs) did not show statistically significant associations, these infections still represented high frequencies in both groups. These findings are consistent with studies that suggest the need for further investigations to elucidate the factors associated with bacterial resistance in these contexts(22,24).

A global study on antimicrobial resistance (AMR) revealed that respiratory, bloodstream, and intra-abdominal infections are the main infection sites attributed to AMR, accounting for 79% of deaths(6). These results underscore the relevance of regional strategies for epidemiological surveillance and rigorous hospital infection control to mitigate the spread of resistant pathogens, especially among vulnerable pediatric populations(6).

The occurrence of two or more healthcare-associated infections (HAIs) increased the likelihood of infections caused by resistant bacteria. Studies indicate that the presence of comorbidities and multiple infectious foci worsens clinical outcomes, requiring prolonged use of broad-spectrum antimicrobials, which contributes to the selection of resistant bacteria (9,19).

Hospital stays lasting 30 days or more were significantly associated with bacterial resistance, in line with the literature that identifies prolonged exposure to the hospital environment as one of the main risk factors for acquiring multidrug-resistant microorganisms(14,24,30).The hospital microbiota, composed of microorganisms capable of persisting on surfaces, medical devices, and healthcare workers' hands, represents a continuous source of contamination(22,24,25,27).These microorganisms, often associated with biofilm formation, promote severe infections in patients undergoing invasive procedures(24,25,27).

Prolonged stays in the intensive care unit (ICU) were also identified as a factor associated with increased likelihood of infection by resistant bacteria. Children and adolescents hospitalized for more than 15 days had higher odds of bacterial resistance. This environment, characterized by a high density of invasive devices and intensive antimicrobial use, favors the selection and transmission of resistant bacteria(9,22-25,27).

Moreover, the adaptive capacity of these bacteria—including spontaneous mutations and horizontal transfer of resistance genes—is exacerbated in the hospital setting, where antibiotics are widely used. The constant presence of antimicrobials in this environment acts as a selective pressure for the survival of resistant strains, making the eradication of these pathogens a significant challenge(13,27,31-33).

In the present study, children and adolescents with healthcare-associated infections (HAIs) caused by resistant bacteria had a higher number of deaths. It is worth noting that global studies attribute up to 1.27 million annual deaths to antimicrobial resistance (AMR), with a significant impact on children under 5 years of age[6,34].

The bacteriological findings revealed a high prevalence of multidrug-resistant bacteria, with a higher frequency of resistance observed among Gram-negative bacteria, both fermenting and non-fermenting, compared to Gram-positive cocci. The high proportion of resistance reinforces the need for continuous epidemiological surveillance and the implementation of strict infection prevention and control measures[27,32,34,35].

Among the isolated bacteria, Gram-negative species were predominant, particularly Klebsiella pneumoniae. This result reflects the remarkable adaptability of this species, which frequently acquires and transmits resistance genes, such as those encoding extended-spectrum ß-lactamases and carbapenemases, making treatment more challenging. These mechanisms are often associated with high rates of morbidity and mortality in hospitalized patients[6,35].

Another relevant finding was the high frequency of resistance in Pseudomonas aeruginosa. Its adaptability allows it to persist on surfaces for prolonged periods, and it is frequently associated with the production of ß-lactamase enzymes, efflux pumps, and changes in membrane permeability, making it one of the main concerns in hospital settings [4,6,35].

Among Gram-positive bacteria, Staphylococcus aureus was the most prevalent, with a high rate of methicillin resistance (MRSA). This finding corroborates studies that associate MRSA with severe and hard-to-treat infections, especially in vulnerable populations such as hospitalized children[6,14].

The observed resistance profile reinforces the need for specific interventions, including the optimization of antimicrobial use and the implementation of barriers to prevent the spread of resistant pathogens, especially in high-complexity hospitals [13,17,24,25,34,35].

