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Coronavirus Pandemic

Antimicrobial consumption and resistance in a tertiary care hospital in Brazil: a 7-year time series

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Abstract

Introduction: Antimicrobial resistance (AMR) is a major public health challenge globally. This study aimed to analyze the antibacterial consumption (ATBc), and the incidence of multidrug-resistant organisms (MDRO), focusing on pathogens *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp. (ESKAPE group), in a Brazilian tertiary care hospital.

Methodology: The ATBc was measured by defined daily doses (DDD) calculated per 1000 patient days. The incidence of MDRO was collected from the hospital infection control committee specialized reports. Changes in ATBc and MDRO incidence over time were explained by the compound annual growth rate (CAGR) represented by the average yearly change as a proportion (%) of consumption in the starting year. This was a time series study using data collected retrospectively from January 2015 to December 2021.

Results: There was an increase in consumption of daptomycin and linezolid during the study period (39.4% and 27.7%, respectively), followed by polymyxins (9.8%). The MDRO of the ESKAPE group with the highest variation in the period were *Staphylococcus* spp (29.2%), *Enterococcus* spp (27.8%), and *Acinetobacter* spp (18.4%). Other MDROs, outside the ESKAPE group, such as *Providencia* sp (51.2%) and *Clostridioides dificille* (37.7%) had significant variation.

Conclusions: The coronavirus disease 2019 (COVID-19) pandemic may have reinforced the deterioration of the scenario of accelerating AMR increase. This warrants investigations of further surveillance data to assess the impact of the pandemic on AMR epidemiological trends.

Key words: antimicrobial stewardship; drug utilization review; drug resistance; outcome assessment; pharmacoepidemiology; COVID-19.

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Introduction

Antimicrobial resistance (AMR) is a major global challenge to public health [1] due to its potential impact on human and animal health, as well as a significant increase in healthcare costs [2–4]. AMR is a natural evolutionary phenomenon for microorganisms that can be accelerated by inappropriate human practices, such as excessive use of antimicrobials [5]. Multiple actions must be implemented to reduce the pace of AMR emergence, such as the provision of basic sanitation, clean water, rigorous protocols to guide the rational use of antimicrobials, investments in public health, and more homogeneous regulatory policies across the globe – both in public and private sectors [1].

Antimicrobial stewardship programs (ASP) represent a useful strategy consisting of actions to promote the responsible use of antimicrobials [6]. Several metrics have been proposed to monitor ASP performance adequately regarding the process and outcome measures; such as quality of antimicrobial use, microbial resistance, *Clostridioides difficile* infection rates, length of hospital stay, readmission rates, mortality estimates, and costs [7].

The emergence of coronavirus disease 2019 (COVID-19) at the end of 2019 resulted in a global health emergency that overstretched healthcare systems and represented an additional challenge to planning actions to reduce the emergence of AMR. Hospital infection control and ASP activities were impacted and

weakened during the COVID-19 pandemic [8]. Several factors contributed to this, such as the burden on health services, complexity of care in the context of the new disease, structural difficulties of services to accommodate patients, changes in hygiene and cleaning procedures, and expansion of the professional staff without proper training for the care of critically ill patients [9].

Trends in antimicrobial use during the pandemic were heterogeneous when compared at the community and hospital levels [8]. Despite the low incidence of secondary bacterial infections, nearly three-quarters of all COVID-19 patients were treated with at least one antimicrobial, especially in the early phase of the pandemic [10,11]; although bacterial infection rates in these patients were around 5% [11]. At the hospital level, an upward trend in antimicrobial use was recorded during the pandemic, which may also be related to the discontinuation of ASP. Together, these factors contributed to the increase in the inappropriate use of antibiotics [8].

The increase in antibacterial consumption (ATBc) resulting from the pandemic jeopardised the progress in combating AMR. It is mandatory to reverse this damage and continue to make progress in antimicrobial stewardship. However, the initiatives are still heterogeneous among high-, middle- and low-income countries [12], and data are still scarce. Such information is critical to support the implementation of effective measures and interventions [8].

