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ORIGINAL ARTICLE

Antimicrobial prescription and bacterial resistance in a Brazilian Intensive Care Unit

Prescrição antimicrobiana e resistência bacteriana em uma Unidade de Terapia Intensiva Brasileira

Prescripción antimicrobiana y resistencia bacteriana en una Unidad de Cuidados Intensivos Brasileña

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ABSTRACT

Background and Objectives: antimicrobial resistance is one of the main public health concerns worldwide. Intensive Care Units have a high prevalence of resistant microorganisms and infections, and the rational use of antibiotics is one of the main strategies for tackling this problem. This work aimed to describe patterns associated with antimicrobial drugs as well as the resistance profile of microorganisms. **Methods:** an observational study was carried out using data from patients hospitalized in the Intensive Care Unit who used antimicrobial agents. **Results:** respiratory and cardiological causes were the most frequent reasons for admission, with cephalosporins (29.02%), with penicillin (25.84%) and macrolides (16.10%) being the most used classes of antibiotics. The predominant microorganisms were *Klebsiella pneumoniae* (13.98%), *Staphylococcus aureus* (13.44%) and *Acinetobacter baumannii* (11.83%). Urine cultures and tracheal aspirate were the culture tests with the highest growth of gram-negative microorganisms. Patients with bacteria isolated in tracheal aspirate had longer hospital stays; 20 patients had positive surveillance cultures; and the mortality rate found was 55.45%. **Conclusion:** the study combined the institution's epidemiological profile with patient characteristics, isolated microorganisms and outcomes.

Keywords: *Anti-Bacterial Agents. Drug Resistance, Microbial. Intensive Care Units. Laboratory Test.*

RESUMO

Justificativa e Objetivos: a resistência antimicrobiana é uma das principais preocupações de saúde pública em todo o mundo. As Unidades de Terapia Intensiva têm uma alta prevalência de microorganismos resistentes e infecções, e o uso racional de antibióticos é uma das principais estratégias para lidar com esse problema. Este trabalho teve como objetivo descrever padrões associados a medicamentos antimicrobianos, bem como o perfil de

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resistência dos microorganismos. **Métodos:** foi realizado um estudo observacional utilizando dados de pacientes hospitalizados na Unidade de Terapia Intensiva que utilizaram agentes antimicrobianos. **Resultados:** causas respiratórias e cardiológicas foram os motivos mais frequentes de admissão, com cefalosporinas (29,02%), penicilina (25,84%) e macrolídeos (16,10%) sendo as classes de antibióticos mais utilizadas. Os microorganismos predominantes foram *Klebsiella pneumoniae* (13,98%), *Staphylococcus aureus* (13,44%) e *Acinetobacter baumannii* (11,83%). Culturas de urina e aspirado traqueal foram os testes de cultura com maior crescimento de microorganismos gram-negativos. Pacientes com bactérias isoladas no aspirado traqueal tiveram internações mais longas; 20 pacientes tiveram culturas de vigilância positivas; e a taxa de mortalidade encontrada foi de 55,45%. **Conclusão:** o estudo combinou o perfil epidemiológico da instituição com características dos pacientes, microorganismos isolados e resultados.

Palavras-chave: *Agentes Antibacterianos. Resistência Microbiana a Medicamentos. Unidades de Terapia Intensiva. Testes Laboratoriais.*

RESUMEN

Antecedentes y Objetivos: la resistencia antimicrobiana es una de las principales preocupaciones de salud pública en todo el mundo. Las Unidades de Cuidados Intensivos tienen una alta prevalencia de microorganismos resistentes e infecciones, y el uso racional de antibióticos es una de las principales estrategias para abordar este problema. Este trabajo tuvo como objetivo describir patrones asociados con medicamentos antimicrobianos, así como el perfil de resistencia de los microorganismos. **Métodos:** se llevó a cabo un estudio observacional utilizando datos de pacientes hospitalizados en la Unidad de Cuidados Intensivos que utilizaron agentes antimicrobianos. **Resultados:** las causas respiratorias y cardiológicas fueron las razones más frecuentes de admisión, con cefalosporinas (29,02%), penicilina (25,84%) y macrólidos (16,10%) siendo las clases de antibióticos más utilizadas. Los microorganismos predominantes fueron *Klebsiella pneumoniae* (13,98%), *Staphylococcus aureus* (13,44%) y *Acinetobacter baumannii* (11,83%). Los cultivos de orina y el aspirado traqueal fueron las pruebas de cultivo con mayor crecimiento de microorganismos gramnegativos. Los pacientes con bacterias aisladas en el aspirado traqueal tuvieron estancias hospitalarias más largas; 20 pacientes tuvieron cultivos de vigilancia positivos; y la tasa de mortalidad encontrada fue del 55,45%. **Conclusión:** el estudio combinó el perfil epidemiológico de la institución con las características de los pacientes, los microorganismos aislados y los resultados.

