ORIGINAL ARTICLE

Antimicrobial resistance in focus: a study on *Klebsiella pneumoniae* in a southern brazilian hospital

Resistência antimicrobiana em Foco: um estudo sobre Klebsiella pneumoniae em hospital do sul do Brasil

Resistencia antimicrobiana en foco: estudio sobre Klebsiella pneumoniae en hospital del sur de Brasil

Laroque, Mariana Fonseca;[1] Martini, Camila de David Tessele;[2] Hartwig, Daiane Drawanz[3]

ABSTRACT

Objective: to identify the antimicrobial sensitivity profile of *Klebsiella pneumoniae* isolates causing infections in a university hospital in southern Brazil. **Method:** this descriptive, observational study analyzed 50 isolates collected from patients hospitalized between August 2022 and May 2023 in a university hospital in southern Brazil. Data collected included date, sex, age, sample type, antibiogram results, and location of hospitalization, obtained from the BD Phoenix™ system. **Results:** all isolates (100%) were sensitive to amikacin, highlighting the potential of aminoglycosides as important therapeutic options. In contrast, none of the isolates showed sensitivity to ampicillin. Notably, 60% of the isolates tested for ceftazidime/avibactam demonstrated sensitivity. The most prevalent resistance markers were carbapenemase production (36%) and extended-spectrum beta-lactamase (32%). **Conclusion:** the study revealed a high level of antibiotic resistance in *K. pneumoniae* isolates.

Descriptors: *Klebsiella pneumoniae*; Cross infection; Drug resistance, multiple

RESUMO

Objetivo: *identificar o perfil de sensibilidade antimicrobiana em isolados de Klebsiella pneumoniae causadores de infecções em um hospital universitário do Sul do Brasil.* ***Método:*** *estudo descritivo e observacional que analisou 50 isolados coletados de pacientes hospitalizados entre agosto de 2022 e maio de 2023 em um hospital universitário no sul do Brasil. Os dados coletados incluíram data, sexo, idade, tipo de amostra, resultados de antibiograma e local de internação, obtidos a partir do sistema BD Phoenix™.* ***Resultados:*** *todos os isolados (100%) foram sensíveis à amicacina, destacando o potencial dos aminoglicosídeos como opções terapêuticas importantes. Em contraste, nenhum dos isolados apresentou sensibilidade à ampicilina. Notavelmente, 60% dos isolados testados para ceftazidima/avibactam foram sensíveis. Os marcadores de resistência mais prevalentes foram produção de carbapenemase (36%) e beta-lactamase de espectro estendido (32%).* ***Conclusão:*** *o estudo revelou alto nível de resistência a antibióticos em isolados de K. pneumoniae.*

Descritores: *Klebsiella pneumoniae; Infecção hospitalar; Resistência a múltiplos medicamentos*

1 Federal University of Pelotas (UFPEL). Pelotas, Rio Grande do Sul (RS). Brazil (BR). E-mail: marianalaroque@yahoo.com.br ORCID: https://orcid.org/0000-0002-8299-9668

2 Federal University of Pelotas (UFPEL). Pelotas, Rio Grande do Sul (RS). Brazil (BR). E-mail: camilatessele@hotmail.com ORCID: https://orcid.org/0000-0002-3605-1294

3 Federal University of Pelotas (UFPEL). Pelotas, Rio Grande do Sul (RS). Brazil (BR). E-mail: daianehartwig@gmail.com ORCID: https://orcid.org/0000-0003-3604-0832

How to cite: Larroque MF, Martini CDT, Hartwig DD. Antimicrobial Resistance in focus: a study on Klebsiella pneumoniae in a southern brazilian hospital. J. nurs. health. 2025;15(1):e1526842. DOI: https://doi.org/10.15210/jonah.v15i1.26842

RESUMEN

Objetivo: *identificar el perfil de sensibilidad antimicrobiana de aislamientos de Klebsiella pneumoniae causantes de infecciones en un hospital universitario del sur de Brasil.* ***Método:*** *estudio descriptivo, transversal, se recogieron 50 aislamientos de pacientes hospitalizados de agosto de 2022 a mayo de 2023 en un hospital universitario del sur de Brasil. Los datos fueron: fecha, sexo, edad, tipo de muestra, antibiograma y lugar de hospitalización, a partir del equipo BD Phoenix™.* ***Resultados:*** *se encontró 100% de sensibilidad a la amikacina, destacando los aminoglucósidos probados como importantes opciones terapéuticas. Por otro lado, ninguno de los aislados mostró sensibilidad a ampicilina. Cabe destacar que el 60% de los aislados sometidos a pruebas de ceftazidima/avibactam fueron sensibles. Los marcadores de resistencia más prevalentes fueron "productor de carbapenemasas" (36%) y "betalactamasa de espectro extendido" (32%).* ***Conclusión:*** *el estudio reveló un alto nivel de resistencia a los antibióticos en los aislados de K. pneumoniae.*
Descriptores: *Klebsiella pneumoniae; Infección hospitalaria; Resistencia a múltiples medicamentos*

