Antimicrobial susceptibility of *Klebsiella pneumoniae* clinical isolates from the lower respiratory tract infection during the COVID-19 pandemic in Brazil (SMART 2020-2021)

Amanda Azevedo Bittencourt; Vinicius Lima Faustino; Paula de Mendonça Batista; Marina Della Negra de Paula; Thales José Polis

Global Medical Affairs, MSD, São Paulo, Brazil

Introduction

During the COVID-19 pandemic, there has been an increase in antibiotic resistance, particularly among gram-negative bacteria, such as *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*.[1] The elevated prevalence of multidrug-resistant bacteria increased the likelihood of mortality and extended hospitalization duration due to complications.[2] The emergence and widespread dissemination of carbapenem resistance in hospitals raise significant public health concerns, especially concerning *K pneumoniae*.[1] The main contributing molecular mechanisms to resistance in this context involve the production of *Klebsiella pneumoniae* carbapenemase (KPC) and New Delhi metallo-β-lactamase (NDM).[1] According to the Infectious Diseases Society of America (IDSA), recommended therapeutic options for treating carbapenem-resistant *Enterobacterales* include imipenem/relebactam (IMR) and ceftazidime/avibactam (CZA).[3] CZA has been available in Brazil since 2019, and IMR was approved in January 2024, offering a new therapeutic option for KPC-producing *K pneumoniae* infections.

Objectives

This study aimed to analyze the in vitro susceptibility of *K pneumoniae* isolates collected from 9 sites in Brazil between 2020 and 2021, as part of the Study for Monitoring Antimicrobial Resistance Trends (SMART) global surveillance program.

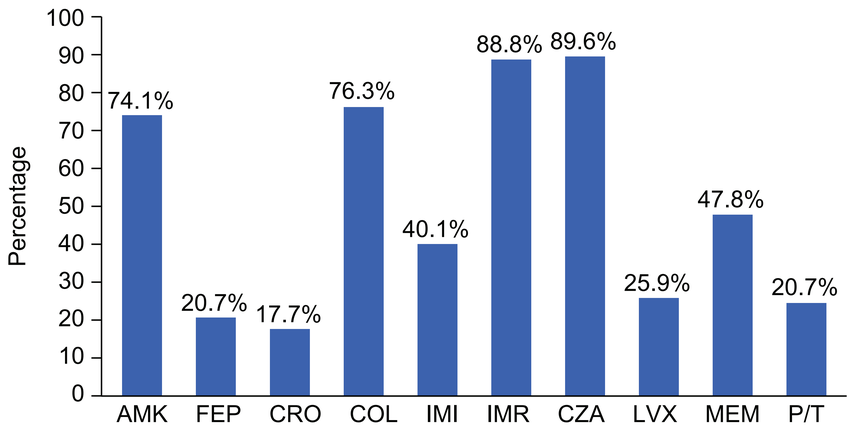
Methods

Nonduplicate clinical isolates of *K pneumoniae* collected from 9 Brazilian sites between January 2020 and December 2021 were analyzed for susceptibility to amikacin (AMK), cefepime (FEP), ceftriaxone (CRO), colistin (COL), imipenem (IMI), IMR, CZA, levofloxacin (LVX), meropenem (MEM), and piperacillin/tazobactam (P/T) according to EUCAST 2023. Only isolates obtained from patients aged 18 years or older and originating from lower respiratory tract infections (LRTI) were considered. Susceptibility patterns and distribution of beta-lactamase encoding genes among KPC-producing isolates were also investigated.

Results

A total of 232 isolates were included in this analysis. The susceptibility rate is demonstrated in **Figure 1**. The commonly used antibiotics, MEM and IMI, exhibited susceptibilities of 47.8% and 40.1%, respectively. COL and AMK, typically reserved for highly resistant isolates due to their associated toxicity, showed susceptibilities of 76.3% and 74.1%, respectively. New antibiotics CZA and IMR demonstrated high in vitro susceptibility rates of 89.6% and 88.8%, respectively.

