

ORIGINAL ARTICLE

Antimicrobial resistance: epidemiological profile of the city of Porto Alegre in 2021-2022.

Resistência antimicrobiana: perfil epidemiológico do município de Porto Alegre em 2021-2022.

Resistencia a los antimicrobianos: perfil epidemiológico de la ciudad de Porto Alegre en 2021-2022

Danilo Lucas Nunes Ribeiro¹ ORCID 0000-0001-6935-2600
Silvia Adriana Mayer Lentz² ORCID 0000-0002-0118-6797
Raquel Cristine Barcella² ORCID 0000-0002-4849-8405

¹Escola de Saúde Pública do Rio Grande do Sul, Programa de residência integrada em Vigilância em Saúde, Porto Alegre, Rio Grande do Sul, Brazil.

²Secretaria Municipal de Saúde, Diretoria de Vigilância em Saúde, Porto Alegre, Rio Grande do Sul, Brazil.

Address: Rua Bento Águido Vieira, 1589, Bela Vista, São José, Santa Catarina, Brasil.
E-mail: danilonunes2@gmail.com

Submetido: 10/03/2025

Aceite: 19/08/2025

ABSTRACT

Background and Objectives: Monitoring multidrug-resistant microorganisms is crucial for containing their spread in healthcare settings. The aim of this study was to describe the main epidemiological characteristics of multidrug-resistant microorganisms identified and reported in Porto Alegre in 2021 and 2022. **Methods:** This quantitative, descriptive epidemiological study is based on an analysis of secondary data from the Porto Alegre Municipal Health Department. **Results:** During the analyzed period, 15,016 multidrug-resistant microorganisms were identified. Enterobacteriales were the most frequently reported microorganisms. An increase in notifications was observed in 2021 and 2022, which was associated with the improvement and strengthening of the city's surveillance process. **Conclusion:** The significant increase in notifications may be related to improvements in epidemiological surveillance, reflecting enhanced monitoring and detection of multidrug-resistant microorganisms in Porto Alegre.

Keywords: *Public Health Surveillance. Drug Resistance. Carbapenems. Drug Resistance Microbial.*

RESUMO

Justificativa e Objetivos: A vigilância de microrganismos multirresistentes é essencial para o controle da disseminação dessas cepas nos serviços de saúde. Este estudo teve

como objetivo descrever as principais características epidemiológicas dos microrganismos multirresistentes identificados e notificados em Porto Alegre nos anos de 2021 e 2022. **Métodos:** Trata-se de um estudo epidemiológico quantitativo e descritivo, baseado na análise de dados secundários provenientes da Secretaria Municipal de Saúde de Porto Alegre. **Resultados:** No período analisado, foram identificados 15.016 microrganismos multirresistentes. As Enterobacteriales permaneceram como os principais microrganismos notificados. Observou-se um aumento no número de notificações nos anos de 2021 e 2022, associado ao fortalecimento e à qualificação do processo de vigilância no município. **Conclusão:** O aumento significativo das notificações pode estar relacionado à melhoria da vigilância epidemiológica, refletindo maior qualificação no monitoramento e detecção dos microrganismos multirresistentes em Porto Alegre.

Descritores: *Vigilância em Saúde Pública. Resistência a Medicamentos. Carbapenêmicos. Resistência Microbiana a Medicamentos.*

RESUMEN

Justificación y Objetivos: La vigilancia de los microorganismos multirresistentes es esencial para el control de la propagación de estas cepas en los servicios de salud. Este estudio tuvo como objetivo describir las principales características epidemiológicas de los microorganismos multirresistentes identificados y notificados en Porto Alegre en los años 2021 y 2022. **Métodos:** Se trata de un estudio epidemiológico cuantitativo y descriptivo, basado en el análisis de datos secundarios provenientes de la Secretaría Municipal de Salud de Porto Alegre. **Resultados:** En el período analizado, se identificaron 15.016 microorganismos multirresistentes. Las Enterobacteriales siguieron siendo los principales microorganismos notificados. Se observó un aumento en el número de notificaciones en los años 2021 y 2022, asociado al fortalecimiento y a la cualificación del proceso de vigilancia en el municipio. **Conclusión:** El aumento significativo de las notificaciones puede estar relacionado con la mejora de la vigilancia epidemiológica, lo que refleja una mayor cualificación en el monitoreo y la detección de los microorganismos multirresistentes en Porto Alegre.