INTRODUCTION

Hospitalization favors the exposure of patients to a wide variety of pathogens. In the hospital environment, invasive procedures are routinely performed, and the administration of broad-spectrum antimicrobials is common. The increased survival of patients with a complex clinical condition is possible due to technological advances, and although it is a positive point in care, it also becomes one of the determining factors for the increased risk of Hospital-Acquired Infections (HAIs) or infections hospital in critical patients.[1]

In hospitalized patients, bloodstream infections are the most frequent, followed by ventilator-associated pneumonia and urinary tract infections.[2] Appropriate treatment depends on identifying the pathogen and analyzing the antimicrobial susceptibility profile. The inappropriate use of these drugs leads to the emergence of resistant strains, which pose a threat to global public health. [2] Among HAIs, those caused by multidrug-resistant enterobacteria stand out, limiting therapeutic resources, mainly due to the production of carbapenemase enzymes, which leads to a worsening of the patient's prognosis.[3]

Antibiotic resistance is one of the greatest threats to global health, with an estimated 700,000 people dying each year worldwide from antimicrobial-resistant infections, and the milestone of 10 million deaths per year be reached by 2050.[4] Bacteria belonging to the *Enterobacteriaceae* family is identified as a top priority for the development of new drugs. [5] Among enterobacteria, *Klebsiella pneumoniae*, stands out as a major concern. Comprises gram-negative encapsulated, non-spore-forming, rod-shaped organisms. While it typically resides within the normal enteric microbiota of human hosts, it can also cause infections in various body systems.[6]

In Brazil, the One Health Brazilian Resistance (OneBR) platform plays a pivotal role in the surveillance of antimicrobial resistance. It compiles epidemiological, phenotypic, and genomic data on critical priority microorganisms, such as the pathogen under study, enabling the monitoring and control of multidrug-resistant bacteria. The platform also facilitates communication among healthcare professionals regarding strains detected in different regions. Of note is the use of artificial intelligence to automate antibiotic susceptibility testing, enhancing rapid responses to outbreaks and advancing research into new treatments. It is worth mentioning that the regions most affected by hospital infections caused by resistant microorganisms are the South and Southeast, with fewer cases reported in the North and Midwest. Between 2015 and 2022, the South region alone recorded 3,068 cases, accounting for 36.25%.[7]

Resistance to antimicrobial treatment has increased at an alarming rate in recent years. A recent Brazilian study reported a case in the Northeast region involving a strain of *K. pneumoniae* resistant to all available antibiotic

options. This strain was isolated from an 86-year-old patient with a urinary tract infection who died within 24 hours of hospital admission. Genome sequencing revealed that the strain had previously been detected in the United States and is now circulating in Brazil, posing a potential global risk.[8]

Based on data made available by 87 countries in 2020, the Global Antimicrobial Resistance Report and recent data from the Antimicrobial Use Surveillance System (GLASS), revealed resistance levels above 50% in bacteria that frequently cause sepsis in hospitals, such as *K. pneumoniae*. These data also revealed that 8% of sepsis caused by this pathogen were resistant to carbapenems, increasing the possibility of death from an intractable infection.[9]

Given the significance of infections caused by multidrug-resistant bacteria and the importance of monitoring susceptibility profiles, antimicrobial selection in HAIs should be guided by this data. This study aimed to determine the antimicrobial sensitivity profile of *K. pneumoniae* isolates responsible for infections in a university hospital in southern Brazil.

METHOD

This study adopts a descriptive, observational design.

Bacterial strains

In this study, *K. pneumoniae* samples were collected from hospitalized patients aged 18 years or older who acquired the infection between August 2022 and May 2023 at the University Hospital of the Federal University of Pelotas (UFPel/EBSERH) in Pelotas, Rio Grande do Sul, Brazil. A total of 50 samples were obtained from various sources, including blood, urine, tracheal secretions, penile secretions, cervical secretions, and surgical wounds. Patients under 18 years old, those who did not consent to the use of their previously collected biological samples or recorded data, and those with negative cultures for *K. pneumoniae* were excluded from the study. The isolates were cultured and analyzed at the Clinical Analysis Laboratory of the University Hospital (UFPel/EBSERH) and the Laboratory of Bacteriology and Bioassays (LaBBio) at the Federal University of Pelotas (UFPel), Pelotas, RS, Brazil. Biological material was collected following the institution's standard requests, protocols, and routines, and was not specifically gathered for this study.