Palabras clave: *Agentes Antibacterianos. Resistencia Microbiana a los Medicamentos. Unidades de Cuidados Intensivos. Pruebas de Laboratorio.*

INTRODUCTION

Antimicrobial resistance has become one of the main public health concerns worldwide.[1,2] Intensive Care Units (ICU) play an important role in this topic, as they have a high prevalence of infections and resistant microorganisms due to several factors, such as the criticality of patients, the use of various invasive devices and the prescription of broad-spectrum antimicrobial agents.[3] The use of antibiotics is essential in combating infections, however their irrational use can lead to the adaptation of microorganisms and bacterial resistance.[4,5] There is a need for caution when using them, since indiscriminate use can lead to resistance, and nosocomial infections caused by resistant microorganisms are important causes of mortality and morbidity in hospitalized patients.[6]

The global epidemiological profile of infections in ICUs is already known.[7,8] The prescription patterns of antimicrobial agents adopted in ICUs as well as the resistance profile of pathogens vary widely. However, studies on the use of medications are important tools for understanding how they are prescribed and used. For the class of antimicrobial agents, the studies make it possible to visualize the prescription pattern, being able to relate it to the types of infection, microorganisms and patient outcomes. These data help to support the development of policies, contributing to the development of actions aimed at the rational use of antimicrobial agents, which is one of the main goals for reducing infections caused by multi-resistant microorganisms. Associated with this, the financial resources required by an ICU are high, and antimicrobial agents are high-cost medications, requiring up to 30% of the total spent by patients during admission.[9]

The work aimed to describe patterns associated with antimicrobial drugs as well as the resistance profile of microorganisms.

METHODS

This is a cross-sectional study, with retrospective data collection of patients admitted to the ICU using antimicrobial agents, carried out between January 1 and December 31, 2019. The ICU analyzed in this study is located in a tertiary hospital specialized in trauma-orthopedics with ten general adult ICU beds in the city of Porto Alegre, Brazil.

Data from all adult patients who received antimicrobial agents, enterally or parenterally, during their ICU stay were included. Consecutive readmissions were considered as new cases. Data from patients hospitalized for immediate postoperative recovery and with a length of stay of less than 48 hours were excluded.

Demographic and clinical data were collected from patients' electronic medical record, such as age, sex, city of origin, comorbidities, length of stay in the ICU and hospital, Body Mass Index (BMI), surveillance cultures, number of laboratory tests, culture exams, in addition to outcomes such as discharge, death, transfer and institution of exclusive palliative care. Reasons for admission were grouped using the International Classification of Diseases and Related Health Problems (ICD), such as respiratory, cardiovascular, renal, neurological, endocrine, digestive and other causes.[8]

The list of patients was obtained from reports from the hospital's pharmacy service, and the number of antibiotics dispensed was obtained from the electronic dispensing system. The cost of materials and medications as well as antimicrobial agents was extracted from the pharmacy service's electronic system, which calculates the mean of acquisition prices for the year, generating reports according to the patients' admission period.