Palabras Clave: *Vigilancia en Salud Pública. Resistencia a Medicamentos. Carbapenêmicos. Farmacorresistencia Microbiana a Medicamentos.*

INTRODUCTION

Antimicrobials represent one of the most important classes of drugs in the history of human health. They have the ability to inhibit or stop the growth of microorganisms, thus resulting in an effective option for treating various diseases. The first antimicrobial, penicillin, appeared in the late 1920s, discovered by physician Alexander Fleming. The importance of antimicrobials became clear during World War II, driving the expansion of research and the emergence of new classes of antimicrobials.^{1,2}

Contemporary to their emergence is antimicrobial resistance (AMR). According to the WHO, AMR occurs when bacteria, viruses, fungi, or parasites can no longer be

destroyed or have their growth limited by a drug to which they were previously sensitive, resulting in difficulties in treating and controlling infections, with prolonged hospitalizations, increasing disease transmission and the risk of death.^{2,3} This resistance can result from several mechanisms: the presence of enzymes that degrade antimicrobials, genetic modification of the target site of the antimicrobial's binding to the microorganism, modification of the microorganism's structures hindering the entry of the antimicrobial, among others.^{4,5}

AMR has been a constant cause for concern. Although it seems like a silent threat, in 2019 it was responsible for a higher mortality rate than other diseases of global concern, such as HIV/AIDS or malaria.⁶ Worldwide, in 2019, an estimated 4.5 million deaths were related to AMR. Of these, 1.27 million were directly attributed to resistance, while the other 3.23 million were deaths associated with it. This data shows how 1.27 million deaths could be prevented simply by using effective antimicrobials against microorganisms.⁷

In the city of Porto Alegre, there has been a significant increase in the number of reports related to the identification of multidrug-resistant microorganisms. Between 2009 and 2018, there was an average annual growth of 33.22% in the number of cases reported by hospitals, from 762 multidrug-resistant microorganisms in 2009 to 6,485 in 2018. Carbapenem-resistant *Klebsiella pneumoniae* accounted for 48.2% of all reported microorganisms, followed by *Acinetobacter* spp. (19.1%) and *Pseudomonas aeruginosa* (10.1%).⁸

In addition to the multidrug-resistant microorganisms reported in Porto Alegre, other examples of antimicrobial resistance have had a significant impact on the incidence of infections on a global scale. A notable case is that of vancomycin-resistant *Enterococcus* spp., which has prevailed in several regions of the world. In the United States, in 2017, approximately 54,500 hospital infections caused by *Enterococcus* spp. resistant to this drug were recorded, resulting in about 5,400 deaths, highlighting the seriousness of the problem.⁹

Given the emergence and spread of multidrug-resistant infections, it is important to understand the current epidemiological situation in the city of Porto Alegre, Rio Grande do Sul. Thus, the main objective of this study is to describe the main epidemiological characteristics of multidrug-resistant microorganisms identified and reported in Porto

Alegre in 2021 and 2022. The current scenario reinforces the need for increased research and studies on the topic, so that standards can be established as a reference for mitigating and combating the occurrence of infections caused by multidrug-resistant microorganisms.

METHODS

This is a quantitative epidemiological study with a descriptive approach. Data collection was based on secondary sources, using official records of hospital notifications of multidrug-resistant microorganisms from the Municipal Health Department of Porto Alegre, referring to the period from 2021 to 2022.

The study scenario comprised all hospitals in the municipality of Porto Alegre capable of reporting MDR, totaling 30 institutions. This network includes hospitals of different sizes and care profiles (public, private, and philanthropic), thus covering the diversity of hospital care in the city, as determined by the municipal surveillance system.

All valid notification records contained in the official databases for the period analyzed were included in the study. As exclusion criteria, notifications that did not correspond to the 2021-2022 time window and duplicate records identified in the data checking and consolidation process were removed.

The databases used were obtained from two systems, since the municipality's notification flow underwent a change in the respective years. Thus, the 2021 data were collected from the Google Forms form provided by the State Health Surveillance Center (CEVS) and Microsoft® Excel spreadsheets in which the hospital institutions made the notifications. The 2022 data was collected from the SENTINELA® Platform. This platform compiles weekly notifications completed in 2022 with information on the detection of multidrug-resistant microorganisms in institutions.