Bacterial strains were identified using BD Phoenix™ automated equipment at the University Hospital of UFPel/EBSERH during the study period. The samples were further confirmed using the Polymerase Chain Reaction (PCR) technique by amplifying the species-specific *dnaA* gene. The primers used were *dnaA*-for (TGCCAAGCGACTGCGCTCAA) and *dnaA*-rev (AGCTCTTTGGCCAGCGCCAT), targeting a 467 bp region of the*dnaA* gene. The PCR reaction was conducted with a 25 µL reaction mixture consisting of 13 µL Go Taq® Colorless Master Mix (Promega, USA), 1 µL of each primer, 5 µL of genomic DNA, and ultrapure water to complete the volume. Amplification conditions included an initial denaturation at 94°C for 5 minutes, followed by 35 cycles of denaturation at 94°C for 1 minute, annealing at 58°C for 30 seconds, and extension at 72°C for 1 minute, with a final extension at 72°C for 7 minutes. PCR products were visualized using 1.2% agarose gel electrophoresis.

Ethical considerations

Patient data collected included the date, gender, age, and hospitalization unit (adult precaution clinic, medical clinic, urgency, and emergency network II and III, intensive care unit, obstetrics, surgical clinic, and day hospital). These data were extracted from the BD Epicenter™ software database of the BD Phoenix™ equipment (Becton, Dickinson and Company, New Jersey, USA), utilized at the Microbiology Laboratory (UFPel/EBSERH). Approval was obtained from the Research Ethics Committee at the Faculty of Medicine of UFPel under opinion nº 5,572.210, adhering to Resolution nº. 466/2012 of the National Health Council. All participants were informed of the study's objectives and provided consent for their information to be used by signing an Informed Consent Form. Anonymity was ensured, and ethical research principles were upheld.

Phenotypic detection of antibiotic resistance

The identification of bacterial strains was conducted at the Clinical Analysis Laboratory of the University Hospital (UFPel/EBSERH) using conventional chromogenic and fluorogenic biochemical tests. This process employed the BD Phoenix™ automated system (Becton, Dickinson and Company, New Jersey, USA). For the identification and sensitivity testing of the pathogen, different panels were utilized depending on the sample type. In urine samples, the UNMIC/ID-407 panel (Becton, Dickinson and Company, New Jersey, USA) was employed, while the NMIC/ID-406, NMIC/ID-503, and NMIC-501 panels (also from Becton, Dickinson and Company, New Jersey, USA) were utilized for other sample types. The UNMIC/ID-407 panel includes susceptibility testing for various antibacterials, including Amikacin, Amoxicillin/Clavulanate, Cefazolin, Cefepime, Cefoxitin, Ceftazidime, Ceftriaxone, Cefuroxime, Ciprofloxacin, Ertapenem, Gentamicin, Imipenem, Levofloxacin, Meropenem, Nitrofurantoin, Norfloxacin, Piperacillin/Tazobactam, Tetracycline, Trimethoprim/Sulfamethoxazole and others. Additionally, it includes tests for ESBLproducing strains such as Cefotaxime/Clavulanate, Ceftazidime/Clavulanate, Cefpodoxime-Proxetil, Ceftazidime, and Ceftriaxone/Clavulanate. The NMIC/ID-406 panel, in addition to the above, includes Phosphomycin and Tigecycline but excludes Nitrofurantoin and Norfloxacin. The NMIC/ID-503 panel includes all the tests from the UNMIC/ID-407 panel and adds susceptibility tests for Colistin, Ceftazidime/Avibactam, and Temcycline. Lastly, the NMIC-501 panel provides identification of resistance markers of the AMBLER classes (A, B, and D), along with susceptibility testing for Ceftolozane/Tazobactam, in addition to the other antimicrobials listed. Bacterial identification and sensitivity testing adhered to the recommendations of the Brazilian Committee on Antimicrobial Susceptibility Testing (BrCAST) and the manufacturer's guidelines. Multidrug-resistant (MDR) *K. pneumoniae* isolates were defined by non-susceptibility to at least one agent in three or more antibiotic categories.[10]

The data were organized and results expressed by descriptive statistics, tabulated, and analyzed using the Microsoft Excel® Program. To improve the dissemination of observational studies, the STROBE Checklist http://strobe-statement.org/ was used.

RESULTS

Regarding the age range and sex of hospitalized patients infected by *K. pneumoniae* in this study, ages ranged from 18 to 84 years, with an average of 62 years. Sixty-four percent (n=32) of the patients were male.

Furthermore, the most frequently contaminated sample type was urine (n=24), representing 48%, followed by 22% blood (n=11). This distribution is further illustrated in Table 1. The distribution of *K. pneumoniae* infections in this study can be seen in Table 2, and they were more frequent in the medical clinic 30% (n=15), and in the Urgency and Emergency Network 28% (n=14).

Regarding the sensitivity profile to antibiotics, the bacteria exhibited greater susceptibility to amikacin (100%), gentamicin (62%), meropenem (34%), imipenem (32%), and ertapenem (26%). Noteworthy is the significant sensitivity observed in samples tested for ceftazidime-avibactam (n=25), with a sensitivity rate of 60%. Conversely, the antimicrobials with the highest resistance rates were ampicillin (100%) and cephalosporins (84% to 92%). These findings are better detailed in Table 3.