Laboratory test results were also collected from the patient's electronic medical record. Surveillance cultures were for *Acinetobacter* sp. (skin swab), methicillin-resistant *Staphylococcus aureus* (MRSA) (nasal swab), vancomycin-resistant *Enterococcus* (VRE) (rectal swab) and carbapenemase (rectal swab). The methodology that the laboratory uses is culture in specific media and identification by MALDI-TOF/MS. For carbapenemase research, the laboratory also uses the "in house" phenotypic (colorimetric) test. For antimicrobial susceptibility testing, the laboratory uses BD Phoenix™ equipment or the Kirby Bauer technique. To define the minimum inhibitory concentration of polymyxin B, amikacin, imipenem and meropenem, the minimum inhibitory concentration technique by microdilution or E-test was used. Parameter analysis was performed by CLSI.

Statistical analysis

The variables observed quantitatively were described by mean, to indicate the central tendency, and by standard deviation (SD), to describe variability. Qualitative variables were described by counts and percentages.

Data normality was tested using the Kolmogorov-Smirnov test, and homogeneity of variances using Levene's test. Tests for differences between distributions were performed using the Kruskall-Wallis or Mann-Whitney U test, when it was not possible to assume variable normality. Association tests were performed using the chi-square test. Correlations of quantitative variables were observed using Pearson correlation analysis. Significance was established at $\alpha=0.05$, and the tests' significance estimate was calculated by two-tailed p-value<0.05.

The study was approved by the *Universidade Federal do Rio Grande do Sul* Research Ethics Committee, under Certificate of Presentation for Ethical Consideration (CAAE - *Certificado de Apresentação para Apreciação Ética*) 36216820.1.0000.5327 and favorable opinion 4.235.870 of August 25, 2020. The Data Use Commitment Form and the institution's Consent and Co-participation Form were signed. The research was conducted in accordance with the required ethical standards (Resolutions 466/2012, 510/2016 and 580/2018 of the Ministry of Health).

RESULTS

In total, data from 211 patients were included in the study. The mean age was 64.75 years (SD=15.89 years), 66.88 years for females (SD=16.02 years) and 62.57 years for males (SD=15.53 years old). The length of hospital stay was 15.29 days on average (SD=12.57 days), while the length of stay in the ICU was 9.69 days (SD=8.59 days). It is noteworthy that 64 (30.33%) patients had palliative care institutions during their admission, four of these (6.25%) were discharged and 60 (93.75%) died. The four palliative care cases that were discharged were allocated to the discharge outcome. Table 1 presents descriptive analysis of the sample.

Table 1. Demographic and clinical characterization of patients.

Patients (n=211)	N (%)
Sex	
Female	107 (50.71)
Male	104 (49.29)
City of origin	
Region Metropolitan	96 (45.49)
Porto Alegre	83 (39.34)
Outros	32 (15.17)
Comorbidities	
Hypertension	104 (49.28)
Diabetes mellitus	71 (33.64)
Chronic obstructive pulmonary disease	60 (28.43)
Chronic kidney disease	29 (13.74)
Stroke	23 (10.90)
Asthma	16 (7.58)
HIV[a] virus infection	13 (6.16)
Previous/active tuberculosis	11 (5.21)
Number of comorbidities (mean of 1.55/patient)	
None	37 (17.54)
1	72 (34.12)
2	61 (28.91)
3	34 (16.11)
>3	7 (3.32)
BMI[b]	
Underweight (BMI <18.5)	14 (6.64)
Normal weight (BMI ≥18.5 and <25.0)	73 (34.60)
Overweight (BMI ≥25 and <30)	67 (31.75)
Obesity (BMI ≥ 30)	57 (27.01)
Reasons for admission	
Respiratory	116 (54.98)
Cardiovascular	23 (10.90)
Renal	11 (5.21)
Neurological	9 (4.27)
Endocrine	7 (3.32)
Digestive	6 (2.84)
Others[c]	39 (18.48)
Outcomes	
Discharge	83 (39.34)
Palliative care – death	60 (28.44)
Death	57 (27.01)
Transfer	11 (5.21)

Laboratory tests-biological samples	
Blood	566 (54.48)
Tracheal aspirate/sputum	247 (23.77)
Urine	88 (8.47)
ABA[d] research in tracheal aspirate	49 (4.72)
VDRL[e]	39 (3.75)
Liquor	11 (1.06)
Others	39 (3.75)
Isolated strains species/genus	
Klebsiella pneumoniae	26 (13.98)
Staphylococcus aureus	25 (13.44)
Acinetobacter baumannii	22 (11.83)
Staphylococcus epidermidis	22 (11.83)
Pseudomonas aeruginosa	17 (9.14)
Escherichia coli	10 (5.37)
Others	64 (34.41)

