OCCURRENCE OF THE BACTERIA IN A HOSPITAL ENVIRONMENT AND THEIR SENSITIVITY PROFILE TO THE MAIN ANTIMICROBIALS IN A REFERENCE GENERAL HOSPITAL IN CURITIBA, BRAZIL

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ABSTRACT: Introduction: Antimicrobial resistance rates are increasing in both hospital and community settings, creating a favorable environment for the development of superbacteria. Therefore, local studies are necessary for the proper management of current antimicrobial arsenals and for addressing the current bacteriological scenario. Aim: The aim of this study is to profile bacterial epidemiology in a hospital in Curitiba, Brazil and associate it with the effectiveness of antimicrobial therapy. Methodology: Data from 2019 to 2021 were collected by the Center for Epidemiology and Hospital Infection Control (CEHIC), and this was a quantitative single-center study. Results: The most commonly detected microorganisms were *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Acinetobacter baumannii*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, and *Enterobacter cloacae*. *A. baumannii* and *K. pneumoniae* had the lowest mean sensitivity coefficients, while *S. aureus* was the most sensitive. Erythromycin was the least effective antimicrobial agent, while daptomycin was the most effective. Conclusion: These results are consistent with the literature and can be used to optimize empiric therapies, as there are already important therapeutic failures associated with antimicrobial resistance.
KEYWORDS: Healthcare-Acquired Infection; Eskape; Antimicrobial Susceptibility.

OCORRÊNCIA DE BACTÉRIAS EM AMBIENTE HOSPITALAR, E SEU PERFIL DE SENSIBILIDADE AOS PRINCIPAIS ANTIMICROBIANOS EM UM HOSPITAL DE REFERÊNCIA EM CURITIBA, BRASIL

RESUMO: Introdução: As taxas de resistência antimicrobiana estão em ascensão tanto em ambientes hospitalares como comunitários, criando um cenário propício para o desenvolvimento de superbactérias e, assim, torna-se necessário estudos locais para uma

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gestão adequada dos arsenais antimicrobianos atuais e frente ao cenário bacteriológico atual. Objetivo: O escopo desse estudo visa traçar o perfil epidemiológico bacteriano num hospital em Curitiba, Brasil e associá-lo à eficácia da terapia antimicrobiana. Metodologia: Os dados de 2019 a 2021 foram recolhidos pelo Centro de Epidemiologia e Controle de Infecções Hospitalares (CECIH), sendo este um estudo unicêntrico quantitativo. Resultados: *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Staphylococcus epidermidis, Pseudomonas aeruginosa, Enterococcus faecalis, Acinetobacter baumannii, Staphylococcus haemolyticus, Staphylococcus hominis*, e *Enterobacter cloacae* foram os microrganismos mais comuns detectados. *A. baumannii* e *K. pneumoniae* tinham as médias de coeficiente de sensibilidade mais baixas, enquanto *S. aureus* era o mais sensível. A eritromicina era o agente antimicrobiano menos eficaz, enquanto a daptomicina era o mais eficaz. Conclusão: Estes resultados estão de acordo com a literatura e podem ser utilizados para otimizar as terapias empíricas, visto que já há falhas terapêuticas importantes associadas a resistência antimicrobiana.
PALAVRAS-CHAVE: Infecção Adquirida em Ambiente de Cuidados de Saúde; Eskape; Suscetibilidade Antimicrobiana.

OCURRENCIA DE BACTERIAS EN AMBIENTE HOSPITALARIO Y SU PERFIL DE SENSIBILIDAD A LOS PRINCIPALES ANTIMICROBIANOS EN UN HOSPITAL DE REFERENCIA EN CURITIBA, BRASIL