According to the results, resistance markers analyzed included Extended Spectrum Beta-lactamases (ESBL), Metallo-beta-lactamase (MBL), and Carbapenemase Producer (CARB). The presence of ESBL was detected in 32% of samples; however, when combined with other resistance markers, this percentage rose to 52%. CARB was identified in 36% of samples individually, and in combination with other markers, it constituted 54% of samples.

Table 1. Types of samples analyzed from 50 patients hospitalized at the University Hospital of the Federal University of Pelotas with K. pneumoniae infection in Pelotas, RS, Brazil, from August 2022 to May 2023.

Sample	Percentage (n)
Urine	48 (24)
Blood	22 (11)
Tracheal secretion	20 (10)
Cervical secretion	02 (1)
Ascitic fluid	02 (1)
Operative wound	02 (1)
Liver puncture sample	02 (1)
Penile secretion	02 (1)

Source: BD Epicenter™ software database of the BD Phoenix™ equipment (Becton, Dickinson and Company, New Jersey, USA), utilized at the Microbiology Laboratory (UFPel/EBSERH), 2022-2023.

Table 2. Distribution of *K. pneumoniae* infections by hospital sector at the University Hospital of the Federal University of Pelotas in Pelotas, RS, Brazil, from August 2022 to May 2023.

Hospitalization sectors	Percentage (n)
Medical Clinic	30 (15)
Urgency and Emergency Network	28 (14)
Adult precaution clinic	22 (11)
Intensive care unit (ICU)	14 (7)
Obstetrics	02 (1)
Surgical clinic	02 (1)
Day hospital	02 (1)

Source: BD Epicenter™ software database of the BD Phoenix™ equipment (Becton, Dickinson and Company, New Jersey, USA), utilized at the Microbiology Laboratory (UFPel/EBSERH), 2022-2023.

Table 3. Percentage of antimicrobial susceptibility to *K. pneumoniae* infections at the University Hospital of the Federal University of Pelotas in Pelotas, RS, Brazil, from August 2022 to May 2023.

Class	Antibiotic	MIC Equivalent Cutoff Points (mg/L)* S≤	R>	S% (n)	I% (n)	R% (n)	NT% (n)
Aminoglycosides	Amikacin	8	>8	100 (50)	00 (0)	0 (0)	00 (0)
	Gentamicin	2	>2	62 (31)	00 (0)	38 (19)	00 (0)
Cephalosporins	Cefepime	1	>4	06 (3)	02 (1)	92 (46)	00 (0)
	Ceftazidime	1	>4	08 (4)	08 (4)	84 (42)	00 (0)
	Ceftriaxone	1	>2	08 (4)	00 (0)	92 (46)	00 (0)
Penicillin	Ampicillin	8	>8	00 (0)	00 (00)	100 (50)	00 (0)
Beta-lactam + beta-lactamase inhibitor	Piperacillin/ Tazobactam	8[5]	>8[5]	20 (10)	00 (0)	80 (40)	00 (0)
Carbapenems	Imipenem	2	>4	32 (16)	14 (7)	54 (27)	00 (0)
	Ertapenem	0,5	>0,5	26 (13)	00 (0)	74 (37)	00 (0)
	Meropenem	2	>8	34 (17)	00 (0)	58 (29)	08 (4)
Fluoroquinolones	Ciprofloxacin	0,25	>0,5	14 (7)	00 (0)	86 (43)	00 (0)
	Levofloxacin	0,5	>1	12 (6)	02 (1)	82 (41)	04 (2)
Sulfonamides Folate metabolic pathway inhibitors	Sulfamethoxazole +Trimethoprim	2	>4	30 (15)	00 (0)	64 (32)	06 (3)

Subtitle: Sensitive (S); Intermediate (I); Resistant (R); Not tested (NT)

* BrCAST – Brazilian Committee of Antimicrobial Sensitivity Testing. Cutoff point tables for interpreting MICs and halo diameters. 2023. Available at: https://brcast.org.br/wp-content/uploads/2022/09/Tabela-pontos-de-corte-rCAST-15-03-2023.pdf.

Source: BD Epicenter™ software database of the BD Phoenix™ equipment (Becton, Dickinson and Company, New Jersey, USA), utilized at the Microbiology Laboratory (UFPel/EBSERH), 2022-2023.

Table 4. Resistance markers related to *K. pneumoniae* infections at the University Hospital of the Federal University of Pelotas in Pelotas, RS, Brazil, from August 2022 to May 2023.

Marcador de Resistência	Percentage (n)
ESBL	32 (16)
ESBL/MBL	04 (2)
CARB	36 (18)
CARB/MBL	02 (1)
ESBL/CARB	16 (8)
Nenhum	10 (5)

Source: BD Epicenter™ software database of the BD Phoenix™ equipment (Becton, Dickinson and Company, New Jersey, USA), utilized at the Microbiology Laboratory (UFPel/EBSERH), 2022-2023.