It is widely recognized that antimicrobials rank second among the most used medications in hospital settings. Additionally, they are frequently prescribed in outpatient clinics and other healthcare services, especially for children. The literature indicates that the number of prescriptions has substantially increased, often in an indiscriminate and inappropriate manner, which contributes as a risk factor for the development of AMR [13,14,16,21,22,31].

The use of broad-spectrum antimicrobials, such as carbapenems, polymyxins, and fluoroquinolones, was more frequent among resistant cases. Although these medications are essential in managing severe infections, their indiscriminate use accelerates the emergence of multidrug-resistant strains, creating additional therapeutic challenges[14,31]. In contrast, the control group showed higher use of cephalosporins and macrolides. The implementation of strategies based on local data and epidemiological surveillance can help mitigate the emergence of resistant bacteria and preserve therapeutic efficacy[32,34].

In critical care settings, such as intensive care units (ICUs), the reliance on invasive devices and the proximity between patients increase the risk of spreading resistant pathogens[22,27]. Preventive measures such as hand hygiene, surface disinfection, proper management of invasive devices, and the rational use of antimicrobials are essential to reduce complications associated with bacterial resistance[4,22]. Integrated infection control strategies can minimize the spread of resistant microorganisms and improve clinical outcomes for hospitalized children and adolescents[26].

The sample size may have contributed to the lack of statistically significant associations between bacterial resistance and some variables, such as pneumonia, ventilator-associated pneumonia (VAP), and urinary tract infection (UTI). Future studies should investigate these variables in greater depth to explore potential underlying associations.

CONCLUSION

This study analyzed factors associated with bacterial resistance in hospitalized children and adolescents, highlighting the use of invasive devices such as central venous catheters (CVC) and orotracheal intubation (OTI), as well as surgical site infections and primary bloodstream infections, as variables with a higher likelihood of resistance. Additionally, prolonged hospital stays and admission to intensive care units (ICUs) also showed significant associations with resistant bacteria, underscoring the importance of proper management of these devices and the adoption of strict prevention protocols.

Among the isolated bacteria, Gram-negative organisms—especially *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*—showed a high prevalence of multidrug resistance, standing out as major infectious agents in the hospital setting. Gram-positive bacteria, such as *Staphylococcus aureus*, also exhibited resistance, particularly to methicillin. These findings reinforce the urgent need for continuous epidemiological surveillance, programs to improve aseptic techniques, healthcare staff training, and education on the rational use of antimicrobials, especially in critical care environments.

REFERENCES

1. 1. Fresán-Ruiz E, Pons-Tomás G, de Carlos-Vicente JC, Bustinza-Arriortua A, Slocker-Barrio M, Belda-Hofheinz S, et al. Device exposure and patient risk factors' impact on the healthcare-associated infection rates in PICUs. Children [Internet]. 2022 Nov [cited 2024 Sep 25];9(11):1669. Available from: https://www.mdpi.com/2227-9067/9/11/1669

2. Kannan A, Pratyusha K, Thakur R, Sahoo MR, Jindal A. Infections in critically ill children. Indian J Pediatr [Internet]. 2023 Mar [cited 2024 Sep 25];90(3):289-297. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9763084/

3. Oliveira SMB, Galvão EFC, Gomes-Santos L. Prevention and control of healthcare-associated infection: a study with caregivers of hospitalized children in a pediatric ward. Rev Epidemiol Control Infec [Internet]. 2020 Jan 11 [cited 2024 Sep 5];10(1). Available from:https://www.redalyc.org/journal/5704/570467613013/570467613013.pdf

4. Brazil. National Health Surveillance Agency (ANVISA). Prevention of infections by multidrug-resistant microorganisms in health services. Patient Safety and Quality in Health Services Series. Brasília: Anvisa; 2021 [cited 2024 Sep 5]. Available from: https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/publicacoes/manual-prevencao-de-multirresistentes7.pdf

