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Bloodstream infection and multidrug resistance in the Intensive Care Unit

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Abstract

Objective: To identify bacterial species and the antimicrobial resistance rate in blood culture samples from patients admitted to an adult ICU. **Methods:** This is an observational and retrospective study, carried out in a tertiary hospital in the Northwest of Minas Gerais, Brazil, between January 1, 2019 and October 31, 2022. Data were obtained from records in the database of blood cultures and electronic medical records of patients admitted to the hospital's adult ICU. **Results:** From 2019 to 2022, Gram positive bacteria were the most isolated, however, a gradual reduction was observed over the years, in parallel with the growth in Gram negative etiology in this period. The frequently isolated microorganisms were coagulase-negative staphylococci, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Enterococcus* spp, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Enterobacter cloacae*. *Staphylococcus aureus* showed low resistance to methicillin, contrary to the results observed in coagulase-negative staphylococcal strains. Resistance rates ≥50% were identified to at least three classes of antimicrobials tested in Gram-negative bacteria, namely *Klebsiella pneumoniae, Enterobacter cloacae, Acinetobacter baumannii, Klebsiella ozaenae* and *Serratia* spp. **Conclusion:** The results indicated multidrug resistance at the study institution, especially concerning in Gram-negative strains.

Keywords: Drug Resistance, Microbial; Intensive Care Units; Drug Resistance, Multiple, Bacterial; Anti-Infective Agents.

Infecção de corrente sanguínea e multirresistência em unidade de terapia intensiva

Resume

Objetivo: Identificar as espécies bacterianas e a taxa de resistência antimicrobiana em amostras de hemoculturas de pacientes internados em uma UTI adulto. **Métodos:** Trata-se de estudo observacional e retrospectivo, realizado em um hospital terciário do Noroeste de Minas Gerais, Brasil, no período entre 1º de janeiro de 2019 a 31 de outubro de 2022. Os dados foram obtidos em registros do banco de dados de hemoculturas e do prontuário eletrônico dos pacientes internados na UTI adulto do hospital. **Resultados:** No acumulado de 2019 a 2022, as bactérias Gram-positivas foram as mais isoladas, entretanto, observou-se redução gradual ao longo dos anos, em paralelo ao crescimento na etiologia por Gram-negativos neste período. Os microrganismos frequentemente isolados foram estafilococos coagulase negativa, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Enterococcus* spp, *Pseudomonas aeruginosa, Acinetobacter baumannii* e *Enterobacter cloacae*. *Staphylococcus aureus* apresentou baixa resistência a meticilina, contrariamente ao resultados observados nas cepas de estafilococos coagulase negativo. Taxas de resistência ≥50% foram identificadas a pelo menos três classes de antimicrobianos testados nas bactérias Gram-negativas, sendo elas *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Acinetobacter baumannii, Klebsiella ozaenae* e *Serratia* spp. **Conclusão:** Os resultados indicaram multirresistência na instituição de estudo, especialmente preocupante em cepas Gram-negativas.

Palavras-chave: Resistência a Antibióticos; Unidade de Terapia Intensiva; Resistência Bacteriana a Múltiplas Drogas; Antimicrobianos.

Introduction

Bloodstream Infections (BSI) acquired in Intensive Care Units (ICUs) are defined as cases in which a positive blood culture is obtained for a clinically significant bacterial pathogen more than 72 hours after admission to the ICU[1-3]. They have particular epidemiological aspects when compared to community or hospital-origin BSI and are often caused by multidrug-resistant (MDR) strains. Early and assertive antimicrobial therapy is the key to improving patient outcomes and should be based on local epidemiology, given the possibility of different microbiological profiles coexisting in the same region/country[4].