Caption: *[a]Human Immunodeficiency Virus; [b]Body Mass Index; [c]Injuries, poisoning and some other consequences of external causes, musculoskeletal system and connective tissue diseases, skin and subcutaneous tissue diseases, infectious and parasitic diseases; [d]Acid-fast bacilli; [e]Venereal Disease Research Laboratory; diagnosis of syphilis.*

Table 2. Resistance profile of microorganisms – excluding duplicates.*

Bacteria	N	Total
Gram-negative		
Carbapenem-resistant *A. baumannii*	20	22
Polymyxin B-resistant *A. baumannii*	3	22
3rd generation cephalosporin-resistant *E. coli*	2	9
Carbapenem-resistant *E. coli*	0	9
3rd generation cephalosporin-resistant *K. pneumoniae*	12	22
Carbapenem-resistant *K. pneumoniae*	8	22
3rd-generation cephalosporin-resistant *Enterobacteriaceae*	0	25
Carbapenem-resistant *Enterobacteriaceae*	1	25
Carbapenem-resistant *P. aeruginosa*	0	14
Gram-positive		
MRSA[a]	3	21
Oxacillin-resistant CNS	9	13

**Duplicates: bacteria isolated from the same person, period less than 30 days; [a]methicillin-resistant Staphylococcus aureus.*

Of the total of 566 blood cultures, 73 (12.90%) showed growth of microbiota suggestive of contamination and 62 (10.95%) were positive, with 72 microorganisms isolated. Of these microorganisms, 36 (50%) were gram-positive, 29 (40.28%) were gram-negative, and seven were fungi (9.72%). Of the 247 tracheal aspirate/sputum collections, 25 (10.12%) showed growth of oropharyngeal microbiota and 61 (24.70%) were positive, isolating 67 microorganisms: 20 (29.85%) isolated bacteria were gram-positive; 47 (70.15%) were gram-negative. A total of 88 urine cultures were collected: 31 (35.23%) were positive, isolating 33 microorganisms, of which five (15.15%) were gram-positive, 17 (51.52%), gram-negative, and 11 (33, 33%), yeast. Table 2 shows resistance profile of isolated microorganisms.

The most prescribed class of antibiotics was cephalosporin, followed by penicillin and macrolide, as shown in table 3. Thus, 503 antibiotics were prescribed, resulting in a mean of 2.39 (SD=1.40) per patient. Furthermore, 79.52% were administered parenterally.

Table 4 shows the mean costs of admission and antimicrobial agents administered, stratified by category of reason for admission.

In Pearson correlation analysis, it was possible to identify a moderate correlation between the number of bacteria isolated from patients and length of stay in the ICU and total admission (ρ=0.540 and ρ=0.418, respectively). A low correlation was observed between total length of stay and quantity of bacteria identified in blood culture (ρ=0.305), tracheal aspirate (ρ=0.380) and urine culture (ρ=0.253). For analysis of length of stay in the ICU and bacteria identified in blood culture (ρ=0.249) and urine culture (ρ=0.248), correlations were low, whereas for tracheal aspirate (ρ=0.578), they can be considered moderate. It was not possible to identify significant associations between the number of bacteria isolated and outcomes.

A significant difference was identified between admission costs (p-value <0.008), antimicrobial costs (p-value <0.001) and percentage of costs related to antimicrobial

Table 3. Antibiotic prescription pattern by class - N (%).