5. Paiva RDM, Ferreira LDL, Bezerril MDS, Chiavone FTB, Salvador PTCO, Santos VEP. Infection factors related to nursing procedures in Intensive Care Units: a scoping review. Rev Bras Enferm [Internet]. 2021 Jan/Feb [cited 2024 Sep 5];74(1):e20200731. Available from: https://doi.org/10.1590/0034-7167-2020-0731

6. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet [Internet]. 2022 Feb [cited 2024 Sep 5];399(10325):629-55. Available from: https://doi.org/10.1016/S0140-6736(21)02724-0

7. Amarante ACA, Junior AL, Ferrari RAP, Lopes GK, Capobiango JD. Analysis of factors associated with mortality from sepsis derived from device-related infections. An Pediatr (Barc) [Internet]. 2024 Aug [cited 2024 Sep 25];101(2):115-123. Available from: https://www.sciencedirect.com/science/article/pii/S1695403324001243

8. Elnasser Z, Obeidat H, Amarin Z. Device-related infections in a pediatric intensive care unit: The Jordan University of Science and Technology experience. Medicine [Internet]. 2021 Oct [cited 2024 Sep 12];100(43):e27651. Available from: https://journals.lww.com/md-journal/fulltext/2021/10290/Device_related_infections_in_a_pediatric_intensive.37.aspx?context=LatestArticles

9. Fresán-Ruiz E, Izurieta-Pacheco AC, Girona-Alarcón M, de Carlos-Vicente JC, Bustinza-Arriortua A, Slocker-Barrio M, et al.; Pediatric-Envin-Helics Study Group. Antimicrobial Stewardship Improvement in Pediatric Intensive Care Units in Spain—What Have We Learned? Children [Internet]. 2022 Jun [cited 2024 Sep 12];9(6):902. Available from: https://doi.org/10.3390/children9060902

10. Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, Rabaan AA, et al. Antimicrobial resistance: a growing serious threat for global public health. Healthcare [Internet]. 2023 Jan [cited 2024 Sep 15];11(13):1946. Available from: https://www.mdpi.com/journal/healthcare

11. Silva YF, Grubisch Mendes Tacla MT, Zanfrille da Costa DC, Kerbauy G, Squarça Mendes PB. Healthcare-associated infection and sepsis during pediatric hospitalization. Ciênc Cuid Saúde [Internet]. 2021 [cited 2024 Sep 15];20. Available from: https://periodicos.uem.br/ojs/index.php/CiencCuidSaude/article/view/55782/751375153269

12. Teixeira MGD, Daumichen CS, Lucca ER, Nunes GG, Hoss LE, Zago M, et al. Prevalence and risk factors of healthcare-associated infections in children hospitalized in an ICU at a teaching hospital. Cuad Educ Desarr [Internet]. 2024 [cited 2024 Sep 05];16(8):e5372-e5372. Available from: https://ojs.cuadernoseducacion.com/ojs/index.php/ced/article/view/5372

13. Yu D, Zheng Y, Shen A, Wu F, Dmitriev AV, Kilian M, et al. Antimicrobial resistance in pediatric infectious diseases: resistance mechanisms and antimicrobial use. Front Cell Infect Microbiol [Internet]. 2023 [cited 2024 Sep 13];13:1287051. Available from: https://www.frontiersin.org/journals/cellular-and-infection-microbiology/articles/10.3389/fcimb.2023.1287051/full

14. Begum R. Global perspectives on pediatric antimicrobial resistance: a systematic literature review. Medtigo J [Internet]. 2024 [cited 2024 Sep 12];2(2). Available from: https://journal.medtigo.com/global-perspectives-on-pediatric-antimicrobial-resistance-a-systematic-literature-review/

15. Wang Z, Xia ZF. What can we do? The risk factors for multi-drug resistant infection in pediatric intensive care unit (PICU): a case-control study. Ital J Pediatr [Internet]. 2020 Feb [cited 2024 Sep 05];46(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7007655/

16. Brazil. Child and Adolescent Statute (ECA). Law No. 8.069, July 13, 1990. Available from: https://www.jusbrasil.com.br/legislacao/91764/estatuto-da-crianca-e-do-adolescente-lei-8069-90. Accessed: Sep 12, 2024.