The files were downloaded in Microsoft Excel® format and cleaned (a process of cleaning and standardization) according to predefined variables of interest, which included: Total number of notifications; Identified microorganisms, Identified enzymes (e.g., KPC, NDM, OXA-48, among others); Type of microbial resistance (resistant to carbapenems, etc.); Classification of the event (infection or colonization); Biological material analyzed for identification of the microorganism (e.g., blood, urine, tracheal

secretion); Hospital unit where the material was collected (e.g., ICU, clinic, emergency room).

The analyses were performed using Epi Info 7.2 software, focusing on the description of the absolute and relative frequencies of the variables analyzed. Comparisons between 2021 and 2022 were made based on the observed proportions.

The research was conducted in accordance with the legal precepts of the National Research Ethics Commission. The project was forwarded and submitted to the Ethics Committee of the Rio Grande do Sul School of Public Health and the SMS Research Ethics Committee, with CAEE number 69173323.7.0000. 5312, and was approved with opinion/protocol No. 6,142,337 on June 26, 2023.

RESULTS

In 2021, 7,700 notifications were recorded, in which 7,825 microorganisms with antimicrobial resistance were identified. In 2022, the total number of notifications was lower, with 7,191 notifications and 7,441 multidrug-resistant microorganisms (MDR) identified (Figure 1).

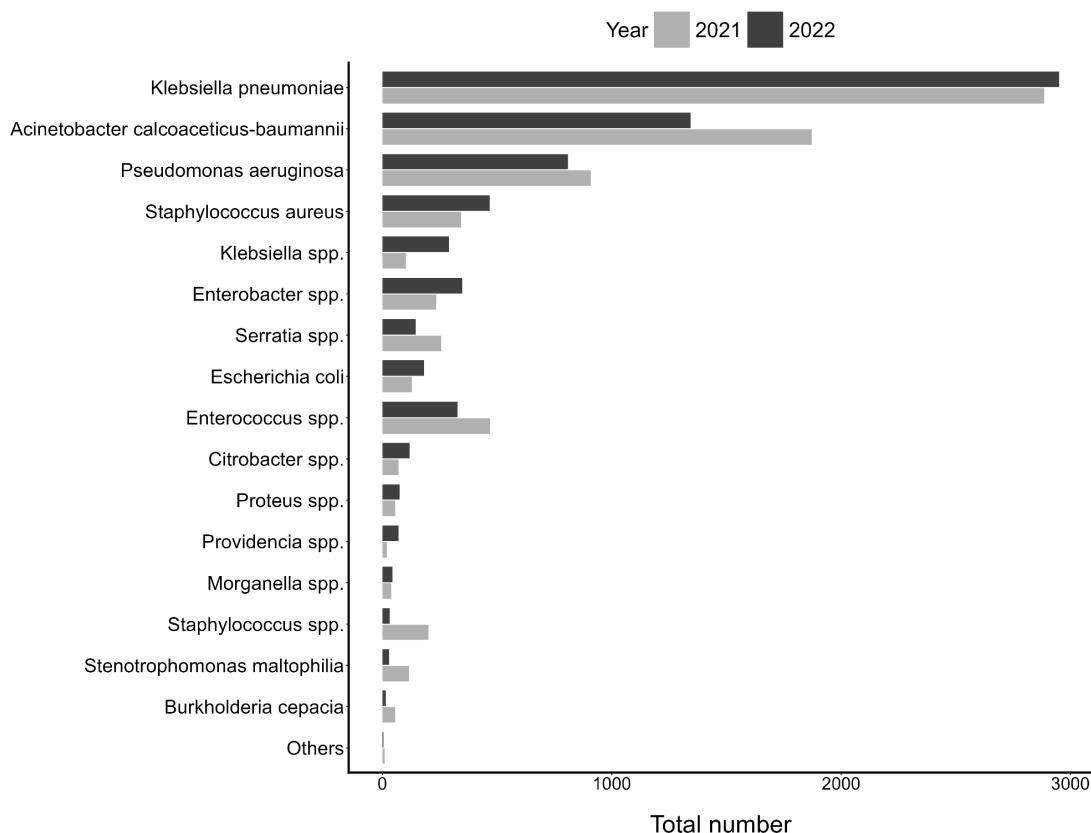


Figure 1. Multidrug-resistant microorganisms identified and reported in the city of Porto Alegre, RS, 2021 and 2022.