Reasons for admission Antibiotic	Respiratory	Renal	Digestive	Endocrine	Neurological	Cardiovascular	Neurological	Others	Total
Cephalosporin	99 (67.81)	9 (6.17)	0 (0)	5 (3.42)	5 (3.42)	9 (6.17)	5 (3.42)	19 (13.01)	**146**
Penicillin	74 (56.92)	8 (6.15)	5 (3.85)	4 (3.08)	6 (4.61)	14 (10.77)	6 (4.61)	19 (14.62)	**130**
Macrolide	66 (81.48)	0 (0)	1 (1.23)	2 (2.47)	1 (1.23)	6 (7.41)	1 (1.23)	5 (6.18)	**81**
Carbapenem	19 (45.24)	2 (4.76)	1 (2.38)	0 (0)	0 (0)	3 (7.14)	0 (0)	17 (40.48)	**42**
Glycopeptide	18 (42.86)	0 (0)	1 (2.38)	0 (0)	1 (2.38)	2 (4.76)	1 (2.38)	20 (47.62)	**42**
Polymyxin	8 (50.00)	1 (6.25)	0 (0)	0 (0)	0 (0)	1 (6.25)	0 (0)	6 (37.50)	**16**
Sulfonamide	7 (46.66)	0 (0)	0 (0)	0 (0)	1 (6.67)	1 (6.67)	1 (6.67)	6 (40.00)	**15**
Antimycobacterial	9 (81.82)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18.18)	**11**
Lincosamide	3 (50.00)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (50.00)	**6**
Aminoglycoside	4 (100.00)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**4**
Quinolone	2 (50.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25.00)	0 (0)	1 (25.00)	**4**
Azole	0 (0)	1 (33.33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (66.67)	**3**
Nitrofuran	1 (50.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.00)	0 (0)	0 (0)	**2**
Oxazolidinone	1 (100.00)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**1**
Total	**311**	**21**	**8**	**11**	**14**	**38**	**14**	**100**	**503**

Table 4. Costs with materials and medications due to admission

Reasons for admission	Admission cost (materials + medications)* (R$) Mean (SD)	Direct cost of antimicrobial agents (R$) Mean (SD)	Costs related to antimicrobial agents (%) Mean (SD)
Respiratory	2,786.97 (2,411.14)	297.95 (353.67)	13.10 (9.42)
Renal	1,164.91 (645.49)	132.63 (93.75)	11.04 (5.08)
Digestive	2,411.40(1,991.95)	132.04(110.83)	9.32 (10.61)
Endocrine	2,026.17 (2,441.31)	148.98 (87.17)	21.24 (23.31)
Neurological	2,229.17 (1,579.13)	176.24 (246.00)	7.70 (5.20)
Cardiovascular	1,394.47 (1,298.11)	196.50 (344.42)	12.34 (8.63)
Others	3,198.70 (5,589.20)	582.70 (1.405.97)	20.19 (12.58)

**Admission cost (materials + medications) corresponds to the total expenditure on materials and medications dispensed by the pharmacy, such as electrodes, bacteriological filter, surgical gloves, catheters, trichotomy device, extension for aspiration, extension for oxygen, sample collection bottle, syringes, probes, dressings, catheters, serums, equipment, masks, all medications available in the institution's therapeutic arsenal; SD: standard deviation.*

agents administered (p-value <0.001). For admission costs, only the distribution of cardiovascular diseases differs from respiratory diseases (p-value <0.017). For antimicrobial costs, the distribution of cardiovascular diseases differs from respiratory diseases (p-value <0.011) and other reasons for admission (p-value <0.002). While the distribution of the percentage of costs related to antimicrobial agents administered for other reasons for admission differs from respiratory (p-value<0.012) and neurological (p-value<0.012) diseases, for all other pairs, it was not possible to identify a significant difference.

As for surveillance cultures, considering the 211 patients included in the study, 844 samples should have been collected, four per patient. However, only 740 were collected. Of these samples, 718 were negative for the microorganisms studied and 22 were positive: 1 (4.55%) acinetobacter (skin swab); 6 (27.27%) MRSA (nasal swab); 13 (59.09%) carbapenemase-producing *Enterobacteriaceae* (rectal swab); and 2 (9.09%) VRE (rectal swab). Of the 20 patients who isolated microorganisms in surveillance swabs, only eight had culture tests showing growth, with 15 bacteria being isolated, ten of which had the same resistance characteristic as the microorganism isolated in the surveillance culture. For patients with positive surveillance cultures, the mean cost of antibiotics was R$213.84 (US$38.88) (SD=R$ 197.45 (US$35.90)). For those with negative surveillance cultures, the mean cost of antibiotics was R$ 339.15 (US$61.66) (SD=R$ 750.19 (US$136.39)). When considering the total costs of materials and medications, the positive ones had a mean of R$ 1,478.76 (US$268.86) (SD=R$ 1,204.07 (US$218.92)), and the negative ones, R$ 2,747.52 (US$499.54) (SD=R$ 3,250.10 (US$590.92)). Regarding the percentage of costs related to antibiotics, patients with isolated microorganisms had a percentage of 18.29% (SD=14.77%) of costs. The negative ones obtained a percentage of 13.40% (SD=10.05%) of costs. Patients with negative surveillance cultures used a mean of 2.1 antibiotics (SD=1.3 antibiotics). Those with positive surveillance cultures used a mean of 2.5 antibiotics (SD=1.4 antibiotics).