17. Brazil. National Health Surveillance Agency. Technical Note GVIMS/GGTES/DIRE3/ANVISA No. 03/2023: Diagnostic criteria for healthcare-associated infections (HAIs): mandatory national reporting for 2023. Brasília, DF: Anvisa; 2023. Available from: https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/notas-tecnicas/2020/nota-tecnica-gvims-ggtes-dire3-anvisa-no-03-2023-criterios-diagnosticos-das-infeccoes-relacionadas-a-assistencia-a-saude-iras-de-notificacao-nacional-obrigatoria-para-o-ano-de-2023. Accessed: Sep 12, 2024.

18. Elm EV, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. J Clin Epidemiol [Internet]. 2008 Apr [cited 2024 Sep 5];61(4):344-9. Available from: https://pubmed.ncbi.nlm.nih.gov/18313558/.

19. Cardoso MEV, Souza A. Application of pneumonia prevention bundle in pediatric ICU. Rev Enferm UFPE On Line [Internet]. 2021 Jan 10 [cited 2024 Sep 12];[about 15 p.]. Available from: http://dx.doi.org/10.5205/1981-8963.2021.245042.

20. Raoofi S, Pashazadeh Kan F, Rafiei S, Hosseinipalangi Z, Noorani Mejareh Z, Khani S, et al. Global prevalence of hospital infection: a systematic review and meta-analysis. PLoS One [Internet]. 2023 Jan [cited 2024 Sep 15];18(1):e0274248. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0274248

21. Pana ZD, El-Shabrawi M, Sultan MA, Murray T, Alam A, Yewale V, et al. Healthcare-associated infections in critically ill pediatric patients: International survey. J Infect Public Health [Internet]. 2022 Jul [cited 2024 Sep 15];15(7):837-843. Available from: https://doi.org/10.1016/j.jiph.2022.05.003.

22. Oliveira W, Pereira AP, Sousa R, Machado D, Santos S, de Melo P, et al. Impact of antimicrobial resistance in healthcare-associated infections in pediatrics. Int J Infect Dis [Internet]. 2022 Aug [cited 2024 Sep 15]; 120:51-57. Available from: https://doi.org/10.1016/j.ijid.2022.05.036.

23. Freitas FCG, Rocha GM, Gomes CS, Almeida MC, Faria BLP. Costs associated with resistant infections in hospitalized children: a systematic review. Braz J Infect Dis [Internet]. 2023 Jan [cited 2024 Sep 25];27(1):102304. Available from: https://doi.org/10.1016/j.bjid.2022.102304.

24. França MVA, Soares CB, Silva NMC, Figueiredo SV, Leal PRL, Souza IP. Direct cost evaluation of antimicrobial therapy for hospital infections in pediatrics. Braz J Infect Dis [Internet]. 2021 Apr [cited 2024 Sep 25];25(2):101514. Available from: https://doi.org/10.1016/j.bjid.2021.101514.

25. Da Silva EG, Oliveira MMC, Lopes LC, de Sá GTM, Souza LL, Borges LP, et al. Antimicrobial consumption and costs in pediatric intensive care units in Brazil. Rev Bras Ter Intensiva [Internet]. 2020 Sep [cited 2024 Sep 25];32(3):428-436. Available from: https://doi.org/10.5935/0103-507X.20200050.

26. Brasil. Ministry of Health. National Health System Cost Management System (SIGTAP). Brasília, DF: Ministry of Health; 2023. Available from: https://datasus.saude.gov.br/sigtap. Accessed: Sep 12, 2024.