DISCUSSION

The data found, compared with the literature, shows that HAIs continue to be an important threat to users and health services, especially to infections caused by multidrug-resistant *K. pneumoniae*, requiring a careful and vigilant approach to issues involving prevention and treatment in the hospital environment.

In a study carried out at the same hospital in 2021, 286 antibiogram reports of microbiological cultures from inpatients and outpatients were analyzed, with *K. pneumoniae* being identified as the most prevalent pathogen, and among the Gram-negative bacilli, it was the most resistant (27.5%).[11] A study aiming to determine the profile and prevalence of healthcare-related infections found that *K. pneumoniae* accounted for 26.3% of 780 HAIs.[12] In another Brazilian study analyzing 466 clinical samples from patients admitted to an adult ICU between 2018 and 2020, 246 were positive for *K. pneumoniae* (53%), underscoring the significance of this pathogen in the hospitalization context.[13]

Given the high prevalence of infections caused by this pathogen, health services (hospitals, clinics and outpatient clinics) must send isolates from samples used in the investigation of HAI outbreaks, in the event of cases of infection or colonization by a microorganism with relevant resistance mechanisms, to the laboratories of the RNLSPA (made up of all the public health laboratories at the three levels of health management, distributed among the National Reference Laboratories, Central Public Health Laboratories (Lacen) and Municipal Laboratories), in accordance with established and agreed flows, to tackle antimicrobial resistance, including investments in the infrastructure of public health laboratories, professional qualification engagement, the Program for the Control of Infections related to healthcare environments, promotion of research, rational use of rational use of medicines and data collection and analysis to understand the national and regional epidemiological and regional epidemiological scenario in order to support decision-making.[7]

These findings align with previous studies indicating that the most common age group affected is over 50 and 70 years old, with males being predominant, representing 64% and 52.8% of the sample, respectively.[11,14] The literature suggests that immune response tends to decrease with advancing age, rendering individuals more susceptible to infections, thus supporting the predominant age group observed in this study.[15]

Corroborating the data found, Jara *et al*. also identified that the majority of samples (56.6%) used in their study came from urine cultures.[11] Urinary tract infection is the most common HAI. This data is important for assessing the infections that occur during hospitalization and the use of antimicrobials, as well as the interventions needed to prevent their spread, which can occur, among other things, due to the ability of *K. pneumoniae* to form biofilm on hospital devices, such as urinary and intravenous catheters. It is therefore essential to pay attention to strict prevention measures such as proper hand hygiene, regular cleaning, and disinfection of equipment and surfaces, as well as the adoption of contact precautions when dealing with colonized or infected patients.[1]

The occurrence of infection by this bacterium in the adult ICU totaled 14% of the samples collected, which is in line with another study carried out at the same institution, which found 23.4%.[11] Although some studies indicate a higher incidence of infections in ICUs, in this study, hospitalization units collectively accounted for 86% of cases.[16-17] It is possible to attribute this difference to the fact that in the study site, the number of beds available in the ICU is much lower than those available in clinical units, making it interesting to take a special look at the prevalence and characteristics of these infections in the ICU, considering its particularities and complexity.

The importance of utilizing and monitoring the sensitivity/resistance patterns of antimicrobials against microorganisms is emphasized considering treatment failures, often necessitating empirical approaches. However, guidance towards new therapeutic strategies enhances treatment success. The escalating prevalence of bacteria resistant to various antimicrobials poses a significant challenge for healthcare professionals, necessitating regular reviews and analyses. Gentamicin and amikacin, commonly prescribed aminoglycosides for Gram-negative infections, act on protein synthesis but are associated with notable toxic effects and limited perfusion in abdominal and pulmonary infection sites.[18-19] Low resistance to aminoglycosides has also been found in other publications, but despite their good results *in vitro*, few studies indicate their use as monotherapy in severe infections, and they are only indicated for some urinary infections caused by carbapenem-resistant Enterobacteriaceae.[20] In a Brazilian study evaluating 224 *K. pneumoniae* isolates, 55.6% exhibited sensitivity to amikacin, and 58.3% to gentamicin.[21] Another study involving 144 patients reported sensitivity rates of 100% for amikacin and 77.2% for gentamicin, imipenem, and meropenem.[22]

In infections caused by *K. pneumoniae*, carbapenems such as ertapenem, imipenem, and meropenem are frequently utilized antibiotics.[23] These antibiotics function by binding to penicillin-binding proteins on the bacterial cell membrane, thereby impeding bacterial synthesis of peptidoglycans, like all beta-lactams, and displaying notable resistance to hydrolysis by beta-lactamases.[24] A study conducted in China in 2017 demonstrated higher rates of resistance to carbapenems, cephalosporins, and fluoroquinolones, along with lower resistance to amikacin, tigecycline, and colistin.[25] The high incidence of resistance to carbapenems, reaching 74% in this study, suggests the importance of more comprehensive strategies, such as the use of molecular methods to detect resistance genes, since genetic monitoring allows for greater attention to the dissemination of these genes and helps with preventive measures.[20]