The outcomes were also observed for these 20 patients identified as colonized by some resistant bacteria. It was not possible to identify a significant association using the chi-square test (p-value>0.396). In these cases, 25% were discharged; 40% died; no patients were transferred; and in 35% palliative care was instituted.

DISCUSSION

Patients admitted to the ICU can have a very different profile and admission characteristics. Moreover, they may present infections during their stay in the unit due to several factors.

In the study, of the 211 patients, 17.5% did not present any comorbidity, unlike a study carried out in 1,265 centers in 75 countries, whose value was 48.5%.[10] When comparing the reasons for admission, the data were similar to those in the literature, such as respiratory causes (54.98%), followed by cardiovascular causes (10.90).[10] Mean length of stay in the ICU (9.69 days) and admission (15.29 days) were similar to those found in a German study, with an average of 14 days of admission,[11] however different from a study in Romania, with an ICU stay of 6.9 days.[3] The high mortality rate found (55.45%) surpassed studies with similar designs and ICU characteristics.[3,10] These differences can be considered by excluding post-operative patients in our study, since they have a shorter hospital stay, fewer complications, a more favorable outcome and, therefore, a shorter hospital stay.

In ICUs, antibiotics are commonly administered via parenteral routes, which was observed in our results (79.52%) and in a study carried out in five ICUs, where 98.7% were administered via this route.[1] The use of azithromycin exclusively orally, in tablet form, may justify this lower rate in the study results. The list of medications available for prescription in the hospital and the form of administration established by protocols can influence the profile of antimicrobial use, limiting the classes used.

The isolated microorganisms were predominantly gram-negative, coinciding with other studies in the literature in Brazilian ICUs[12,13] and studies with data from 83 countries.[8] *K. pneumoniae*, *S. aureus, A. baumannii, S. epidermidis* and *P. aeruginosa* were the most frequently found microorganisms.[3,6] ICUs are favorable environments for the spread of microorganisms. In this regard, gram-negative microorganisms cause greater concern, as they present high rates of resistance and have fewer therapeutic options available in these cases.[13]

The results of this study showed that 90.91% of *A. baumannii* isolates were carbapenem-resistant, a profile similar to that found in two Brazilian ICUs (100% and 83.3%).[14] Regarding the prevalence of *Escherichia coli*, the result was similar to that found in the review of data from the Region of the Americas - 16% to 22%.[15] No samples of carbapenem-resistant *E. coli* were found, in agreement with data from other Brazilian ICUs, which were also not found.[14] The results for 3rd generation cephalosporin-resistant *K. pneumoniae* (54.54%) support those reported for the Region of the Americas[8] and Brazilian ICUs.[14] However, a significantly higher number of carbapenem-resistant *K. pneumoniae* was reported (36.36%) compared to 7.9% and 5.1% found in other Brazilian ICUs,[14] and 9% to 11%, found in the Region of the Americas.[15] For MRSA, the study result was 14.29%, different from other Brazilian ICUs, where 80% were reported,[14] and from a review study, which identified 42% to 55% of resistance.[15]

The most prescribed classes of antimicrobial agents were cephalosporin, penicillin and macrolide. Meanwhile, in a study including 1,150 centers in 88 countries, the classes were penicillin, carbapenem and cephalosporin.[8] A lower prevalence of carbapenem prescription was found when compared to global data,[8] which may indicate a preservation of this broad-spectrum antibiotic in the study ICU. The different epidemiological and clinical profiles and protocols of each institution may also justify the differences in the prescription pattern.