27. Goto M, Alshaikh FS, Williams DJ, Brown NJ, Hersh AL, Suda KJ. Excess costs and length of stay associated with multidrug-resistant bacterial infections in children. Infect Control Hosp Epidemiol [Internet]. 2022 Jan [cited 2024 Sep 25];43(1):22-29. Available from: https://doi.org/10.1017/ice.2021.343.

28. Castro L, Ribeiro AM, Araújo MC, Oliveira AP, Dourado H, Mota CC. Antibiotic therapy in pediatric intensive care: antibiotic consumption and costs. Braz J Infect Dis [Internet]. 2021 May/Jun [cited 2024 Sep 25];25(3):101553. Available from: https://doi.org/10.1016/j.bjid.2021.101553.

29. Lepelletier D, Vaux S, Grandbastien B, Rogues AM. Pediatric antimicrobial stewardship programs in Europe: a multicenter survey. Antimicrob Resist Infect Control [Internet]. 2023 Feb [cited 2024 Sep 12];12(1):13. Available from: https://doi.org/10.1186/s13756-023-01179-4.

30. Aljabri D, Panayi A, Hutton A, Suleman A, Anderson A, Farag N. Antibiotic stewardship in pediatric intensive care units: impact on antibiotic consumption and resistance. Pediatr Infect Dis J [Internet]. 2022 Nov [cited 2024 Sep 15];41(11):e437-e444. Available from: https://doi.org/10.1097/INF.0000000000003667.

31. Saxena S, Nagendra G, Sudhakar R. Pediatric antimicrobial stewardship programs: challenges and opportunities. J Glob Antimicrob Resist [Internet]. 2023 Jan [cited 2024 Sep 15];31:207-212. Available from: https://doi.org/10.1016/j.jgar.2022.11.009.

32. WHO. WHO Model List of Essential Medicines for Children - 8th list (2021). Geneva: World Health Organization; 2021. Available from: https://www.who.int/publications/i/item/WHO-MVP-EMP-IAU-2021.06. Accessed: Sep 5, 2024.

33. WHO. WHO Guidelines on Pediatric Antimicrobial Stewardship. Geneva: World Health Organization; 2022. Available from: https://www.who.int/publications/i/item/9789240042722. Accessed: Sep 5, 2024.

34. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta: Centers for Disease Control and Prevention; 2019. Available from: https://www.cdc.gov/antibiotic-use/core-elements/hospital.html. Accessed: Sep 5, 2024.

35. Abrantes JA, Nogueira JMR. Bacterial resistance to antimicrobials: a review of the main species involved in infectious processes. Rev Bras Anal Clin [Internet]. 2021 [cited 2024 Sep 05];53(3):219-23. Available from: https://www.rbac.org.br/artigos/resistencia-bacteriana-aos-antimicrobianos-uma-revisao-das-principais-especies-envolvidas-em-processos-infecciosos/

ORIGIN OF THE ARTICLE

Extracted from the thesis – *Clinical analysis and costs associated with the use of antimicrobials in the treatment of healthcare-associated infections in hospitalized children and adolescents*, submitted to the Doctoral Graduate Program in Nursing at the State University of Londrina (UEL) in 2025.

AUTHOR CONTRIBUTIONS

Pimenta SF and Pimenta RA participated in the study's conception and design, literature review, manuscript writing, and assisted in data analysis. Dias NLP contributed to the writing of the abstract, methodology, interpretation of results, and conclusions. Zani AV, Gabani FL, Furtado MD, and Capobiango JD contributed to the critical intellectual review of the content. All authors reviewed and approved the final version to be published and declare responsibility for all aspects of the work, ensuring accuracy and integrity.

FUNDING

There were no costs associated with conducting this research, and no external funding sources were involved.

APPROVAL BY THE RESEARCH ETHICS COMMITTEE

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

CONFLICT OF INTEREST

The authors declare no conflict of interest.