RESUMEN: Introducción: Las tasas de resistencia antimicrobiana están en aumento tanto en el ámbito hospitalario como en el comunitario, creando un escenario propicio para el desarrollo de superbacterias, por lo que son necesarios estudios locales para una gestión adecuada de los actuales arsenales antimicrobianos y hacer frente al escenario bacteriológico actual. Objetivo: El alcance de este estudio pretende trazar el perfil epidemiológico bacteriano en un hospital de Curitiba, Brasil y asociarlo a la eficacia de la terapia antimicrobiana. Metodología: Los datos de 2019 a 2021 fueron recogidos por el Centro de Epidemiología y Control de Infecciones Hospitalarias (CECIH), siendo un estudio cuantitativo unicéntrico. Resultados: Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Staphylococcus epidermidis, Pseudomonas aeruginosa, Enterococcus faecalis, Acinetobacter baumannii, Staphylococcus haemolyticus, Staphylococcus hominis y Enterobacter cloacae fueron los microorganismos más frecuentes detectados. A. baumannii y K. pneumoniae presentaron los coeficientes medios de sensibilidad más bajos, mientras que S. aureus fue el más sensible. La eritromicina fue el agente antimicrobiano menos eficaz, mientras que la daptomicina fue el más eficaz. Conclusión: Estos resultados concuerdan con la literatura y pueden ser utilizados para optimizar las terapias empíricas, pues ya existen importantes fracasos terapéuticos asociados a la resistencia antimicrobiana.
PALABRAS CLAVE: Infección Adquirida en la Asistencia Sanitaria; Eskape; Susceptibilidad Antimicrobiana.

1. INTRODUCTION

With the increasing rates of antimicrobial resistance in nosocomial and community infections, therapeutic options are becoming scarce. The spectrum of antimicrobials used to treat bacterial infections varies according to local and regional epidemiology and the resistance mechanisms present, as there is statistical variability in the sensitivity and resistance profiles of superbacteria among hospitals worldwide. This variation stems from the influence of factors that favor the development of antibiotic resistance mechanisms, such as the irrational use of antimicrobials. The advancement of such mechanisms creates a vulnerable scenario in therapeutics against super bacteria and patient safety in hospital settings, causing higher monetary costs for the public health system (SALEEM et al., 2019).

The development of this research is justified by the need for regular studies that track the incidence of pathogens in hospital environments and their sensitivity profiles. This is necessary to contribute to the literary arsenal on the subject and improve the effectiveness of both empirical and defined measures to control the spread of these bacteria.

Thus, this study aimed to trace the bacterial epidemiological profile in a general reference hospital in Curitiba, Paraná, Brazil, and associate this profile with the effectiveness of antimicrobial therapies of greater clinical use.

2. MATERIALS AND METHODS

This study evaluated the main bacteria identified by culture and their sensitivity coefficients to the antimicrobials for which they were tested. It is a descriptive study, with a documental character and quantitative approach, conducted at the Center for Epidemiology and Hospital Infection Control (CEHIC) of a general hospital in Curitiba, PR, Brazil. Data were collected from May to July 2021, encompassing data from January 1, 2019, to July 13, 2021.

The data were mostly collected using Excel spreadsheets made available on computers at CEHIC, and information about the death and transfer of some patients was collected from the electronic medical records in the hospital's information system.

This study included data referring to positive cultures for microorganisms of bacterial origin within the collection period defined above, regardless of age, sex, and hospital sector. Records outside the defined collection period and microorganisms of nonbacterial origin were excluded.

Data were collected from all cultures that were positive for microorganisms of bacterial origin at three distinct intervals: January 1 to December 31, 2019; January 1 to December 31, 2020; and January 1 to July 13, 2021. Within each interval, information was obtained on the identified species and their respective quantities. It also included data to define the sensitivity profile (quantity of specimens tested and sensitivity for each antimicrobial evaluated) of each species to the antimicrobials for which they were tested.

All data were checked and analyzed using Excel 2013 software. The development and analysis of the results were performed using descriptive statistics, mainly using the mean as a measure of central tendency, and highlighting the maximum and minimum values as measures of variability.

2.1 Microorganisms of Bacterial Origin Identified by Culture

All microorganisms of bacterial origin identified by culture in the hospital are listed and grouped by species in each of the three intervals considered for the organization of these data. In this study, only the ten most prevalent pathogens, which coincided in the three periods considered, were selected for analysis in each of the defined intervals.