In 2021, Enterobacterales were predominant, accounting for 51.5% of notifications. Within this group, the *Klebsiella pneumoniae* complex was the most prevalent, with 36.89% of notifications. The *Acinetobacter calcoaceticus-baumannii* complex was the second most reported microorganism (23.93%), followed by *Pseudomonas aeruginosa* (11.62%) and *Enterococcus* spp. (5.99%) (Figure 1).

In 2022, *Klebsiella pneumoniae* continued to lead the notifications, with 39.65%, followed by the *Acinetobacter calcoaceticus-baumannii* complex (18.06%), *Pseudomonas aeruginosa* (10.87%), and *Staphylococcus aureus* (6.29%) (Figure 1).

Among the classes of antimicrobials analyzed, carbapenems had the highest resistance rates, accounting for 55.2% of notifications in 2021, with an increase to 66.7% in 2022. Resistance to third- and fourth-generation cephalosporins showed a statistically significant increase ($p < 0.001$), rising from 0.2% (2021) to 10.9% (2022). Additionally, in 2022, there were reports of resistance to sulfamethoxazole/trimethoprim, which had not been observed in the previous year (Figure 2).

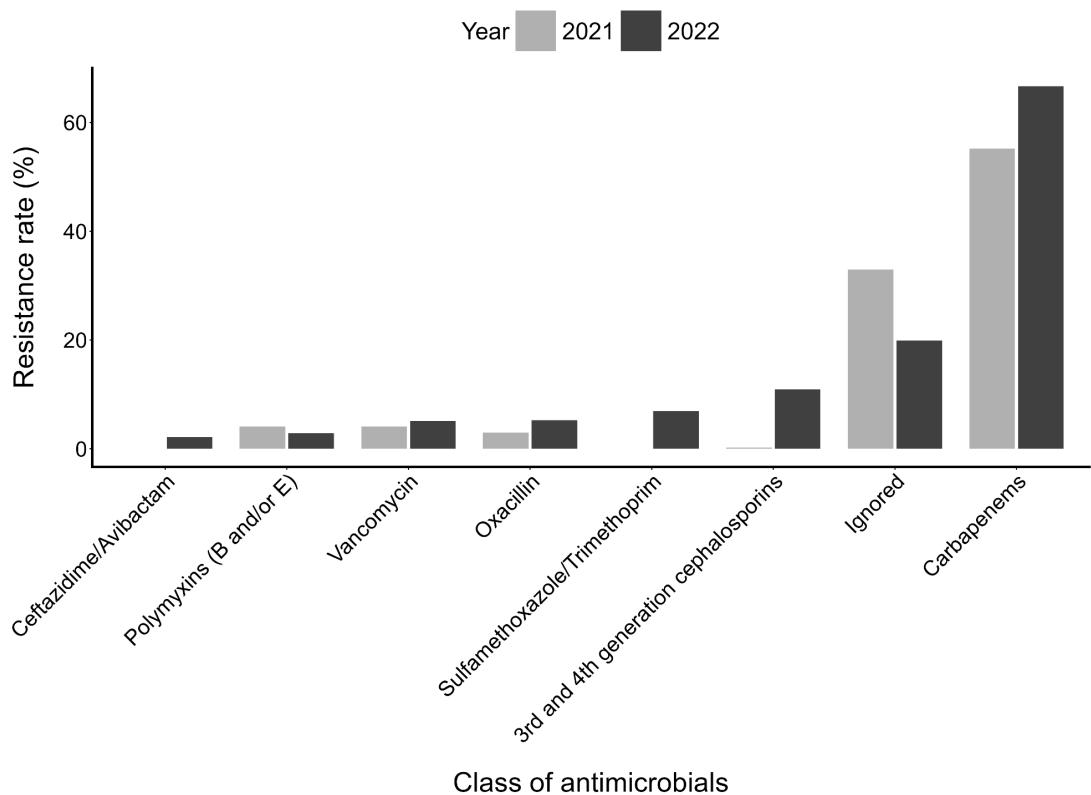


Figure 2. Distribution of antimicrobial resistance by antibiotic class in Porto Alegre, RS, 2021 and 2022.

It is worth noting that in 2021, in 33% of cases, the microbial resistance field was ignored, while in 2022 this omission fell to 19.92% (Figure 2).