Adequate microbiological surveillance is highlighted in the WHO (World Health Organization) Global Action Plan. As such, it is strongly recommended that countries implement or improve their National Action Plan, including a Surveillance Program, to properly assess local resistance patterns and trends[5]. In 2017, Brazil joined GLASS and, in 2018, started its own national antimicrobial surveillance program (BR-GLASS). This program is an ongoing project that aims to cover at least 95 hospitals over the next few years, distributed across Brazil's five geographical regions, and is proving to be a major step forward in measuring and discussing resistance in the country, although the data is still incipient[6].

In Minas Gerais, studies on the sensitivity profile in the ICU are often related to the urinary tract[7,8]. However, in 2019, data from the multicenter study of healthcare-related infections in adult Intensive Care Units, carried out in hospitals in the ten planning regions of the state of Minas Gerais (Alto Paranaíba; Central; Midwest Minas; Jequitinhonha/Mucuri; Mata; Noroeste de Minas; Norte de Minas; Rio Doce; Sul de Minas and Triângulo), indicated during the one-off survey that among the samples evaluated, approximately half were resistant to antibiotics (45.4%), with the highest resistance among samples of Gram-negative bacilli (63.0%)[9]. This study also observed a significant empirical use of antimicrobials, especially broad-spectrum ones, which contributed to, as well as justified, the significantly higher frequency of resistance/multi-resistance in these units.

These results point to and reinforce the need to investigate the microbiological and antimicrobial sensitivity profile, specific to each hospital, in order to protect against the irrational use of antimicrobials and help prevent the spread of resistance. It is estimated that by 2050, if the current scenario does not change, infections caused by multidrug-resistant bacteria will be the leading cause of death in the world and will kill more people than cancer, diabetes and traffic accidents, for example[10]. In light of this, the purpose of this study was to identify the bacterial species that cause BSI in the adult ICU of a medium-sized regional hospital and the antimicrobial resistance rate in blood culture samples.

Methods

This is an observational and retrospective study, approved by the Research Ethics Committee under number CAEE 58907222.7.0000.5119, carried out in a tertiary hospital in the northwest of Minas Gerais, Brazil, between January 1, 2019, and October 31, 2022. The sample was obtained by convenience in a non-probabilistic way, based on the availability of records in the blood culture database of patients admitted to the hospital's adult ICU. Routine blood culture collection is not practiced in the ICU, so all positive blood cultures were considered indicative of suspected infection.

Patients admitted to the adult ICU with positive blood cultures obtained more than 72 hours after admission were eligible for the study. Common skin contaminants (Bacillus spp., CONS [coagulase-negative staphylococci] [including S. epidermidis] and *viridans streptococci*) were considered only when identified from two or more blood cultures taken on separate occasions, no more than 48h[11] hours apart, or when retrospective clinical analysis yielded strong clinical suspicion of being a true infection, e.g. obvious clinical signs of BSI, sample positive time <48h, patient untreated and not improving or treated and improving, absence of documented parallel infection and of another microorganism in the same sample.

The methods used for collecting, seeding, and incubating inocula from blood culture samples follow the standard operating procedures adopted by the institution's laboratory. These were based on the recommendations of ANVISA (National Health Surveillance Agency) and CSLI (Clinical and Laboratory Standards Institute) M100 (2019 to 2022). The standard routine consisted of receiving the samples collected aseptically in two vials, one for anaerobes and the other for aerobes, both with the presence of antimicrobial inhibitors. The volume of the blood sample collected is 8 to 10 ml per vial. The samples are incubated in the BACTEC® 9050 device at 37°C for five days. When the alarm indicating the positivity of a sample occurs, the samples are removed from the equipment and the procedure for identifying the microorganism and the antimicrobial susceptibility test (ASCT) is carried out in accordance with the established operating procedure.