2.2 Sensitivity Profile of Microorganisms of Bacterial Origin Identified by Culture

Each microorganism identified in the study hospital was categorized by the CEHIC team through antimicrobial susceptibility testing as sensitive, intermediate, or resistant interpretative categories. These are defined by the Clinical and Laboratory Standards Institute (CLSI) guideline M23–Performance Standards for Antimicrobial Susceptibility Testing. Selection by the CEHIC team, in which antimicrobials were tested for each of the microorganisms identified in the study hospital, was made through standardized evaluations by the CLSI and the Brazilian Committee on Antimicrobial Susceptibility Testing (BRCAST).

Based on this categorization, the sensitivity coefficients of the microorganisms to the antimicrobials tested at each of the three intervals were calculated and are presented as percentages. This calculation was based on the definition presented by Administrative Rule No. 2616 of May 12, 1998, from the Ministry of Health, which regulates the Hospital Infection Control Program in Brazil.

To perform a population estimate, only the results in which the total number of specimens tested was greater than or equal to 30 in the period in question were considered valid. The results of the sensitivity tests with fewer than 30 specimens of a microorganism for a specific agent in one of the three periods were considered untested, along with the antimicrobials for which no tests were performed. Sensitivity coefficients that were missing due to a lack of testing and those considered invalid were not highlighted in the results of this study. Subsequently, only antimicrobials suggested by the CLSI were selected for routine testing within the analysis of each of the highlighted pathogens, as defined by the M001S guidelines.

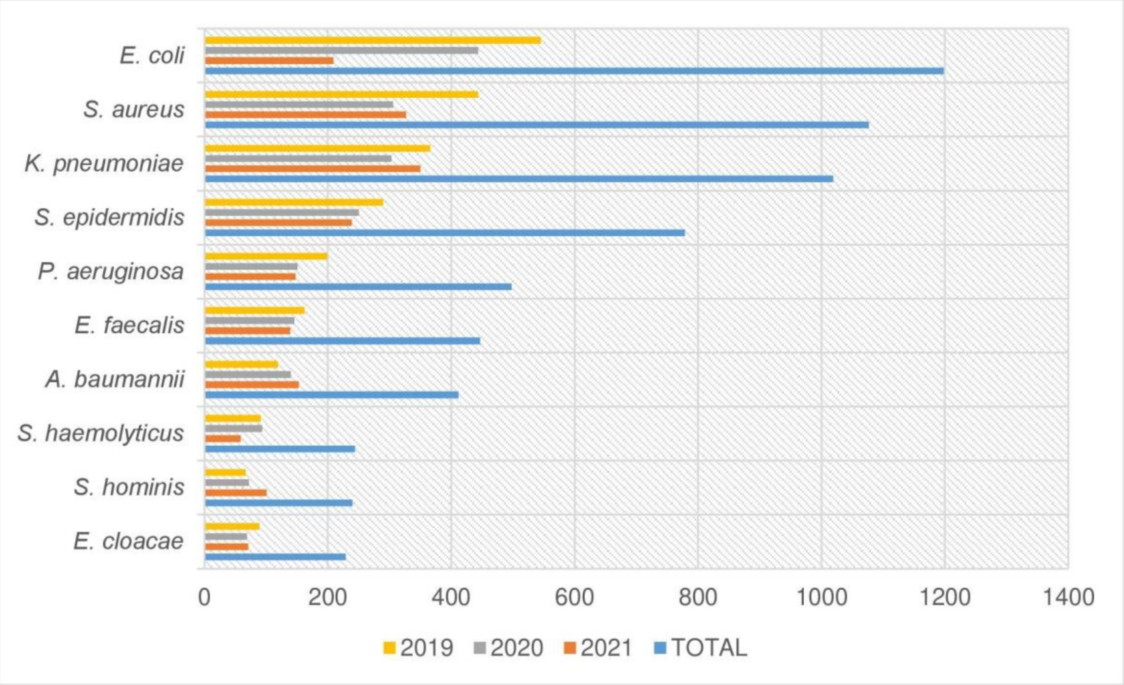
The ten most prevalent pathogens in this study were listed in ascending order of sensitivity profile, defined by the authors from the averages of all valid sensitivity coefficients for each species. During the analysis of the sensitivity profile of each of these, the antimicrobials with the highest and lowest mean sensitivity coefficients were highlighted.