In 2021, infections accounted for 31.90% of notifications, while colonizations accounted for 20.94%. In 47.16% of cases, this field was not filled in. In 2022, there was an increase in colonizations, which totaled 41.88%, while infections accounted for 38.2%. Only 19.92% of notifications did not have the classification reported (Table 1).

Table 1. Distribution of cases by final classification, material analyzed, hospital unit, and inhibitory enzyme (2021-2022), Porto Alegre, RS.

Variable	2021 N (%) ¹	2022 N (%) ¹	Total N (%) ²	p-valor ³
Final Classification				<0.001
Infection	2.496 (31.90)	2.842 (38.2)	5.338 (35.0)	
Colonization	1.638 (20.94)	3.116 (41.88)	4.754 (31.1)	
Unclassified	3.691 (47.16)	1.482 (19.92)	5.172 (33.9)	
Material Analyzed				<0.001
Surveillance swab	1.811 (23.15)	2.563 (34.45)	4.374 (28.7)	
Urine	1.217 (15.55)	1.490 (20.03)	2.707 (17.7)	
Tracheal aspirate	2.103 (26.88)	1.282 (17.23)	3.385 (22.2)	

Blood	1.289 (16.45)	740 (9.95)	2.027 (13.3)
Sputum	504 (6.46)	369 (4.96)	873 (5.7)
Surgical wound	69 (0.88)	159 (2.14)	228 (1.5)
Bronchial Lavage	61 (0.78)	151 (2.03)	212 (1.4)
Soft Tissues	0	99 (1.33)	99 (0.6)
Cerebrospinal Fluid	7 (0.09)	12 (0.16)	19 (0.1)
Others	764 (9.76)	575 (7.73)	1.339 (8.8)
Hospital Unit			<0.001
Adult ICU	4.289 (54.8)	2.843 (38.21)	7.132 (43.9)
Clinic	2.728 (34.8)	2.715 (36.49)	5.443 (33.5)
Emergency Room	351 (4.49)	810 (10.89)	1.161 (7.1)
Surgical	191 (2.4)	459 (5.4)	650 (4.0)
Outpatient Clinic	169 (2.2)	1.168 (13.85)	1.337 (8.2)
Pediatric ICU	0	136 (1.6)	136 (0.8)
Pediatric Clinic	11 (0.1)	100 (1.2)	111 (0.7)
Oncology	35 (0.4)	69 (0.8)	104 (0.6)
Neonatal ICU	0	63 (0.7)	63 (0.4)
Cardiology	2 (0.02)	24 (0.32)	26 (0.2)
Obstetrics/Gynecology	6 (0.08)	13 (0.17)	19 (0.1)
Neurology	0	010 (0.13)	10 (0.1)
Hemodialysis	1 (0.01)	9 (0.12)	10 (0.1)
Infectious Diseases	3 (0.04)	8 (0.11)	11 (0.1)
Others	38 (0.76)	13 (0.17)	51 (0.3)
Inhibitory Enzyme			<0.001 ⁴
KPC	1.591 (20.33)	1.979 (26.57)	3.570 (23.4)
NDM	225 (2.87)	1.274 (17.12)	1.499 (9.8)
OXA-48	0	20 (0.32)	20 (0.1)
VIM	0	3 (0.04)	3 (0.0)
IMP	0	2 (0.02)	2 (0.0)
Other	0	272 (3.64)	272 (1.8)
Unidentified	6.009 (76.79)	3.890 (52.28)	9.899 (64.8)

Legend: N: number of cases; 1: proportion in relation to the total for the year; 2: proportion in relation to the combined total for the two years (2021+2022); 3: Pearson's chi-square test for final classification, material analyzed, and hospital unit; 4: Fisher's exact test with Monte Carlo simulation (B= 10,000) for Inhibitory Enzyme. ICU: Intensive Care Unit. KPC: *Klebsiella pneumoniae* Carbapenemase; NDM: New Delhi Metallo-beta-lactamase; OXA-48: Oxacillinase-48; VIM: Verona imipenemase; IMP: Imipenemase.

Regarding enzymatic resistance mechanisms, *Klebsiella pneumoniae* carbapenemase (KPC) was the most prevalent enzyme in both years, accounting for 20.33% of notifications in 2021 and increasing to 26.57% in 2022. New Delhi Metallo-

β -lactamase (NDM) showed a significant increase, from 2.87% in 2021 to 17.12% in 2022. IMP, OXA-48 Like, and VIM enzymes were reported in smaller proportions, all with frequencies below 1% (Table 1).