The TSA used the Kirby-Bauer qualitative method and was interpreted according to the CLSI cut-off points (2019-2022). The choice of antimicrobials for testing followed internal standardization, drawn up based on CLSI recommendations and agreed between the Hospital Infection Control Commission (HICC), the Pharmacy and the unit's Laboratory. The final result is given in the form of a spreadsheet which includes a qualitative interpretation for each antimicrobial; the strain can be, as follows: sensitive (S), intermediate (I) or resistant (R). For analysis purposes, in this study the microorganisms classified as sensitive or with intermediate resistance were grouped together. According to the established standardizations, the Etest strip is used when methicillin-resistant *Staphylococcus aureus* (MRSA+), vancomycin is tested; and when carbapenem-resistant enterobacteriaceae, meropenem, imipinem and ertapenem are tested.

The tests for phenotypic detection of antimicrobial resistance were carried out in accordance with CLSI and ANVISA recommendations. Screening for inducible Amp C-type β-lactamases is carried out on all bacteria in the CESP group (*Citrobacter* spp., *Enterobacter* spp., *Serratia* sp. and *Proteus* spp.) and *Pseudomonas aeruginosa.* Screening for carbapenemases is carried out on all enterobacteria, while ESBL (extended spectrum betalactamases) screening excludes those in the CESP group. With effect from 2021, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were included in the group for carbapenemase screening, following alerts from ANVISA.

The laboratory carries out internal and external quality control on a regular basis in order to ensure the integration of the monitoring, evaluation and applicability processes, while promoting the continuous improvement and reliability of the identification procedures and antimicrobial sensitivity tests carried out. The standard strains ATCC 27853, 25923, 25922, 35218 and 29212 are used to evaluate these controls.

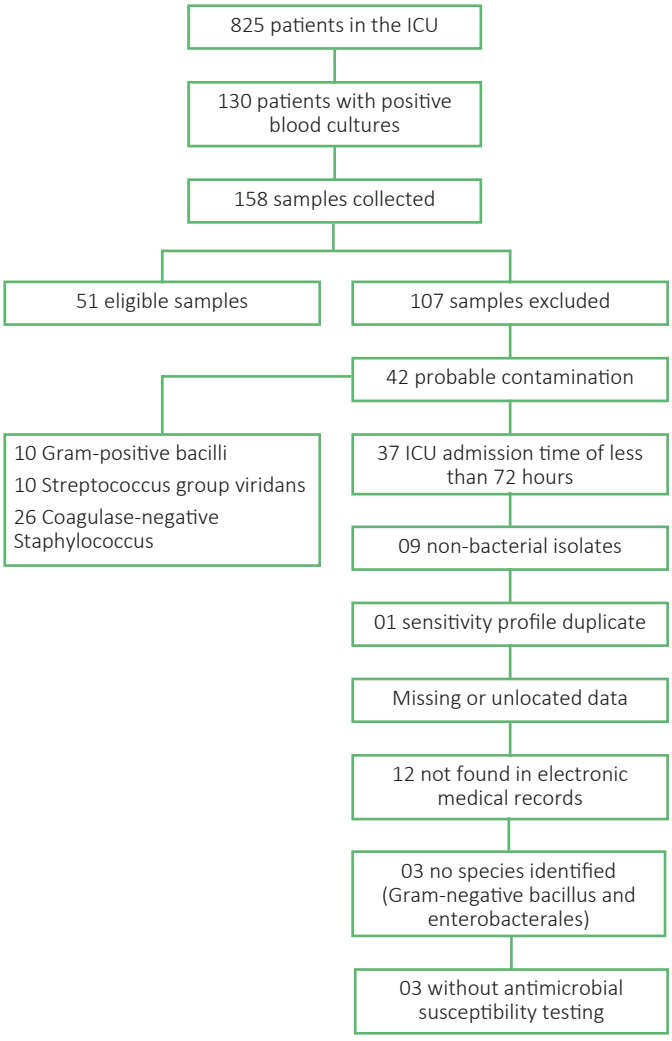
All the procedures carried out and the results found during laboratory analysis are listed in the laboratory's logbook and this, together with the Integrated Hospital Management System (Sistema Integrado de Gestão Hospitalar, SIGH) and the webdesktop report from the Pentaho system, served as a source of data collection for the research.