To combat the escalating antimicrobial resistance, pharmacological combinations of beta-lactam antibiotics and beta-lactamase inhibitors, such as ceftazidime-avibactam, have been explored as treatment options. In this study, 25 isolates were tested for susceptibility to ceftazidime-avibactam, of which 15 (60%) were sensitive to the drug. Supporting this, a study conducted in Egypt from 2020 to 2021 involving 134 cancer patients with positive *K. pneumoniae* cultures suggested ceftazidime/avibactam as a potential therapeutic alternative for carbapenem-resistant *K. pneumoniae* infections.[26] Additionally, Scientific Technical Opinion 1/2023 of Hospital HE-UFPE/EBSERH indicated that ceftazidime-avibactam demonstrated scientific evidence of non-inferiority compared to carbapenems in treating infections caused by ESBL-producing bacteria, exhibiting superior outcomes in terms of clinical response, mortality, clinical cure, and nephrotoxicity.[27] Even so, it is worth mentioning that the Epidemiological Bulletin on carbapenem-resistant microorganisms and their distribution in Brazil, 2015 to 2022, highlights the significant increase in the *blaNDM* gene, which confers resistance not only to carbapenems but also to new combinations of drugs, such as beta-lactams combined with beta-lactamase inhibitors, such as ceftazidime-avibactam, with the potential to make NDM-producing

bacteria resistant to all available antibiotics.[7] Regarding the result of sensitivity to ampicillin, it is worth highlighting that some bacteria present intrinsic resistance to some antibiotics, as is the case of *K. pneumoniae* to ampicillin, as this medication does not play a role in bacteria that produce beta-lactamase.[22]

The high rates of resistance are primarily attributed to the dissemination of resistance mechanisms, such as the production of enzymes known as beta-lactamases, capable of hydrolyzing beta-lactams. Given this, more government investment is needed in measures to prevent and control infections caused by resistant microorganisms, as well as encouraging the technological development of new antibacterial classes.[28]

In searching for the characteristics of microbial factors in healthcare-associated infections, in Poland from 2011 to 2018, the second most common pathogen found was *K. pneumoniae* ESBL, which demonstrated 93.7% resistance to fluoroquinolones and insensitivity to aminoglycosides only at a level of 41.7%. Unlike the findings of the present study, among the *K. pneumoniae* ESBL strains, they did not observe resistance to carbapenems and reported a slight decrease in resistance to amikacin.[29] In a study carried out in a teaching hospital in western Pará on the bacterial resistance profile of *K. pneumoniae*, it was observed that 32% of cases presented ESBL, 24% presented greater resistance to the cephalosporin class, 28% to beta-lactams and 16% to other antimicrobials.[14] In the analysis of microbial resistance in 28 clinical isolates of *K. pneumoniae* in bacteremia, the presence of carbapenemases was identified in 10 samples, while metallo-beta-lactamases were not found. In the present study, three samples (6%) were found with this resistance marker.[30] The emerging threat of resistant bacteria has put the world on alert, especially when it comes to thinking about prevention and control measures, such as improving hygiene conditions in areas at risk, access to drinking water, the development of new vaccines, informing the population about the conscious use of antibiotics, promoting technological innovation, developing diagnostic tools and techniques and changing paradigms in the prescription of antimicrobial drugs.[28]

CONCLUSIONS

In this study, among the strains of *K. pneumoniae* isolates analyzed, coming from cultures of hospitalized patients, a sensitivity of 100% to amikacin was found, highlighting the aminoglycosides tested as important therapeutic options, on the other hand, in line with several studies, no sample showed sensitivity to ampicillin. A high percentage of sensitivity to ceftazidime/avibactam stands out among the samples tested for this antimicrobial, corroborating findings in the literature. Regarding the resistance markers analyzed, the most prevalent were Carbapenemase Producer (CARB) and Extended Spectrum Beta-lactamase (ESBL), thus raising concern about the high resistance to antimicrobials, especially in the hospital environment, added to the limitation in the treatment of multi-resistant pathogens. For all of the above, retrospective studies and constant epidemiological monitoring of bacteria in healthcare services are essential strategies for monitoring the evolution of bacterial resistance to antimicrobials.

A limitation of the study is that it was carried out in a single hospital, and although the data was collected over a long period, it covered 50 users, so the findings may differ from those emerging from other experiences.

It is important to emphasize that the susceptibility profiles found in this study only relate to the population studied, but are in line with findings in other locations, revealing a major challenge for the treatment of these infections, especially in the hospital setting.