Regarding the clinical materials analyzed, in 2021, tracheal aspirate was the main material, representing 26.88% of the samples, followed by surveillance swabs (23.15%), blood (16.45%), and urine (15.55%). In 2022, surveillance swabs became the most analyzed material, corresponding to 34.45% of samples, followed by urine (20.03%) and tracheal aspirate (17.23%) (Table 1).

Intensive Care Units (ICUs) and Clinical Units were the hospital sectors that most identified multidrug-resistant microorganisms in 2021, with 54.8% and 34.8% of notifications, respectively. However, there was no distinction between the different types of ICUs this year. In 2022, due to changes in the reporting system, it was possible to differentiate between ICUs, with the Adult ICU accounting for 38.21% of reports and Clinical Units accounting for 36.49%. Other sectors, such as Emergency (10.89%) and Surgical Units (6.17%), were also reported (Table 1).

DISCUSSION

This study analyzed the dynamics of notifications of multidrug-resistant microorganisms (MDR) in the hospital network of Porto Alegre in 2021 and 2022. The results confirm a substantial and continuous burden of MDR in the municipality, with 7,700 notifications recorded in 2021 and 7,191 in 2022.

This scenario maintains the high level observed in previous years and continues the significant growth trend already documented in the city, which recorded an average increase of 35% per year between 2009 and 2018⁸. It is worth noting that the year 2020, marked by the onset of the COVID-19 pandemic, showed an atypical drop (5,011 notifications), suggesting possible underreporting or deprioritization of MDR surveillance during that period. Thus, the high number of notifications in 2021 (an increase of approximately 52% compared to 2020) may represent, in part, a resumption of surveillance capacity, in addition to the actual growth of the phenomenon. The slight reduction observed in 2022 (6.61% compared to 2021), while still maintaining a high

level, indicates the endemic persistence of MDR as a critical challenge for local public health.¹⁰

The year 2021 marked the highest number of notifications in the history of MDR surveillance in Porto Alegre. This increase can be attributed to several factors, such as the strengthening of the notification process, changes in registration platforms, data qualification, and greater awareness of hospital units for the surveillance of antimicrobial resistance.⁸

During the period analyzed, the pattern of the main microorganisms reported remained consistent, with three pathogens standing out: the *Klebsiella pneumoniae* complex, the *Acinetobacter calcoaceticus-baumannii* complex, and *Pseudomonas aeruginosa*. The predominance of the *Klebsiella pneumoniae* complex in antimicrobial resistance is a global phenomenon. High resistance rates have been observed in several regions, such as South Africa (68.3%) and Equatorial Guinea (97.17%).¹¹ In Europe, rates vary significantly, with Greece presenting 60% of *K. pneumoniae* strains resistant to carbapenems, while in Italy this rate is 40%.¹¹ In the United States, *K. pneumoniae* is the most prevalent Enterobacterale in the country.¹²

The empirical use of antibiotics in clinical practice and the persistent exposure of *K. pneumoniae* to various antimicrobials are the main factors contributing to the development of resistant strains.¹¹ The mechanisms of co-resistance and co-selection are fundamental in this process. Co-resistance occurs when resistance genes are located on the same genetic element, such as plasmids, transposons, or integrons, facilitating the transmission of resistance between microorganisms. This linkage of genetic elements enables co-selection for other genes located on the same element, thus culminating in the transmission of resistance genes from one microorganism to another.¹³

Like *K. pneumoniae*, the *Acinetobacter calcoaceticus-baumannii* complex has been recognized as an emerging threat for nosocomial infections and antimicrobial resistance, with mortality rates ranging from 40% to 70%.¹⁴ *Pseudomonas aeruginosa*, included in the list of priority pathogens for the development of new antimicrobials, stands out for its metabolic versatility and ability to adapt to different environments, causing acute and chronic infections.^{14,15}

Carbapenems continue to be the class of antimicrobials with the highest resistance in the municipality, reflecting the scenario observed in other South American

countries, where the growth of MDR is marked.¹⁶ While in some countries, such as Australia, resistance to carbapenems is still rare, in others, such as Iran, it reached 56.3% in 2008, a figure close to that observed in Porto Alegre (55% in 2021 and 60% in 2022).¹⁷