According to Our World in Data, by October 2022, Brazil ranked 15th in the world for proportionate deaths from COVID-19, with 3,221 deaths per million inhabitants [13]. In this context, discussing pre- and post-pandemic ASP outcomes and exploring potential impacts on ATBc and AMR would be relevant. This study aimed to analyse ATBc and the epidemiological distribution of multidrug-resistant organisms (MDRO) in a Brazilian teaching hospital in 2021.

Methodology

The study was conducted in a public general teaching hospital which is affiliated to the Brazilian Unified Health System. This 392-bed hospital is a referral center for more than 1.2 million people living in the region of Belo Horizonte, Minas Gerais State, in Southeast Brazil. The hospital provides care for about 50,000 patients annually, encompassing medium and high-complexity assistance for clinical, surgical, and polytrauma emergencies, as well as maternal and childcare. The population assisted includes mainly adults and has a heterogeneous profile.

The antimicrobial formulary, including the standardized drugs, is available in the computerised physician order entry (CPOE). The computer system requires the record of the reason for indication of all antimicrobials prescribed. Reserve antimicrobials, broad-spectrum, and/or high-cost antimicrobials are dispensed only after review by a clinical pharmacist and by the hospital infection control committee (HICC). The main strategies for infection control focused on AMR at the hospital of study involve active search, antimicrobial evaluation, analysis and dissemination of epidemiological results, and technical visits.

This study was a time series using data collected retrospectively from January 2021 to December 2021, analysing aggregated data from the hospital database. The Institutional Ethics Committee of the Universidade Federal de Minas Gerais approved the study protocol (CAAE 54060321.8.0000.5149). The requirement for informed consent form was waived because no individual participants were recruited.

Medication consumption data were obtained through the hospital pharmacy reports issued via the computerised management software – MV 2000i®/MV Soul®. Microbial resistance data were obtained from the laboratory management software – Matrix BI© (Copyright 2024 © Matrix Sistems, Brazil).

The consumption of antibacterial agents and the frequency of MDRO were variables of interest in this study. The consumption of antimicrobials was measured by defined daily doses (DDD) – the metrics adopted by the HICC, following the guidelines proposed by the World Health Organisation (WHO) [14]. The DDD was calculated per 1,000 patient days, and the most recent ATC/DDD index was applied to the study period. Data on antimicrobial consumption was collected from reports and calculated by subtracting the number of antimicrobial units dispensed from the number of antimicrobial units returned to the hospital pharmacy. Data on antimicrobial consumption was extracted from MV 2000i® (version 2006, MV Informática Nordeste, Imbiribeira, Brazil), MV Soul® (version 2021, MV Informática Nordeste, Imbiribeira, Brazil), and MatrixBI © software (Copyright 2024 © Matrix Sistems, Brazil). Afterwards, data were tabulated in a Microsoft Office Excel (2003) spreadsheet and plotted serially, monthly from January 2021 to December 2021. The antibacterial agents of interest in this study that were standardised in the hospital and listed by the Brazilian Health Regulatory Agency (Anvisa) with mandatory monitoring for hospitals providing intensive care unit (ICU). Data on antibacterials were presented by drug (categorised by

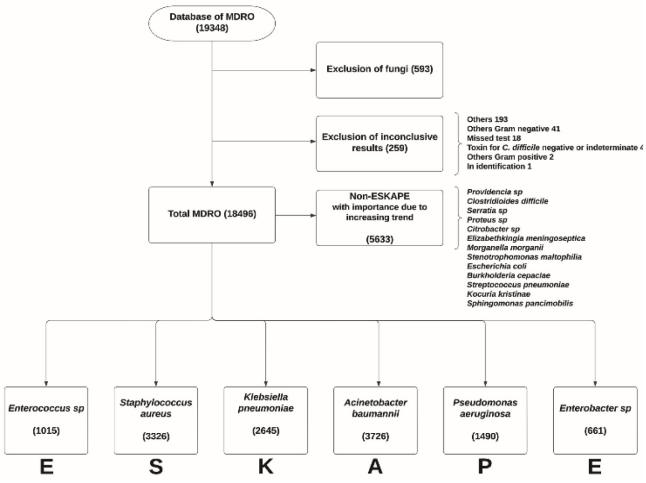
2021 ATC code and 2021 AWaRe classification) and then by therapeutic class (ATC 2021 classification).