Samples with incomplete or inconsistent data in both the laboratory record book and SIGH, such as the absence of the patient's name, the isolated microorganism, and the sensitivity profile, were excluded from the study. Samples from the same patient with the same sensitivity profile and polymicrobial growth were also discarded. The remaining data was compiled and analyzed in a Microsoft Excel® spreadsheet using descriptive statistics.

Results

During the study period, a total of 825 patients were admitted to the adult ICU, 130 of whom had at least one positive blood culture. Data was collected from 158 samples, 107 of which were excluded because they did not meet the criteria defined for the study, as illustrated in the flowchart (Figure 01).

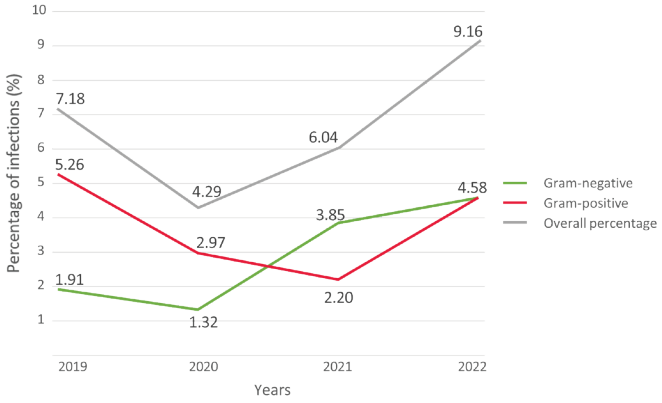
Figure 01. Flowchart for inclusion and exclusion of blood cultures in the study.



Subtitle: ICU: Intensive Care Unit.

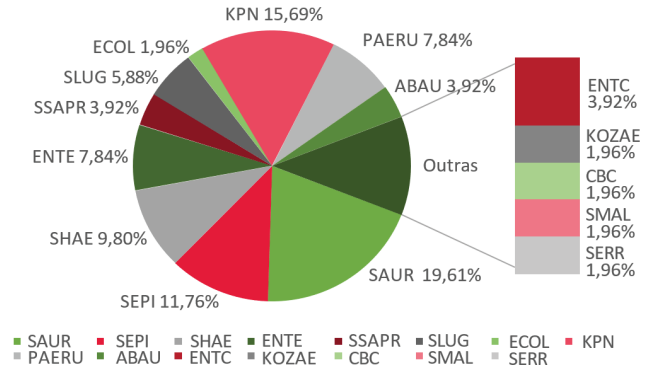
Though, in absolute numbers, 2019 had more cases of BSI (7.18% - 15/209), 2022 had the highest rate of BSI per hospitalized patient (9.16%- 12/131). From 2019 to 2022, Gram-positive bacteria (58.82% - 30/51) were the most isolated, but with a gradual reduction over the years. At the same time, there was an increase in Gram-negative etiology and convergence of results in 2022 (Figure 02).

Figure 02. Percentage of bloodstream infections acquired in the Intensive Care Unit by Gram-positive and Gram-negative bacteria in a tertiary hospital in the northwest of Minas Gerais, between 2019 and 2022, Patos de Minas, Brazil.



The most frequently isolated microorganisms were *Staphylococcus aureus* 19,61% (10/51), *Klebsiella pneumoniae* 15,69% (8/51), *Staphylococcus epidermidis* 11,76% (6/51), *Staphylococcus haemolyticus* 9,80% (5/51), *Enterococcus* spp. 7,84% (4/51), *Pseudomonas aeruginosa* 7,84% (4/51), *Staphylococcus lugdunensis* 5,88% (3/51), *Staphylococcus saprophyticus, Acinetobacter baumannii* e *Enterobacter cloacae* 3, 92% (2/51) each. The other bacteria identified represented 1.96% (1/51) each (Figure 03).