3. RESULTS

3.1 Bacteria Identified by Culture

All bacterial specimens were identified using hospital cultures. In each of the three periods considered, ten bacteria were the most prevalent. Among them, *Escherichia coli* was the most frequent (1198 specimens), considering the entire collection period, and *Enterobacter cloacae* (229) was less prevalent. The number of specimens observed during each period is shown in Figure 1.

Figure 1 - The most prevalent pathogens among all those identified by culture in the study hospital.

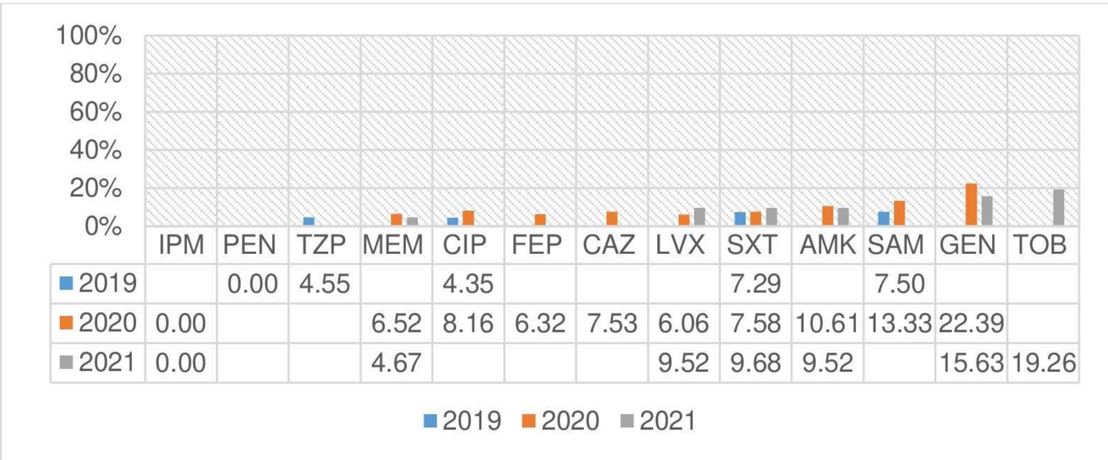


3.2 Sensitivity Profile of Bacteria Identified by Culture

The sensitivity coefficients of the 10 most prevalent species to the antimicrobials were analyzed. The results showed that Acinetobacter baumannii had the lowest overall average sensitivity coefficient (8.20%), followed by Klebsiella pneumoniae (35.61%), Staphylococcus non-aureus (50.35%), E. cloacae (54.81%), Enterococcus faecalis (73.17%), Pseudomonas aeruginosa (74.37%), E. coli (74.73%), and Staphylococcus aureus (77.66%). *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, and *Staphylococcus hominis* were grouped into a single group: *S. non-aureus*.

With the most concerning sensitivity profile, *A. baumannii* presented the lowest sensitivity coefficients to imipenem and penicillin, for which the microorganism had already documented intrinsic resistance. The highest sensitivity coefficient did not exceed 30%, with most of the results below 20% (Figure 2).