The results for all microbiological cultures (including clinical and surveillance cultures) were recorded in the hospital management software by the HICC nurses to guide the healthcare team on specific procedures required by patients, such as contact precautions. There was no change in the surveillance criteria during the period of study. Thus, the incidence of MDRO was collected from the HICC specialised reports and then exported to a Microsoft Excel (2003) spreadsheet. An MDRO was defined as a microorganism that was resistant to three or more classes of tested antimicrobials [4]. Over the years, the system for entering information into the data management system has been improved. For this reason, the microorganisms in this study were grouped by genus.

Data on MDRO were classified according to the list proposed by WHO that mentions the global priority pathogens. The group, designated by the acronym ESKAPE, (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp.) was assigned the highest priority status due to its significant threat to humans [15]. Inconclusive results, encompassing microorganisms categorised in the laboratory database as “other Gram-positive”, "other Gram-negative", "other", "missed test", “toxin for *Clostridioides dificille* negative or indeterminate” or "under identification", were excluded from the study sample. The other microorganisms not belonging to the ESKAPE group were categorised as non-ESKAPE. A flowchart detailing the study design is depicted in Figure 1.

The compound annual growth rate (CAGR) was used to calculate the yearly changes in antimicrobial consumption and the incidence of MDRO pathogens. The first calculation of CAGR was obtained by using the returns on interest rate (RRI function) of Microsoft Excel® (2003), subtracting the last year of the study (2021) from the first year (2015), corresponding to the notation CAGRt. The second calculation of CAGR was obtained by the same function (RRI), subtracting the last year (2021) until the first year before the pandemic (2019), corresponding to the notation CAGRp. Delta coefficient (Δ) was calculated by subtracting CAGRp from CAGRt. This coefficient was used to assess whether there were changes in trends in antimicrobial consumption and the incidence of pathogens, analysing the COVID-19 pre-pandemic period with the pandemic period. All statistical analyses were performed using R

Figure 1. Protocol design - inclusion and exclusion criteria.



ESKAPE group: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter* species. MDRO, multidrug-resistant organisms.

statistical software (version 4.0; R Foundation for Statistical Computing, Vienna, Austria). The study was conducted and reported according to the guidelines of the strengthening the reporting of observational studies in epidemiology (STROBE-AMS), reporting epidemiological studies focused on the relationship between MDRO and antimicrobial use.

Results

The CAGRt revealed four antibacterials with an increasing consumption trend (ceftriaxone, piperacillin-tazobactam, levofloxacin oral, and ampicillin-sulbactam), two with a decreasing trend (daptomycin and ceftazidime), and 11 with a stable trend (Figure 2A). The consumption of polymyxin E could not be estimated because of null DDD in the first year of analysis.

Overall, the results for CAGRp revealed seven antimicrobials with an upward consumption trend (daptomycin, linezolid parenteral, levofloxacin parenteral, tigecycline, vancomycin, ceftriaxone, piperacillin-tazobactam); two with a downward trend (ciprofloxacin parenteral and ceftazidime); and the others, shown in Figure 2A, had a stable trend. The variation of DDD per 1000 patient days by each antimicrobial assessed across years is also presented in Figure 2A.

Polymyxin E, also called colistin, was not included in the antimicrobial hospital formulary at the beginning of this time series. However, due to market fluctuations and drug shortage of polymyxin B, colistin came to be incorporated as a therapeutic alternative and, therefore,

Figure 2. A, Variation of the defined daily dose (DDD) of antibacterials per 1000 patient-days. B, Variation of the DDD per 1000 patient-days of therapeutic classes (ATC Classification, 2021).