Figure 03. Microbiological profile of bacteria isolated in blood culture samples from patients admitted to the Adult Intensive Care Unit of a Tertiary Hospital in the Northwest of Minas Gerais, Patos de Minas, Brazil, 2019- 2022.



SAUR	*Staphylococcus aureus*	PAERU	*Pseudomonas aeruginosa*
SEPI	*Staphylococcus epidermidis*	ABAU	*Acinetobacter baumannii*
SHAE	*Staphylococcus haemolyticus*	ENTC	*Enterobacter cloacae*
ENTE	*Enterococcus spp.*	KOZAE	*Klebsiella ozaenae*
SSAPR	*Staphylococcus saprophyticus*	CBC	*Complexo Burkholderia cepacia*
SLUG	*Staphylococcus lugdunensis*	SMAL	*Stenotrophomonas maltophilia*
ECOL	*Escherichia coli*	SERR	*Serratia spp.*
KPN	*Klebsiella pneumoniae*		

Staphylococcus aureus was the main bacterium isolated in individuals with BSI at this institution. Of ten isolates, 80% (8/10) were resistant to ciprofloxacin, 70% (7/10) to penicillin, 60% (6/10) to erythromycin and 50% (5/10) to clindamycin. Only one strain of MRSA was identified, resulting in 14.29% (1/7) resistance to oxacillin - the anti-staphylococcal penicillin chosen as the agent for testing the sensitivity of *S. aureus*. No resistance to vancomycin was identified.

Staphylococcus epidermidis, the second most commonly isolated Gram-positive bacterium (11.76% - 6/30), showed high resistance rates (>50%). Resistance to oxacillin was observed in approximately 84.00% (5/6) of the isolates. Other CoNS showed a similar resistance pattern. *Staphylococcus haemolyticus* showed 100% resistance to most of the antimicrobials tested, with the sole exception of rifampicin (20%) and tetracycline (0%). *Staphylococcus lugdunensis* showed sensitivity (100%) to gentamicin and rifampicin, although a rate of 33.33% resistance to tetracycline and 100% resistance to the other antimicrobials were observed. Finally, *Staphylococcus saprophyticus* showed 100% resistance to ciprofloxacin, clindamycin, oxacillin, penicillin, and erythromycin and 50% resistance to gentamicin, rifampicin, and tetracycline. Fourteen of the 15 isolates (93.33%) of CoNS showed resistance to oxacillin (Table 01).

Enterococcus spp. was the third most frequently identified Gram-positive bacterium (4/30). It was resistant to penicillin in 50% of cases, as well as to streptomycin and levofloxacin. Resistance to ciprofloxacin and gentamicin was observed in 33% of cases. No resistance to vancomycin was observed in the four isolates tested.

Klebsiella pneumoniae was the most isolated Gram-negative bacterium (15.69% - 8/21). The phenotypic test to identify ESBL was positive in 50% (4/8) of the isolates (Table 02). Screening for carbapenemase enzymes was positive in three of the strains that showed resistance to carbapenems. The resistance rate was 100% for ampicillin, 60% for amoxicillin + clavulanate, 37.50% for piperacillin + tazobactam, 33.33% for amikacin and 0% for imipinem, meropenem and erythromycin. Resistance rates of 50% were observed for the other antimicrobials.

Four isolates of *Pseudomonas aeruginosa* were identified, all AmpC producers (Table 02). Sensitivity to levofloxacin, ciprofloxacin, and piperacillin + tazobactam was seen in all the bacteria, while a 25% resistance rate was observed to the other antimicrobials tested. Similarly to *Pseudomonas aeruginosa*, the two *Enterobacter cloacae* isolates screened positive for AmpC. The resistance rate to ampicillin, amoxicillin + clavulanate, ampicillin + sulbactam, cefepime, cefoxitin and ceftazidime was 100%.

Table 01. Percentage of antimicrobial resistance in bacterial isolates obtained from blood cultures of patients admitted to the Intensive Care Unit of a tertiary hospital in Minas Gerais, Patos de Minas, Brazil, 2019-2022.