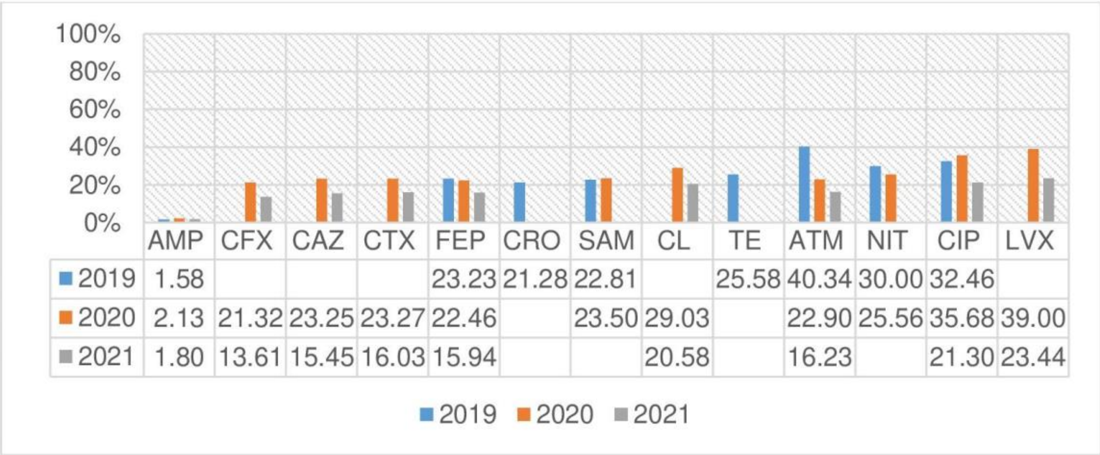
Figure 2 - A. baumannii sensitivity profile as a percentage. IPM - Imipenem, PEN - Penicillin not specified, TZP - Piperacillin and Tazobactam, MEM - Meropenem, CIP - Ciprofloxacin, FEP - Cefepime, CAZ - Ceftazidime, LVX - Levofloxacin, SXT - Sulfamethoxazole and Trimethoprim, AMK - Amikacin, SAM - Ampicillin and Sulbactam, GEN - Gentamicin, TOB - Tobramycin.

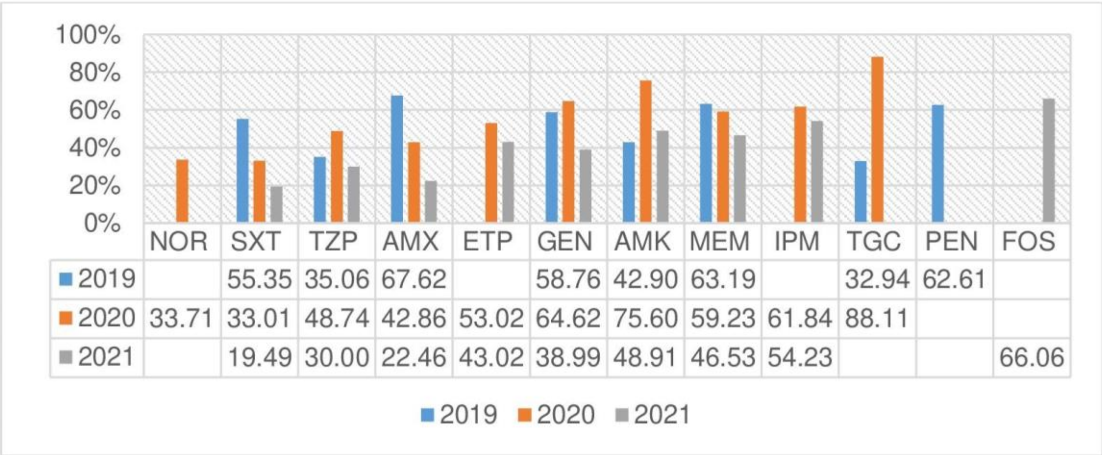


	IPM	PEN	TZP	MEM	CIP	FEP	CAZ	LVX	SXT	AMK	SAM	GEN	TOB
2019		0.00	4.55		4.35				7.29		7.50		
2020	0.00			6.52	8.16	6.32	7.53	6.06	7.58	10.61	13.33	22.39	
2021	0.00			4.67				9.52	9.68	9.52		15.63	19.26

With the second-lowest overall mean, *K. pneumoniae* showed the lowest sensitivity coefficient to ampicillin (for which the microorganism has already documented intrinsic resistance). The best results were observed for amikacin in 2020 and tigecycline in 2020 (Figure 3).

Figure 3 - K. pneumoniae sensitivity profile in percentages. AMP - Ampicillin, CFX - Cefuroxime, CAZ - Ceftazidime, CTX - Cefotaxime, FEP - Cefepime, CRO - Ceftriaxone, SAM - Ampicillin and Sulbactam, CL - Chloramphenicol, TE - Tetracycline, ATM - Aztreonam, NIT - Nitrofurantoin, CIP - Ciprofloxacin, LVX - Levofloxacin, NOR - Norfloxacin, SXT - Sulfamethoxazole and Trimethoprim, TZP - Piperacillin and Tazobactam, AMX - Amoxicillin, ETP - Ertapenem, GEN - Gentamicin, AMK - Amikacin, MEM - Meropenem, IPM - Imipenem, TGC - Tigecycline, PEN - Penicillin not specified, FOS - Phosphomycin.