Figure 1. *K pneumoniae* susceptibility rate among isolates from LRTI-SMART Brazil 2020-2021 (n=232)



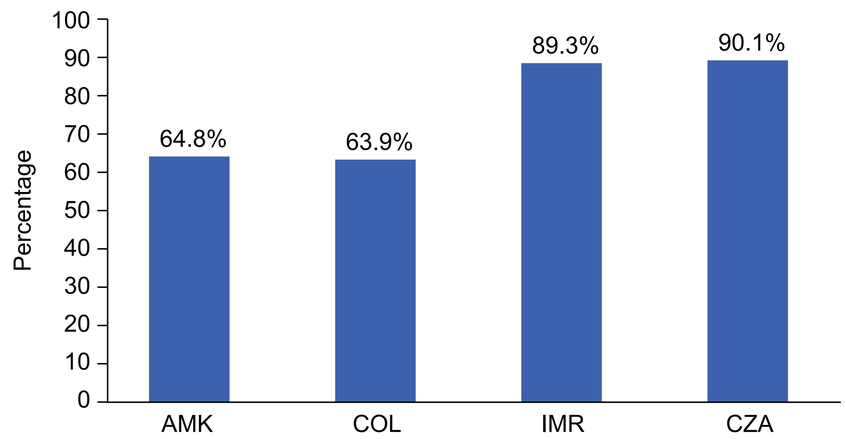
AMK, amikacin; FEP, cefepime; CRO, ceftriaxone; COL, colistin; IMI, imipenem; IMR, imipenem/relebactam; CZA, ceftazidime/avibactam; LVX, levofloxacin; MEM, meropenem; P/T, piperacillin/tazobactam.

Regarding beta-lactamase encoding genes in KPC-producing isolates (n=122), almost all isolates (97.5%) exhibited KPC-2 production (**Table 1**). Novel β-lactam/β-lactamase inhibitors (BL/BLI) exhibited a susceptibility rate of approximately 90% (**Figure 2**).

Table 1. Distribution of beta-lactamase encoding genes according to participating Brazilian medical centers in KPC-producing *K pneumoniae* isolates from LRTI (2020-2021)

Beta-lactamase	No. (% of all isolates)
KPC-2	119 (97.5%)
CTX-M-1-240G	49 (40.1%)
CTX-M-2-240D	27 (22.1%)
CTX-M-9-240D	25 (20.4%)
NDM-1	7 (5.7%)
NDM-7	4 (3.2%)
KPC-3	2 (1.6%)
CTX-M-9-TYPE	1 (0.8%)
KPC-31	1 (0.8%)
VIM-1	1 (0.8%)

Figure 2. Susceptibility rate among KPC-producing *K pneumoniae* isolates from LRTI-SMART Brazil 2020-2021 (n=122)



AMK, amikacin; COL, colistin; IMR, imipenem/relebactam; CZA: ceftazidime/avibactam.

Cross-susceptibility to COL, AMK, IMR, and CZA is demonstrated in **Table 2**. In KPC isolates nonsusceptible to COL, CZA and IMR maintained susceptibility of 97.7% and 95.4%, respectively. As for KPC isolates nonsusceptible to AMK, IMR and CZA maintained susceptibility of 97.6% and 95.3%, respectively.

Table 2. Cross-susceptibility among KPC-producing *K pneumoniae* isolates from LRTI with different phenotypes

Phenotype	No. (% of all isolates)	Antimicrobial agent, % susceptible			
		COL	AMK	IMR	CZA
COL-NS	44 (36)	0	34	95.4	97.7
AMK-NS	43 (35)	32.5	0	97.6	95.3

AMK, amikacin; COL, colistin; IMR, imipenem/relebactam; CZA, ceftazidime/avibactam; NS, nonsusceptible.

Conclusion

This study highlights an elevated prevalence of KPC-producing *K pneumoniae* from the LRTI in Brazil, which underscores the urgent need to implement strategies to combat antimicrobial resistance and to provide effective treatment options for patients with resistant infections. CZA, available in Brazil for several years, has demonstrated a highly potent in vitro activity in this study. IMR, a newly approved antibiotic in Brazil, has also shown highly potent in vitro activity, including against resistant bacterial strains, and can serve as an important treatment option for respiratory infections caused by *K pneumoniae*.

References:

1. Al Sulayyim HJ, et al. *Int J Environ Res Public Health*. 2022;19(19):11931.
2. Petrakis V, et al. *Pathogens*. 2023;12(6):780.
3. Tamma PD, et al. Infectious Diseases Society of America antimicrobial-resistant treatment guidance: Gram-negative bacterial infections. Infectious Diseases Society of America; Version 3.0. 2023. Available at: https://www.idsociety.org/practice-guideline/amr-guidance/. Accessed 03/18/2024.

Presented at ISPOR; Atlanta, GA, USA; May 5-8, 2024.