It can be inferred from the data found in this study that the qualification of reported data is crucial, as evidenced by the significant reduction in microorganisms without identified resistance in 2022, compared to 2021. In addition, an increase in resistance to third- and fourth-generation cephalosporins was observed in 2022. Resistance to cephalosporins is particularly relevant in *Neisseria gonorrhoeae* infections, one of the most common community-acquired infections worldwide, highlighting the importance of continuous monitoring.¹⁸

K. pneumoniae resistance to carbapenems, mediated by carbapenemases, poses a global threat to public health due to its ability to inactivate most beta-lactams.^{12,18} The most prevalent enzyme in Porto Alegre is *Klebsiella pneumoniae* Carbapenemase (KPC), whose presence is associated with up to a threefold increase in the hospital mortality rate.¹⁹

The New Delhi Metallo-β-lactamase (NDM) enzyme has also gained prominence, with its prevalence increasing significantly in the municipality ($p < 0.001$), from 2.9% in 2021 to 17.1% in 2022 (Table 1). First identified in India in 2010, NDM is known for its rapid spread among different species of Enterobacterales, and the growth observed in Porto Alegre reinforces its potential for expansion.^{19,20}

Classifying the event as colonization or infection provides information that can be extremely useful in managing and monitoring cases, not only in terms of treatment but also prevention. In the United States, identifying patients colonized by vancomycin-resistant *Enterococcus* has been an effective strategy for preventing gastrointestinal infections, given that asymptomatic colonization of the intestine is a key factor in infection by gastrointestinal bacteria.^{9,16} Thus, the importance of adequate monitoring of these aspects is understood, since it allows surveillance to be an instrument for qualifying the process of preventing multidrug-resistant infections.²¹

The appropriate choice of materials collected for sensitivity testing is crucial, since the cut-off points for resistance vary according to the sample site (urinary tract, skin, blood, etc.).^{22,23} In addition, an appropriate choice of sample origin is essential, as each pathogen may be more abundantly present in a particular sample. For example: for the

detection of carbapenemase-producing *Enterobacteriales*, rectal or perirectal swab collection is recommended; for *Acinetobacter calcoaceticus-baumannii* and *Pseudomonas aeruginosa*, oropharyngeal, endotracheal, or wound samples are indicated; while for *Staphylococcus aureus*, nasal swab collection is mandatory.²³

The data presented in this article highlight the importance of a continuous process of qualification in MDR monitoring for establishing the epidemiological profile. Significant changes observed in 2022 highlight the impact of implementing a new reporting platform.

This study has some limitations that should be considered when interpreting the results. First, the use of secondary data from hospital notifications may be subject to underreporting or inconsistencies in data quality, since the completeness and accuracy of the information depend on proper completion by health professionals. In addition, the change in the reporting system between 2021 (Google Forms and Excel spreadsheets) and 2022 (SENTINELA® Platform) may have introduced variations in the way data were collected and recorded, making it difficult to directly compare the two years. Another limitation is the lack of detailed information on the clinical profile of patients, such as comorbidities, previous use of antimicrobials, and clinical outcomes, which could enrich the analysis of factors associated with antimicrobial resistance.

Nevertheless, the high rate of carbapenem resistance in the city of Porto Alegre underscores the urgent need to revise antibiotic prescribing guidelines, focusing on alternative treatments and more judicious use of broad-spectrum antimicrobials.

It is essential that further research evaluate the effectiveness of antibiotic management programs and new protocols for preventing hospital infections, with a view to containing the growth of antimicrobial resistance.

Finally, it is important to monitor multidrug-resistant microorganisms, given the significant increase in the number of notifications made by hospitals in the municipality, as well as endemic variations by microorganism species and their mechanisms of resistance to antimicrobials, which modify the epidemiological profile of MDR in the municipality. Surveillance of the information obtained through notification forms allows for the planning and implementation of effective strategies to mitigate the impacts of antimicrobial resistance.

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AUTHORS' CONTRIBUTIONS

Danilo Lucas Nunes Ribeiro contributed to the bibliographic research, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables and graphs, conclusions, review, and statistics. **Silvia Adriana Mayer Lentz** contributed to the writing of the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, and review. **Raquel Cristine Barcella** contributed to the writing of the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, and revision.

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