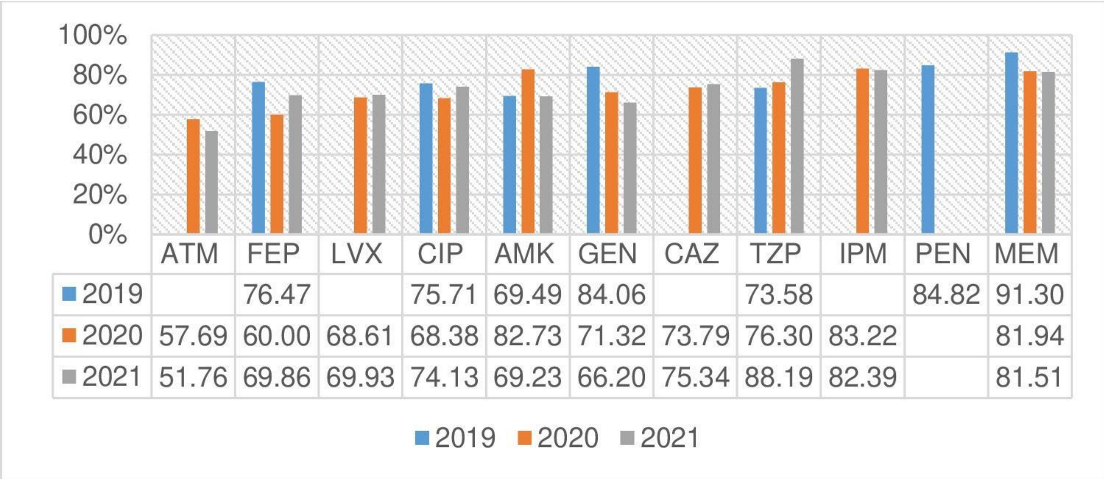
Additionally, *S. non-aureus* showed the worst sensitivity profile for erythromycin. The best results were obtained with linezolid and vancomycin in tests conducted in 2020 and daptomycin in tests conducted in 2020 and 2021.

E. cloacae showed lower sensitivity to ampicillin and its association with sulbactam, with documented intrinsic resistance to both antibiotics. In contrast, meropenem showed the highest mean sensitivity coefficient.

E. faecalis showed lower sensitivity to the antimicrobial streptomycin in 2021, and unspecified tetracycline, for which it showed its prior results in 2020 and 2021, compared to a sensitivity coefficient of 100% in 2019 for this same agent. The best results were obtained in tests performed with nitrofurantoin in 2020 and 2021, and ampicillin in 2019, 2020, and 2021.

P. aeruginosa, despite being the fifth most identified pathogen through cultures performed in the hospital under study, was placed as the third microorganism with the best sensitivity profile to the antimicrobials tested. The lowest sensitivity coefficient for aztreonam is 51.76% in 2021. The best results were obtained with meropenem, with 91.30% sensitivity in tests performed in 2019 (Figure 4).

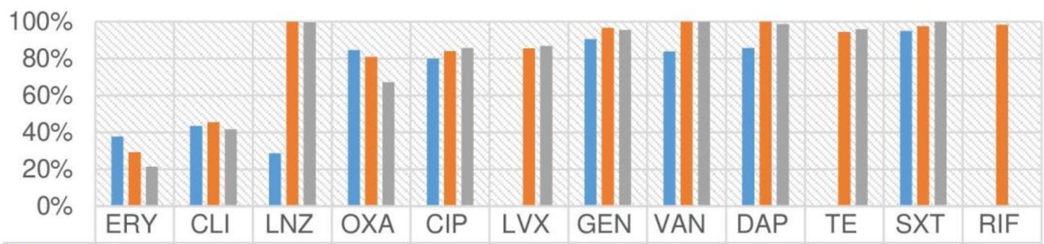
Figure 4 - P. aeruginosa sensitivity profile in percentage. ATM - Aztreonam, FEP - Cefepime, LVX - Levofloxacin, CIP - Ciprofloxacin, AMK - Amikacin, GEN - Gentamicin, CAZ - Ceftazidime, TZP - Piperacillin and Tazobactam, IPM - Imipenem, PEN - Penicillin not specified, MEM - Meropenem.