	S. aureus	*Coagulase-positive staphylococci*	*Enterococcus spp*	*K. pneumoniae*	*P. aeruginosa*	*E. cloacae*	*A. baumanni*	*K. ozaenae*	*Serratia spp.*
Amikacin	N/A	N/A	N/A	33.33	25	50	50	100	0
Amoxicilin + clavulanate	N/A	N/A	N/A	60	N/A	100	N/A	N/A	100
Ampicilin	N/A	N/A	N/A	100	N/A	100	N/A	N/A	N/A
Ampicilin + sulbactam	N/A	N/A	N/A	N/A	N/A	100	50	100	100
Aztreonam	N/A	N/A	N/A	50	25	0	N/A	0	100
Cefepime	N/A	N/A	N/A	50	25	100	50	0	100
Cefoxitin	N/A	N/A	N/A	50	N/A	100	N/A	100	100
Ceftazidime	N/A	N/A	N/A	50	N/A	100	100	0	100
Ceftriaxonae	N/A	N/A	N/A	50	N/A	N/A	100	N/A	N/A
Ciprofloxacin	80	100	33.33	50	0	0	50	N/A	N/A
Clindamicina	50	95.83	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ertapenem	N/A	N/A	N/A	50	N/A	0	N/A	N/A	N/A
Streptomycin 300	N/A	N/A	50	N/A	N/A	N/A	N/A	N/A	N/A
Gentamicin	0	56.25	33.33	50	25	0	0	100	N/A
Imipenem	N/A	N/A	N/A	0	25	0	50	0	100
Levofloxacin	0	83.33	50	N/A	0	0	50	N/A	N/A
Meropenem	N/A	N/A	N/A	0	25	0	50	0	100
Oxacillin	14.29	95.83	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Penicilin g	70	100	50	N/A	N/A	N/A	N/A	N/A	N/A
Piperacilin + tazobactam	N/A	N/A	N/A	37.50	0	N/A	50	0	N/A
Rifampicin	0	25.83	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Sulfamethoxazole + trimethoprim	0	83.33	N/A	50	N/A	50	0	0	0
Tetracycline	0	20.83	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Vancomycin	0	NT	0	N/A	N/A	N/A	N/A	N/A	N/A
Erytromycin	60	95	N/A	0	N/A	0	N/A	0	100

A: *Acinetobacter*, E: *Enterobacter*, K: *Klebsiella,* P: *Pseudomonas,* S: *Staphylococcus*, N/A: not applicable

One of the two strains of *Acinetobacter baumannii* isolated during the study period showed resistance to amikacin, ampicillin + sulbactam, cefepime, ciprofloxacin, imipinem, levofloxacin, meropenem and piperacillin + tazobactam. Ceftazidime and ceftriaxone were resistant to both isolates. No resistance phenotypes were reported and/or identified (Table 02).

Table 02. Resistance phenotypes of bacterial isolates obtained from blood cultures of patients admitted to the Intensive Care Unit of a tertiary hospital in Minas Gerais, Patos de Minas, Brazil, 2019-2022.

Bactérias	N (%)	AmpC (%)	ESBL (%)	Carbapenemase (%)
A. baumannii	2 (3.92)	NA	NA	0
E. cloacae	2 (3.92)	2 (100)	NA	0
Escherichia coli	1 (1.96)	NA	0	0
K. ozaenae	1 (1.96)	NA	0	0
K. pneumoniae	8 (15.69)	NA	4 (50)	3 (37.5)
P. aeruginosa	4 (7.84)	4 (100)	NA	0
Serratia spp.	1 (1.96)	0	NA	1 (100)
Total	19	6	4	4

Legend: A: *Acinetobacter,* E: *Enterobacter,* K: *Klebsiella,* P: *Pseudomonas,* ESBL: extended-spectrum beta-lactamases

Only one isolate of *Escherichia coli* was identified. The strain was resistant only to ciprofloxacin. *Klebsiella ozaenae*, also identified in a single sample, showed resistance to four of the 12 antimicrobials tested, amikacin, ampicillin + sulbactam, cefoxitin and gentamicin.