Figure 2A - Variation of the DDD (defined daily dose) per 1000 patient-days of antibacterials monitored in Brazilian ICUs

DDD (defined daily dose) per 1000 patient-days	2015	2016	2017	2018	2019	2020	2021	Time Series	CAGRt	CAGRp	Δ
Polymyxin E - Colistin	0,0	0,0	0,0	0,0	0,0	33,5	111,6		N/A	N/A	N/A
Daptomycin	140,7	72,2	38,6	26,8	8,7	18,4	11,4		-30,2%	9,2%	39,4%
Linezolid parenteral	36,8	78,9	53,0	39,2	16,9	39,7	34,5		-0,9%	26,7%	27,7%
Parenteral levofloxacin	60,0	64,8	72,1	43,7	57,1	43,2	85,6		5,2%	14,5%	9,2%
Amikacin	222,3	75,6	84,5	119,1	143,6	101,5	154,6		-5,1%	2,5%	7,5%
Tigecycline	88,1	100,7	78,5	86,0	81,3	92,5	105,9		2,7%	9,2%	6,5%
Vancomycin	558,0	537,2	473,3	535,7	525,2	558,8	687,1		3,0%	9,4%	6,4%
Ceftriaxone	790,9	757,5	891,5	855,3	986,5	1450,4	1521,3		9,8%	15,5%	5,7%
Cefepime	450,3	458,2	401,1	454,7	416,2	412,4	455,5		0,2%	3,1%	2,9%
Piperacillin-tazobactam	296,1	327,1	493,8	428,2	442,6	517,2	654,5		12,0%	13,9%	1,9%
Polymyxin B	426,8	383,6	338,5	299,8	258,8	291,4	186,3		-11,2%	-10,4%	0,8%
Meropenem	769,6	854,0	812,5	924,0	909,5	934,9	966,5		3,3%	2,0%	-1,3%
Teicoplanin	315,1	331,9	329,7	308,0	242,8	291,0	181,3		-7,6%	-9,3%	-1,7%
Ciprofloxacin oral	139,5	142,1	123,2	162,5	117,6	63,7	82,3		-7,3%	-11,2%	-4,0%
Parenteral ciprofloxacin	129,9	68,4	78,1	95,3	76,4	39,5	28,3		-19,6%	-28,2%	-8,6%
Levofloxacin oral	98,6	208,9	209,4	344,7	371,0	232,5	267,0		15,3%	-10,4%	-25,7%
Ceftazidime	95,8	82,5	46,1	91,7	146,0	66,5	9,5		-28,1%	-59,8%	-31,7%
Ampicillin-sulbactam	2,06	24,4	20,2	27,4	16,0	21,5	15,7		33,7%	-0,6%	-34,3%

Figure2B - Variation of the DDD (defined daily dose) per 1000 patient-days of antibacterial therapeutic classes, monitored in Brazilian ICUs

DDD (defined daily dose) per 1000 patient-days	2015	2016	2017	2018	2019	2020	2021	Time Series	CAGRt	CAGRp	Δ
Lipopeptides	141	72	39	27	9	18	11		-30,2%	9,2%	39,4%
Oxazolidinones	37	79	53	39	17	40	34		-0,9%	26,7%	27,7%
Polypeptides	427	384	338	300	259	325	298		-5,0%	4,8%	9,8%
Aminoglycosides	222	76	84	119	144	101	155		-5,1%	2,5%	7,5%
Glycylcyclines	88	101	79	86	81	93	106		2,7%	9,2%	6,5%
Glycopeptides	873	869	803	844	768	850	868		-0,1%	4,2%	4,3%
Cephalosporins	1337	1298	1339	1402	1549	1929	1986		5,8%	8,6%	2,8%
ß-Lactams - Penicillins	298	351	514	456	459	539	670		12,3%	13,5%	1,2%
ß-Lactams - Carbapenems	770	854	812	924	909	935	967		3,3%	2,0%	-1,3%
Quinolones	428	484	483	646	622	379	463		1,1%	-9,4%	-10,5%