For *E. coli*, the worst results were observed in tests with ampicillin. Tests performed with imipenem and ertapenem, on the other hand, generated an average sensitivity coefficient above 99%.

The microorganism that responded best to the tested antimicrobials was *S. aureus* (data for this microorganism included both methicillin/oxacillin-sensitive and methicillin-resistant strains). Despite a higher overall mean sensitivity coefficient, the pathogen still showed low sensitivity to some agents such as erythromycin and clindamycin. In contrast, 100% sensitivity was observed for tests performed using linezolid, vancomycin, daptomycin, and sulfamethoxazole in combination with trimethoprim (Figure 5).

Figure 5 - S. aureus sensitivity profile in percent. ERY - Erythromycin, CLI - Clindamycin, LNZ - Linezolid, OXA - Oxacillin, CIP - Ciprofloxacin, LVX - Levofloxacin, GEN - Gentamicin, VAN - Vancomycin, DAP - Daptomycin, TE - Unspecified Tetracycline, SXT - Sulfamethoxazole and Trimethoprim, RIF - Rifampicin.



	ERY	CLI	LNZ	OXA	CIP	LVX	GEN	VAN	DAP	TE	SXT	RIF
2019	37.67	43.51	28.76	84.62	80.00		90.48	83.89	85.71		94.94	
2020	29.33	45.45	100.0	80.95	84.09	85.58	96.76	100.0	100.0	94.42	97.66	98.26
2021	21.54	41.63	99.59	67.30	85.66	86.80	95.55	100.0	98.80	95.88	100.0	

2019 2020 2021

4. DISCUSSION

4.1 Microorganisms of Bacterial Origin Identified by Culture

The prevalence of bacteria found by culture in the general hospital environment in this study showed a predominance of *E. coli* (1198). Despite not belonging to the *Enterococcus faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, and Enterobacter species* (ESKAPE) group, it is on the World Health Organization (WHO) priority list for antimicrobial control. Furthermore, ESKAPE specimens such as *S. aureus* (1077), *K. pneumoniae* (1019), *P. aeruginosa* (498), *A. baumannii* (412), and *E. cloacae* (229) were, in descending order, the most prevalent pathogens in the hospital under study. In addition to the considerable prevalence already documented in several other studies, these specimens have an extensive arsenal of antimicrobial resistance, which hinders therapeutic effectiveness, as highlighted in studies by Gipson et al. and Pérez-Lazo et al (GIPSON et al., 2020; PÉREZ-LAZO et al., 2021).

4.2 Sensitivity Profile of Microorganisms of Bacterial Origin Identified by Culture

The profiles of resistance and sensitivity of pathogens to antibiotics are important points to be analyzed to define an effective therapy. The incidence of resistant specimens has increased not only in hospital-acquired infections but also in infections of community origin. According to Pulingam et al. (2021), the microorganisms most resistant to bacterial infections worldwide include *Enterococcus spp.*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, and *P. aeruginosa*. Of these, *K. pneumoniae* and *E. coli* are most commonly resistant to a wide range of antimicrobials. In Brazil, the overall indexes from the Global

Antimicrobial Resistance and Use Surveillance System (GLASS) in 2021 show that specimens of *Acinetobacter spp, E. coli, K. pneumoniae* and *S. aureus* have a low antimicrobial sensitivity profile in the country, with samples having reported resistances of up to 90% (PULINGAM et al., 2022; SHRIVASTAVA et al., 2018).

Among the susceptibility profiles highlighted in this study, *that of A. baumannii* was the most concerning. A study by Genteluci et al. conducted with 72 isolates of such bacteria from two public hospitals in Rio de Janeiro, Brazil, showed a 96% rate of resistance to carbapenems among the strains under analysis. As this antimicrobial class is one of the main lines of treatment for the offending pathogen, these results are critical. In addition, *A. baumannii* with low sensitivity to carbapenems is highly on the WHO's list of research priorities for antimicrobial control (GENTELUCI et al., 2020; KYRIAKIDIS et al., 2021).