The *Burkholderia cepacia* complex and *Stenotrophomonas maltophilia* were sensitive to all the antimicrobials tested. *Serratia* spp. showed resistance to amikacin and sulfamethoxazole+trimethropine. Phenotypic screening for carbapenemase production was positive in this strain.

Discussion

The resistance of pathogens to antimicrobials is a global challenge, especially with the increase in morbidity and mortality and the decline in the availability of new medications on the market. The indiscriminate use of antibiotics during the COVID-19 pandemic has further increased concern about the development and spread of resistance mechanisms in pathogenic bacteria[12,13]. In this study, microbiological cultures of blood samples provided clinically relevant information on the epidemiological distribution and antimicrobial resistance rate. Our data show that, in the period between 2019 and 2022, Gram-positive bacteria were the most identified pathogens in blood cultures, much of it attributable to CoNS and *S. aureus*. This profile has also been observed in other countries around the world[14,15].

Despite this, the data in Brazil is diverse. A national surveillance study carried out in 16 Brazilian hospitals spread across the five regions of Brazil showed that from 2007 to 2010 there was a higher prevalence of Gram-negative bacteria (59%) in Intensive Care Units[16]. On the other hand, results similar to those of this study were observed in a tertiary hospital in Minas Gerais. Between 2012 and 2014, approximately 60% of ICU BSI were of Gram-positive etiology, with a large predominance of CoNS (82.22% - 394/528)[17]. Brazil is an extensive country with heterogeneous socio-demographic characteristics, with more developed regions concentrated in the south of the country. Heterogeneity can also be seen in health care, institutional protocols, preventive practices, and the management of nosocomial infection. Thus, different patterns of antimicrobial resistance can coexist in the country[16].

High oxacillin resistance rates were observed in coagulase-negative staphylococci. Similar rates were observed in Brazil by Marra *et al*. (86.4%) and by Guzek *et al*. in Poland (87.20%)[15,16]. Fortunately, these findings were not reproduced in isolates of *S. aureus*, which makes this drug an option for empirical therapy in the institution when BSI is suspected of being caused by this pathogen[18]. All the CoNS isolates showed high rates of resistance to ciprofloxacin, clindamycin, penicillin, and erythromycin. The *mecA*, *blaZ*, *ermA/B/C*, *aac-aphD* and *SCC-mec* genes isolated in hospitals in Belo Horizonte were associated with a multidrug resistance profile similar to that found in this study[19]. Options such as vancomycin, teicoplanin and linezolid, although they have not been tested, could be a therapeutic alternative for patients with suspected MRCoNS infection. Data suggests low resistance to these drugs in Brazil (1.7%)[15].

In line with our data, a Chinese study carried out in six ICUs of a large tertiary hospital identified a low frequency of VRE (vancomycin-resistant *Enterococcus*), with only five isolates in 681 positive blood cultures from adult patients[10]. Ampicillin combined with gentamicin or ceftriaxone, or penicillin plus gentamicin can be alternatives for empirical treatment in these cases[20,21].

Despite the higher frequency of infections by Gram-positive bacteria, in 2021 the number of infections by Gram-negative bacteria was higher, and in 2022 the curve converged. This is in line with the SENTRY study, which highlighted *K. pneumoniae* (15.69%), *P. aeruginosa* (7.84%), *E. cloacae* (3.92%) and *A. baumannii* (3.92%) as the most isolated Gram-negative rods (GNR) in BSI[22]. This growing increase in Gram-negatives in the institution, as has already been observed elsewhere in Brazil, is of practical importance, where, in agreement with the present data, it makes it mandatory to have an agent aimed at covering Gram-negatives for empirical therapy in ICU-acquired BSI.