REFERENCES

1 Gugliotta C, Deiana G, Dettori M, Sotgiu G, Azara A, Castiglia P. Prevalence study on health-care associated infections and on the use of antimicrobials carried out with the light protocol of the European Centre for Disease Prevention and Control. Ann Ig. 2020;32(4):357-367. DOI: https://doi.org/10.7416/ai.2020.2359

2 Pasetti ES, Caiana ABS, Ribeiro KO, Freitas EL, Gomes ECS, Pereira LGS, et al. Antimicrobial sensitivity profile of nosocomial bacteria in a hospital in ABC São Paulo, in 2020. Braz. J. Infect. Dis. (Online). 2022;26. DOI: https://doi.org/10.1016/j.bjid.2021.101822

3 Kalın G, Alp E, Chouaikhi A, Roger C. Resistance to multiple antimicrobial drugs: clinical implications for the management of infections in critically ill patients. Microrganisms. 2023;11(10):2575. DOI: https://doi.org/10.3390/microorganisms11102575

4 O'Neill J. Review on Antimicrobial Resistance. Tackling drug-resistant infections globally. 2016. Available from: https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf

5 World Health Organization (WHO). Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug resistant bacterial infections, including tuberculosis. 2017. Available from: https://www.who.int/publications/i/item/WHO-EMP-IAU-2017.12

6 Podschun R, Ullmann U. *Klebsiella spp*. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev. 1998;11(4):589-603. DOI: https://doi.org/10.1128/cmr.11.4.589

7 Ministério da Saúde (BR). Secretaria de Vigilância em Saúde e Ambiente. Boletim Epidemiológico: Microorganismos resistentes aos cabapenêmicos e sua distribuição no Brasil, 2015 a 2022. 2024;55(2). Disponível em: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edicoes/2024/boletim-epidem-vol-55-n-2

8 Vásquez-Ponce F, Vianello M, Becerra J, Pariona JGM, Dantas K, Melocco G, et al. Global epidemiological trend of *Klebsiella pneumoniae* ST340: emergence of subclade KL15 co-producing *K pneumoniae* carbapenemase-2 and New Delhi metallo-ß-lactamase-7 in the Americas. The Lancet microbe. 2025;6(2). DOI: https://doi.org/10.1016/j.lanmic.2024.100990

9 World Health Organization (WHO). GLASS Report: Early Implementation 2020. (Online). 2020. Available from: https://www.who.int/publications/i/item/9789240005587

10 Awoke T, Teka B, Seman A, Sebre S, Yeshitela B, Aseffa A, et al. High Prevalence of Multidrug-Resistant Klebsiella pneumoniae in a Tertiary Care Hospital in Ethiopia. Antibiotics (Basel). 2021;10(8):1007. DOI: https://doi.org/10.3390/antibiotics10081007

11 Jara MC, Frediani AV, Zehetmeyer FK, Bruhn FRP, Müller MR, Miller RG, et a*l*. Multidrug-Resistant Hospital Bacteria: Epidemiological Factors and Susceptibility Profile. Microb Drug Resist. 2021;27(3). DOI: https://doi.org/10.1089/mdr.2019.0209

12 Dudkiewicz FM, Bail L, Ito CAS, Gaspar MDR, Castro JPW, Montes EG. Estudo da frequência e da caracterização das infecções por Klebsiella pneumoniae

carbapenemase em um hospital dos Campos Gerais. Research, Society and Development. 2022;11(16):1-16. DOI: https://doi.org/10.33448/rsd-v11i16.38275

13 Gaspar GG, Ferreira LR, Feliciano CS, Campos Júnior CP, Molina FMR, Vendruscolo ACS, et al. Pre-and post-covid-19 evaluation of antimicrobial susceptibility for healthcare-associated infections in the intensive care unit of a tertiary hospital. Rev. Soc. Bras. Med. Trop. (Online). 2021;54. DOI: https://doi.org/10.1590/0037-8682-0090-2021

14 Gato PC, Maia AL, Santos KAS, Santos LA, Silva EMR. Perfil de resistência bacteriana da klebsiella pneumoniae na unidade de terapia intensiva em um hospital de ensino no oeste do Pará no período de 2018 a 2019. Brazilian Journal of Development. 2022;8(1):1208–25. DOI: https://doi.org/10.34117/bjdv8n1-077

15 Wang Y, Dong C, Han Y, Gu Z, Sun C. Immunosenescence, aging and successful aging. Front Immunol. 2022;13:942796.

DOI: https://doi.org/10.3389/fimmu.2022.942796

16 Rafa E, Wałaszek MZ, Wałaszek MJ, Domański A, Różańska A. The Incidence of Healthcare-Associated Infections, Their Clinical Forms, and Microbiological Agents in Intensive Care Units in Southern Poland in a Multicentre Study from 2016 to 2019. Int J Environ Res Public Health. 2021;18(5):2238. DOI: https://doi.org/10.3390/ijerph18052238

17 Sousa ABA, Ramalho FL, Camargo B. Prevalência de Infecções nosocomiais ocasionadas por Klebsiella pneumoniae produtora de carbapenemase (KPC) em indivíduos hospitalizados. Brazilian Journal of Health Review. 2020;3(2):1915-32. DOI: https://doi.org/10.34119/bjhrv3n2-051