Furthermore, according to a multicenter study by Yoon et al., beta-lactam agents generally have low efficacy. The study shows The sensitivity profile of this pathogen was 39.4% for ampicillin/sulbactam, 28% for piperacillin/tazobactam, 16.7% for ceftazidime, 36.7% for imipenem, and 30.3% for meropenem, an antimicrobial class mentioned above (YOON et al., 2019).

Our study used data from a retrospective analysis by Le et al., which included both community and hospital infections. *K. pneumoniae* showed high resistance to ampicillin (98.41%), cefuroxime (52.50%), and ceftazidime (38.5%) but a low resistance rate to tigecycline (1.58%). Tests performed with carbapenems showed resistance rates of approximately 22% for imipenem, meropenem, and ertapenem (LE et al., 2021).

The resistance rates presented by Le et al. corroborated the sensitivity profiles obtained in our study. It is worth noting that carbapenems are the last line of treatment for multidrug-resistant gram-negative microorganisms. *Klebsiella pneumonia Carbapenemase* (KPC) is the major cause of antibiotic resistance in hospital worldwide. The KPC enzyme makes bacteria resistant to all β-lactam antibiotics and is easily transferred between different species, causing various infections like urinary tract infections, pneumonia, and meningitis (VIEIRA; VICENTINO VIREIRA, 2018). With the increased prevalence of KPC in hospital infections, added to the reserved prognosis, the progressive development of resistance may culminate in increasing threat to public health worldwide (LE et al., 2021; ZHENG et al., 2017).

P. aeruginosa showed the third-best sensitivity profile in this study, despite its high prevalence in hospital settings. Similar results were obtained by Saleem and

Bokhari's analysis of 88 samples collected from infected wound patients admitted to a hospital in Pakistan that were positive for P. aeruginosa. Ciprofloxacin (73.3%), amikacin, imipenem (57.0%), and colistin (58.8%) were used. However, resistance rates to ceftazidime (98%), cefotaxime (97.7%), and tigecycline (94.2%) were high (SALEEM et al., 2019).

Similarly, Yoon et al. demonstrated a good antimicrobial susceptibility profile of *P. aeruginosa*, mainly for carbapenems such as imipenem (77.4%) and meropenem (81.1%), fluoroquinolones such as ciprofloxacin (83.5%), and aminoglycosides such as gentamicin (90.5%) and amikacin (94.5%) (YOON et al., 2019).

Staphylococcus aureus showed the best overall sensitivity profile. A longitudinal study by Stelling et al. showed the susceptibility profiles of the strains collected against oxacillin (71%), erythromycin (52%), gentamicin (98%), and sulfamethoxazole/trimethoprim (98%), corroborating the data presented in this study (STELLING et al., 2021).

5. CONCLUSION

As an answer to the research question, the epidemiological profile found in the hospital under study is consistent with the data presented in the literature. The most common bacteria identified here belong to the ESKAPE group or listed as a priority by the WHO. *A. baumannii* and *K. pneumoniae* were identified as low-sensitivity profile pathogens by GLASS 2021. Other studies corroborate the findings of this research, showing low rates of sensitivity of *Staphylococcus spp.* to erythromycin, in addition to alarming data on *K. pneumoniae, E. coli,* and *E. cloacae* to ampicillin and sulfamethoxazole with trimethoprim.

The results obtained in this research help society and academia by demonstrating a universal tendency of several pathogens to reduce the susceptibility to antimicrobials of wide clinical use. This fact the need for the scientific community to search for alternative therapies, in order to prevent a possible future crisis due to the lack of effective antimicrobials to combat the most common infections. Therefore, we recommend conducting more studies like this one to continuously update the evolution of the epidemiological profiles in hospitals in diverse locations, and to search for possible solutions to the problem presented here.

The limitations of this study include the manual records of the data collected by the study hospital and the authors, which may predispose to typing and proportion errors.

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