ICU, intensive care unit; ATC code, a tool for drug utilization monitoring and research to improve the quality of drug use; DDD, defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults; CAGRt, compound annual growth rate of the total period (2015 to 2021); CAGRp, compound annual growth rate of the pandemic period (2019 to 2021); Δ, variation of CAGRp-CAGRt; N/A, not applicable, trend analyses were not performed and CAGR was not calculated because of missing data, changes in the type of data, or changes in the data process. Time-series black and red dots indicate maximal and minimal values in the time interval.
A, AWaRe classification, a tool for monitoring antibiotic consumption, defining targets, and monitoring the effects of stewardship policies that aim to optimize antibiotic use and curb antimicrobial resistance; B, "Name" is defined as the name of the substance (normally the INN name) or the name of the ATC level.

could be monitored for DDD results until 2020. The DDD of polymyxins showed a downward trend in the total period (CAGRt = – 5.0%), but an upward trend in the pandemic period (CAGRp = 4.8%), indicating an increase in consumption of 9.8%.

ATBc assessment grouped by class showed a downward trend before the pandemic for "other antibacterials" (CAGRt = – 17.6%), "polymyxins" (CAGRt = – 5.0), "other aminoglycosides" (CAGRt = – 5.1), "tetracyclines" (CAGRt = 2.7), "glycopeptide antibacterials" (CAGRt = – 0.1), and "fourth-generation cephalosporins" (CAGRt = 0.2). The class "combinations of penicillins, including beta-lactamase inhibitors and carbapenems" showed an increasing trend. The other classes revealed a stable trend in consumption. The variation of DDD by each antibacterials class assessed across years is detailed in Figure 2B.

Regarding the occurrence of MDRO, among the pathogens included in the ESKAPE group, *Acinetobacter* spp, *Pseudomonas aeruginosa*, and *Enterobacter* spp, presented a decreasing trend in CAGRt. Upon evaluating CAGRp, the incidence of *Staphylococcus* spp and *Enterococcus* spp tended to increase (CAGRp = 49.6% and 47.6%, respectively). The evaluation of the variation between CAGRt and CAGRp for the MDROs showed the most significant increase in the trend for *Enterococcus* spp, *Staphylococcus* spp, and *Acinetobacter* spp. Detailed data on MDRO results across years is presented in Figure 3A.

Figure 3. A, Variation of the multidrug-resistant organisms (MDRO) grouped according to the World Health organization (WHO) list of global priority pathogens. B, MDRO pathogens categorized as "Non-ESKAPE".

Figure 3A - Variation of the MDRO grouped according to the WHO list of global priority pathogens

Multidrug-resistant organism	2015	2016	2017	2018	2019	2020	2021	Time Series	CAGRt	CAGRp	Δ
Enterococcus sp	132	132	83	45	94	227	302		12,6%	47,6%	35,0%
Staphylococcus aureus	399	240	152	147	333	941	1114		15,8%	49,6%	33,8%
Acinetobacter baumannii	852	793	499	329	352	351	550		-6,1%	16,0%	22,1%
Non-ESKAPE	350	202	317	394	842	1798	1730		25,6%	27,1%	1,5%
Pseudomonas aeruginosa	183	143	140	139	248	326	311		7,9%	7,8%	0,0%
Klebsiella pneumoniae	156	170	258	370	393	579	719		24,4%	22,3%	-2,1%
Enterobacter sp	65	73	80	62	98	168	115		8,5%	5,5%	-3,0%

Figure 3B - Discrimination of pathogens MDRO categorized as "Non-ESKAPE"