18 Abrantes JA, Nogueira JMR. Resistência bacteriana aos antimicrobianos: uma revisão das principais espécies envolvidas em processos infecciosos. Rev. bras. anal. clin. 2021;53(3):219-223. DOI: https://doi.org/10.21877/2448-3877.202102156

19 Vardakas KZ, Falagas ME. Colistin versus polymyxin B for the treatment of patients with multidrug-resistant Gram-negative infections: a systematic review and meta-analysis. Int J Antimicrob Agents. 2017;49(2):233-8. DOI: https://doi.org/10.1016/j.ijantimicag.2016.07.023

20 Terra E, de Mello W, Santos D. Avaliação do perfil de suscetibilidade aos antimicrobianos de bactérias gram-negativas de origem clínica. Revista Científica do UBM. 2024;26(51):39-50. DOI: https://doi.org/10.52397/rcubm.v26i51.2114

21 Braun G, Cayô R, Matos AP, Fonseca JM, Gales AC. Temporal evolution of polymyxin B-resistant Klebsiella pneumoniae clones recovered from blood cultures in a teaching hospital during 7 years. Int J Antimicrob Agents. 2018;51(3):522-7. DOI: https://doi.org/10.1016/j.ijantimicag.2017.08.031

22 Naue CR, Leite MIM, Colombo A, Silva CF. Prevalência e perfil de sensibilidade antimicrobiana de bactérias isoladas de pacientes internados em Unidade de Terapia Intensiva de um hospital universitário do Sertão de Pernambuco. Semina: Ciências Biológicas e da Saúde. 2021;42(1):15-28. DOI: https://doi.org/10.5433/1679-0367.2021v42n1p15

23 Sharma R, Patel S, Abboud C, Diep J, Ly NS, Pogue JM, *et al*. Polymyxin B in combination with meropenem against carbapenemase-producing *Klebsiella pneumoniae*: pharmacodynamics and morphological changes. Int. j. antimicrob. Agents. 2017;49(2):224-32. DOI: https://doi.org/10.1016/j.ijantimicag.2016.10.025

24 Mora-Ochomogo M, Lohans CT. Β-Lactam antibiotic targets and resistance mechanisms: from covalent inhibitors to substrates. RSC Med Chem. 2021;12(10):1623-39. DOI: https://doi.org/10.1039/d1md00200g

25 Wang S, Dong H, Wang M, Ma W, Cheng Y, Zhou J, et al. Molecular Epidemiology of Carbapenem-Resistant *Klebsiella pneumoniae* in a Tertiary Hospital in Northern China. Can J Infect Dis Med Microbiol. 2022. DOI: https://doi.org/10.1155/2022/2615753

26 El-Kady RAEH, Elbaiomy MA, Elnagar RM. Molecular Mechanisms Mediating Ceftazidime/ Avibactam Resistance Amongst Carbapenem-Resistant *Klebsiella pneumoniae* Isolates from Cancer Patients. Infect Drug Resist. 2022;15. DOI: https://doi.org/10.2147/IDR.S384972

27 Ângelo BHB, Facundes EMN, Paiva GS, Nascimento LR, Silva NVN, Cavalcanti NG, et al. Uso da ceftazidima-avibactam para tratamento de infecções por Enterobactérias multidroga resistentes. Parecer Técnico Científico 1/2023. Hospital das Clínicas da Universidade Federal de Pernambuco. Núcleo de Avaliação da Tecnologia em Saúde. 2023. Disponível em: https://www.gov.br/ebserh/pt-br/hospitais-universitarios/regiao-nordeste/hc-ufpe/ensino-e-pesquisa/sitenovogep/publicacoes/PTC/PARECER_15_CEFTAZIDIMA_AVIBACTAM.pdf

28 Schirmer AA, Beccaria CS, Coser HS. Carbapenemase producing enterobacteria (KPC): alternatives for current pharmacotherapy. Brazilian Journal of Surgery and Clinical Research. 2021;33(3):62-9. Disponível em: https://www.mastereditora.com.br/periodico/20210207_100930.pdf

29 Litwin A, Fedorwicz O, Duszynska W. Characteristics of Microbial Factors of Healthcare-Associated Infections Including Multidrug-Resistant Pathogens and Antibiotic Consumption at the University Intensive Care Unit in Poland in the Years 2011–2018. Int J Environ Res Public Health. 2020;17(19). DOI: http://dx.doi.org/10.3390/ijerph17196943

30 Palmeira DCC. *Bacteremias por Klebsiella pneumoniae: epidemiologia, clínica e mecanismos de resistência microbiana.* [dissertação]. Recife: Programa de Pós-graduação em Medicina Tropical, Universidade Federal de Pernambuco, Recife; 2019. 122 p. Disponível em: https://repositorio.ufpe.br/handle/123456789/35582

Recebido em: 16/04/2024
Aceito em: 26/11/2024
Publicado em: 07/03/2025