From the data analyzed, it can be seen that the resistance of Gram-negative bacteria to carbapenems is worrying, especially in isolates of *K. pneumoniae* and *A. bau-mannii*. It is known that bloodstream infections secondary to ESBL-positive and/or carbapenem-resistant *K. pneumoniae* have higher 30-day lethality or in-hospital mortality[23]. Results from the SENTRY Antimicrobial Surveillance Program (Latin America, 2008-2010) already indicated a wide dissemination of *Enterobacteriaceae* producing *Klebsiella pneumoniae* Carbapenemases (KPC) and a decrease in susceptibility to carbapenems by *Acinetobacter* spp. in Latin America, especially in Brazil[18]. Of the *K. pneumoniae* isolates tested, approximately 40% were resistant to at least one carbapenem, with positive screening for carbapenemase production. The KPC-2 gene is endemic in the study hospital, as it is in Brazil. In a study carried out in the city of São Paulo, a significant increase in *K. pneumoniae* resistant to carbapenems was observed (2011 - 6.8% to 2015 - 35.5%), with detection of KPC-2 in 96.2% of the isolates in 2015[24].

In addition to the production of carbapenemases, another resistance phenotype was identified in *K. pneumoniae* strains. Extended-spectrum β-lactamases were observed in two of the three carbapenem-resistant strains. A total of four isolates were ESBL positive and, as a result, a 50% rate of resistance to 2nd to 4th generation cephalosporins, as well as aztreonam, was observed. The *A. baumannii* strains also showed 50% resistance to carbapenems, but no resistance phenotype was reported. Polymyxin alone or in combination with another antimicrobial

can be an alternative of choice for empirical BSI therapy in patients with risk factors for infection by multidrug-resistant Gram-negative bacteria and high risk, aminoglycosides can be an alternative when there are no other options, in both cases with the proviso that a de-escalation strategy must be implemented after culture results[25,26]. Although the *K. pneumoniae* strain has shown a resistance rate of 37.5% to piperacillin + tazobactam, current evidence suggests the use of this antimicrobial only in low-inoculum infections such as urinary tract and biliary tract infections, even when secondary bacteremia is present. For high-inoculum infections (e.g. undrained abscesses or pneumonia) or for patients with septic shock, broader spectrum therapies are suggested[26]. It is worth noting that inadequate empirical therapy is an important prognostic factor for unsatisfactory results[23].

The participation of the multi-professional team in the management of antimicrobial therapy in the Intensive Care Unit is fundamental, especially the participation of pharmacists. This professional contributes to selection, monitoring effectiveness and safety, auditing the results of antimicrobial consumption prospectively and retrospectively, optimizing prescribed regimens, developing, and managing antimicrobial guidelines and policies, and training and educating clinical teams and patients. The data presented here supports decision-making by these professionals throughout the antibiotic use management process, by providing information to support more assertive empirical choices.

There are some significant limitations to this study: the study is subject to bias due to its retrospective nature; the standard volume used for the blood culture samples (only two vials) limits the recovery of all the microorganisms that cause BSI, the literature suggests 4 vials; as this was a single-center study, the findings cannot be generalized to other hospitals. Finally, we would like to point out that the possible risk factors for the etiology of BSI could not be explored in this analysis.

Conclusion

Multidrug resistance was observed in the study institution and was particularly worrying in Gram-negative strains. The results suggest that agents covering both Gram-positive and Gram-negative strains should be used for empirical treatment of BSI in ICUs. For Gram-negative strains, broad-spectrum antimicrobials such as polymyxin should be considered in patients with risk factors for multidrug-resistant germs.

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Collaborators

ECS: Project design, data analysis and interpretation; article writing; DGR: Critical review relevant to the intellectual content; CAA: Critical review relevant to the intellectual content.

Conflict of interests statement

The authors declare that there are no conflicts of interest regarding this article.

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