The moderate correlation between length of stay and quantity of bacteria can be explained by the length of treatment with antimicrobial agents necessary to complete the treatment of the infection. A study to assess the request for blood cultures demonstrated that there was no change in antimicrobial agent consumption with the reduction in the request for blood cultures.[16] The study hypothesis that patients without request for cultures would use antibiotics for longer was not empirically observed, demonstrating that treatment duration with antimicrobial agents tends to be longer when there are positive cultures.[16] When cultures were negative due to the absence of infection, the shorter length of stay can be explained because patients who do not have infection in intensive care do better,[10] being discharged earlier.

The moderate correlation between tracheal aspirate and the number of bacteria can be explained by the profile of microorganisms isolated in these samples, predominantly gram-negative. Although the majority of gram-negative urine cultures were also observed in urine cultures, positive urine cultures in asymptomatic patients are considered asymptomatic bacteriuria and treatment is not necessary.[17] Gram-negative bacteria found in tracheal aspirates are microorganisms closely related to pneumonia associated with mechanical ventilation,[18] which have high rates of multidrug resistance and fewer therapeutic options,[19] in addition to being associated with worse outcomes,[18] which may justify this increase in length of admission. In a study carried out in an Istanbul hospital, with follow-up for four years, a predominance of gram-negative microorganisms in tracheal aspirate was observed.[18]

The financial resources spent on antibiotics corresponded, on average, to 14.15% of direct costs of medications and materials. The results showed a lower cost of antibiotics in cardiovascular admissions, in line with the results highlighted by the Greek study.[9]

Among the 211 patients observed, 20 (9.48%) had positive results for surveillance cultures, and, for the institution's epidemiological profile, it is necessary to reflect on whether surveillance culture collection is really useful, since the collection criteria end up covering practically all patients admitted to the ICU. In order to rationalize the institution's resources, possibly carrying out only carbapenemase research, which was the surveillance culture with the highest positive rate, would be sufficient.

A study on the use of antibiotics in palliative care in ICUs stated that there is a vicious circle that involves the following order: length of stay; increased infection rate; use of antibiotics; infection by resistant microorganisms; use of broad-spectrum antibiotics; and longer hospital stay. Therefore, the use of antibiotics for patients in palliative care is contrary to the philosophy of palliative care itself, and is contraindicated.[20] In our study, palliative care was instituted in 30.33% of patients at the beginning or during ICU admission. Palliative care is still a new approach and requires more research to promote greater comfort and avoid the use of antibiotics unnecessarily.[20]

This work has the limitations inherent to single-center, cross-sectional observational studies. Furthermore, the specific characteristics of this ICU, with its epidemiological profile, the teams of prescribers and the list of medications available do not allow generalizing the results; furthermore, they provide understanding and encourage reflection on adopted procedures. Cost data should also be considered with caution, as it only considers data on direct costs with antimicrobial agents and total costs with materials and medications.

This study provides information that may assist in the development of institutional policies aimed at the rational use of antimicrobial medications and laboratory tests.

REFERENCES

1. Plantinga NL, Wittekamp BH, Van Duijn PJ, et al. Fighting antibiotic resistance in the intensive care unit using antibiotics. Future Microbiol. 2015;10(3):391-406. doi: 10.2217/fmb.14.146.
2. Pulingam T, Parumasivam T, Gazzali AM, et al. Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome. Eur J Pharm Sci. 2022;170:e106103. doi: 10.1016/j.ejps.2021.106103.
3. Axente C, Licker M, Moldovan R, et al. Antimicrobial consumption, costs and resistance patterns: A two year prospective study in a Romanian intensive care unit. BMC Infect

Dis. 2017;17:358. doi: 10.1186/s12879-017-2440-7.