"Non-ESKAPE" Multidrug-resistant organism	2015	2016	2017	2018	2019	2020	2021	Time Series	CAGRt	CAGRp	Δ
Providencia sp	25	5	4	15	4	15	13		-8,9%	48,1%	57,0%
Clostridioides dificille	15	11	0	0	6	14	15		0,0%	35,7%	35,7%
Serratia sp	88	4	68	100	80	162	146		7,5%	22,2%	14,7%
Proteus sp	71	51	45	57	89	181	221		17,6%	35,4%	17,8%
Citrobacter sp	15	5	11	7	23	61	54		20,1%	32,9%	12,8%
Elizabethkingia meningoseptica	0	0	0	1	0	0	0		0,0%	0,0%	0,0%
Morganella morganii	10	10	10	6	25	73	60		29,2%	33,9%	4,7%
Stenotrophomonas maltophilia	22	20	19	27	33	25	39		8,5%	5,7%	-2,8%
Escherichia coli	83	84	157	178	556	1136	1063		43,9%	24,1%	-19,8%
Burkholderia cepaciae	13	10	3	3	12	14	1		-30,7%	-56,3%	-25,6%
Streptococcus pneumoniae	0	0	0	0	14	117	117		N/A	N/A	N/A
Kocuria kristinae	6	1	0	0	0	0	0		N/A	N/A	N/A
Sphingomonas pancimobilis	2	1	0	0	0	0	1		N/A	N/A	N/A

CAGRt, compound annual growth rate of the total period (2015 to 2021); CAGRp, compound annual growth rate of the pandemic period (2019 to 2021); Δ, variation of CAGRp-CAGRt; N/A, not applicable, trend analyses were not performed and CAGR was not calculated because of missing data, changes in the type of data or changes in data process; Time-series black and red dots indicate maximal and minimal values in the time interval; The ESKAPE group includes *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species; The non-ESKAPE represents all other multidrug-resistant organisms MDROs identified, with importance due to the increasing trend.

The incidence of "Non-ESKAPE" MDRO increased considerably in the pandemic years, ranging from 17% of MDRO in 2015, to approximately 45% in 2020, and 35% in 2021. Data on "Non-ESKAPE" bacteria is presented in Figure 3 and Figure 4. In this context, the most significant increase in incidence was of the bacteria of the genus *Providencia* (Δ = 57.0%), followed by *Clostridioides difficile* (Δ = 35.7%). Detailed data on "Non-ESKAPE" MDRO results across years is presented in Figure 3B.

Figure 4. Absolute and relative frequency of incidence of multidrug-resistant organisms.

The ESKAPE pathogens include *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* species.

Discussion

In this seven-year retrospective study assessing important ASP metrics, there was a change in the trend for ATBc, and in the incidence of MDROs with the occurrence of the COVID-19 pandemic. Three of the ten antibacterial classes monitored had their trends altered by the pandemic, represented by an increase in lipopeptides and oxazolidinones, and a decrease in quinolones. Two of the six microorganisms of the ESKAPE group had considerably increased incidence – *Enterococcus* spp and *Staphylococcus* spp.

The increased consumption of antimicrobials has been previously highlighted in healthcare contexts with a low rate of bacterial co-infections in patients with COVID-19, which has been paradoxically related to excessive prescription of antibacterials [16,17]. However, such findings are limited to single-center retrospective studies and deserve further investigations. A systematic review with meta-analysis reported an estimated incidence of 7–8% of hospitalized patients in general hospitals and 14% of ICU patients diagnosed

with secondary infection (sepsis, nosocomial pneumonia). However, 72% of COVID-19 patients received broad-spectrum antibacterials [18].

The classes with the highest variation in ATBc were the lipopeptides and the oxazolidinones, represented by daptomycin and linezolid, respectively. These antimicrobials were selected for reserved use in the hospital of study and are indicated for infections caused by vancomycin-resistant enterococci (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA) in patients allergic to glycopeptides (vancomycin or teicoplanin), and patients with renal or hematological dysfunction (leucopenia). This increase may suggest an increased prevalence of VRE and MRSA, which other authors have pointed out in the same period [19,20]. However, further investigations should confirm this hypothesis since the method employed in the present study categorized MDROs with no specification of the resistance mechanisms involved.

Polymixins represented another class with increasing consumption that was analyzed using the combined data for polymyxin B and colistin consumption. Polymyxins are active against a large portion of the Gram-negative bacilli of clinical relevance, especially *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterobacter* spp., *Klebsiella pneumonae*, and *Escherichia coli*. These same microorganisms also showed an upward trend in other studies [21–23]. With no availability of polymyxin, colistin had been used during specific periods; and without both, the drug of choice was tigecycline, administered in double doses. Inappropriate drug replacements have been reported as a consequence of drug shortages with a potential impact on the quality and safety of drug therapy [24].