4. Willmann M, El-Hadidi M, Huson DH, et al. Antibiotic selection pressure determination through sequence-based metagenomics. Antimicrob Agents Chemother. 2015;59:7335-45. doi: 10.1128/aac.01504-15
5. Jung SH, Ryu CM, Kim JS. Bacterial persistence: Fundamentals and clinical importance. J Microbiol. 2019;10:829-35. doi: 10.1007/s12275-019-9218-0
6. Saxena S, Priyadarshi M, Saxena A, et al. Antimicrobial consumption and bacterial resistance pattern in patients admitted in I.C.U at a tertiary care center. J Infect Public Health. 2019;12:695-9. doi: 10.1016/j.jiph.2019.03.014
7. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395:200-11. doi: 10.1016/S0140-6736(19)32989-7
8. Vincent JL, Sakr Y, Singer M, et al. Prevalence and Outcomes of Infection among Patients in Intensive Care Units in 2017. JAMA. 2020; 323:1478-87. doi: 10.1001/jama.2020.2717
9. Karabatsou D, Tsironi M, Tsigou E, et al. Variable cost of ICU care, a micro-costing analysis. Intensive Crit Care Nurs. 2016;35:66-73. doi: 10.1016/j.iccn.2016.01.001
10. Vincent JL, Rello J, Marshall J, et al. International Study of the Prevalence and Outcomes of Infection in Intensive Care Units. JAMA. 2009;302:2323-9. doi: 10.1001/jama.2009.1754
11. Stocker H, Mehlhorn C, Jordan K, et al. Clinical and economic effects of an antimicrobial stewardship intervention in a surgical intensive care unit. Infection. 2020;48:509-19. doi: 10.1007/s15010-020-01421-8
12. Sabino SS, Lima CA, Machado LG, et al. Infections and antimicrobial resistance in an adult intensive care unit in a Brazilian hospital and the influence of drug resistance on the thirty-day mortality among patients with bloodstream infections. Rev Soc Bras Med Trop. 2020; 53:e20190106. doi: 10.1590/0037-8682-0106-2019
13. Mota FS, Oliveira HA, Souto RCF. Perfil e prevalência de resistência aos antimicrobianos de bactérias Gram-negativas isoladas de pacientes de uma unidade de terapia intensiva. Revista Brasileira de Análises Clínicas. 2018;50(3):270-7. doi: 10.21877/2448-3877.201800740
14. Silva ARA, Jaszkowski E, Schober T, et al. Patterns of antimicrobial consumption in neonatal and pediatric intensive care units in Germany and Brazil. Eur J Clin Microbiol Infect Dis. 2020;39:249-55. doi: 10.1007/s10096-019-03714-9
15. Timsit JF, Bassetti M, Cremer O, et al. Rationalizing antimicrobial therapy in the ICU: a narrative review. Intensive Care Med. 2019;45:172-89. doi: /10.1007/s00134-019-05520-5
16. Sick-Samuels AC, Woods-Hill CZ, Fackler JC, et al. Association of a blood culture utilization intervention on antibiotic use in a pediatric intensive care unit. Infect Control Hosp Epidemiol. 2019;40:482-90. doi: 10.1017/ice.2019.10
17. Henderson JT, Webber EM, Bean SI. Screening for Asymptomatic Bacteriuria in Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2019;322:1195-205. doi: 10.1001/jama.2019.10060
18. Caskurlu H, Kocoglu ME, Cag Y, et al. Examination of blood and tracheal aspirate culture results in intensive care patients: 5-year analysis. Medeni Med J. 2020;35:128-35. doi: 10.5222/MMJ.2020.89138
19. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. Review on Antimicrobial Resistence. HM Government and Wellcome Trust; 2016. Disponível em: https://amr-review.org/Publications.html.
20. Dagli O, Tasdemir E, Ulutasdemir N. Palliative care infections and antibiotic cost: a vicious circle. Aging Male. 2020;23:98-105. doi: 10.1080/13685538.2019.1575353.

AUTHORS' CONTRIBUTIONS

Lucia Collares Meirelles contributed to abstract conception, bibliographical research, writing, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions and final review of research. **Vera Lúcia Milani Martins** contributed to methodology, discussion, interpretation and description of results, preparation of tables, statistics and final review of research. **Diogo Pilger** contributed to research conception, methodology, discussion, interpretation of results, conclusions and final review.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.