Studies have demonstrated a sustained increase in the spread of multidrug-resistant bacteria, endorsing the framing of reliable and comparable methods for generating data on AMR globally [2,25]. The microorganisms considered a global priority by WHO were also the most prevalent MDROs in the hospital of study. The upward trend for *Staphylococcus* spp intensified during the pandemic, which is in line with reports from other countries [26,27]. *Enterococcus* spp also significantly increased during the pandemic. Viral infections are suspected of altering the bacterial microbiome, which benefits the growth of *Enterococcus* and increases intestinal permeability, favoring the development of invasive infections [28]. The third highest variation among the MDRO was related to *Acinetobacter* spp, an opportunistic pathogen that is highly prevalent in ventilator-associated pneumonia and bloodstream infections; with increased incidence during the COVID-19 pandemic also reported in several countries [16,21,29]. The cytokine storm generated in response to the viral infection required clinical management with immunosuppressive drugs, such as corticoids. Immunosuppression could facilitate the proliferation of opportunistic pathogens, such as *Acinetobacter* spp and this assumption needs clarification.

Part of the burden imposed by the COVID-19 pandemic was related to the overload of healthcare systems, which had repercussions on infection prevention and control routines in institutions [5]. The hospital structure could also influence the incidence of healthcare-associated infections (HCAI) and work processes [23]. Some of the changes in the structure and processes were observed worldwide, such as the limited supply of personal protective equipment and medicines, such as polymyxins; changes in cleaning and procedures for environment disinfection; and difficulty in allocating patients to private rooms/cohort units; among other factors [4,22]. This multifactorial impact on the structure and work processes may explain the increased incidence of *Clostridioides dificille*, which recognized as a marker of antibacterial overuse, and is easily transmissible by spores.

The strengths of our study include a long-term computerized database with no missing data since 2015 regarding outcomes recommendations for ASP follow-up. We did not find any large study in literature with comparative information covering the period before and during the COVID-19 pandemic. Our data provide helpful information for a better understanding of how antimicrobial consumption and resistance have evolved in a public hospital in a middle-income country. The results of this study suggest that further studies should be carried out and signal priorities for actions to improve healthcare practices for infection control in the studied hospital. A legacy of this study is the systematization of a tool to continue monitoring the DDD and the incidence of MDRO in a more automated way, facilitating the work of the HICC, hospital pharmacy, and the ASP operational team.

Drug utilization studies should consider the COVID-19 pandemic to measure the impact of policy changes or prescriptions that overlap with the pandemic. We suggest accounting for these changes by comparing them to historical controls, contextualizing drug utilization shifts during this period, and interpreting that it could be due to the COVID-19 pandemic.

There are some limitations in this study. Firstly, it is a single-center study, hindering the possibility of generalising the findings to our country. Secondly, although the microorganisms were classified as MDRO, their resistance profiles were not determined in this study.

Conclusions

This study analyzed the consumption of antimicrobials and the distribution of the main MDROs from 2015 to 2021 in a public teaching hospital in Brazil. There was a significant increase in the consumption of "other antibacterials" (daptomycin and linezolid), and polymyxins. *Staphylococcus* spp, *Enterococcus* spp, and *Acinetobacter* spp had the highest increasing tendency in the hospital during the COVID-19 pandemic. Further deterioration in the scenario of accelerating AMR increase may be associated with the occurrence of the pandemic. This warrants further investigations of surveillance data to assess the AMR epidemiological trends and establish strategies to mitigate the problem.

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Authors' contributions

AFM, MAPM, and CMB: study design; BCFD: data collection; RPS: statistical analyses; EML, MHNGA, LRV, CDCA, and AFFS: data interpretation; AFM: manuscript draft. All authors critically reviewed and approved the final version of the manuscript.

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