Clinical characteristics of patients in the intensive care unit with infections caused by multiresistant Gram-negative bacteria.

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BACKGROUND

- Antimicrobial resistance may vary according to the geographical location, across distinct periods of time and even within an institution. It is alarming that this resistance is increasingly common in different pathologies, such as complicated urinary tract infection¹, complicated intra-abdominal infection², and hospital-acquired and ventilator-associated pneumonia³, thus becoming a threat to global public health^{4,5}.
- Infections by multidrug resistant bacteria occur frequently in patients admitted to intensive care unit (ICU)⁶, been more common than in other hospital wards⁷.
- In Colombia, national reports have described that, among isolated *K. pneumoniae* in ICU, 9.3% to 14.6% have exhibited carbapenem-resistance, 8.8% to 12.7% in general hospitalization rooms⁸, and in the case of Bogota—as reported by the Health Secretariat—in 2017, 1.5% of *E. coli* isolations and 21.2% of *K. pneumoniae* isolations in ICUs exhibited carbapenem-resistance. For non-ICU isolations, 0.9% was found to be carbapenem-resistant in *E. coli*, and 23.4% in *K. pneumoniae*⁹.

OBJECTIVE

• To describe the clinical characteristic and treatment patterns in patients in the intensive care unit (ICU) with infections caused by multiresistant Gram-negative bacteria.

METHODS

- This is an observational, retrospective study in ICU patients with any of the following infections caused by resistant gram-negative bacteria: bacteremia, urinary tract, pneumonia, and intra-abdominal.
- The index point was when the patient was diagnosed with an infection of study in ICU or from another place and confirmed isolated of multiresistant Gram-negative bacteria.
- The start of antibiotic treatment and dosing was defined by the treating physician according to relevant criteria and institutional guidelines.
- Patients were followed up until 30 days in the hospital, hospital discharge or death.
- It was performed in two Colombian hospitals and involved the review of medical records between 2018 to 2021.
- Patients' demographics, clinical conditions, comorbidity, history of previous exposure to antibiotics, severity of disease, treatment characteristics, clinical outcomes such as mortality during follow-up and hospital and ICU Length of Stay (LOS) were collected.
- Clinical laboratory reports, database of institution in the infection committee and clinical records were used as source of information, from which the target population was identified based on inclusion and exclusion criteria.
- Dichotomous and polychotomous variables were given in percentage. For continuous variables, the mean, median, interquartile range, and standard deviation were estimated.

RESULTS

- One hundred sixty-two patients were included in the study. The mean age was 59.1 years [Standard deviation (SD) 16.1], mainly males (59.9%).
- The most frequent diagnosis of ICU was community-acquired pneumonia (13.6%), primary bacteremia (9.9%), hospital-acquired pneumonia (8.6%), and intrabdominal infections (8.0%).
- The mean time in ICU was 27.6±33.5 days. The mean APACHE II score at the ICU admission was 40.8 (SD 23.9). Mechanical ventilation (MV) was required in 132 patients. The mean MV duration was 23.8±32.6 days.
- The main etiological causes of infection were *K. pneumoniae* (45.0%), *E. coli* (13.6%), *P. aeruginosa* (12.3%), and *Enterobacter spp.* (9.8%). Carbapenemases were the most frequent mechanism of resistance (83.3%).

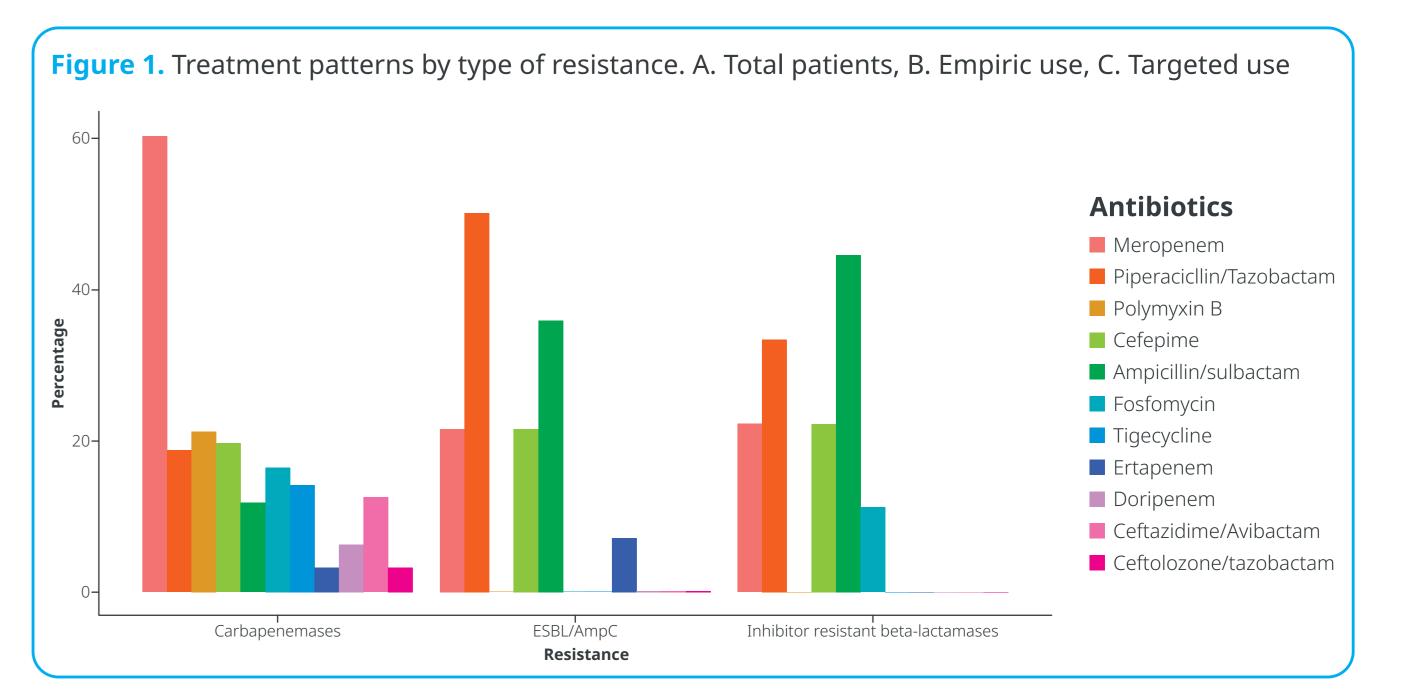
RESULTS (cont)

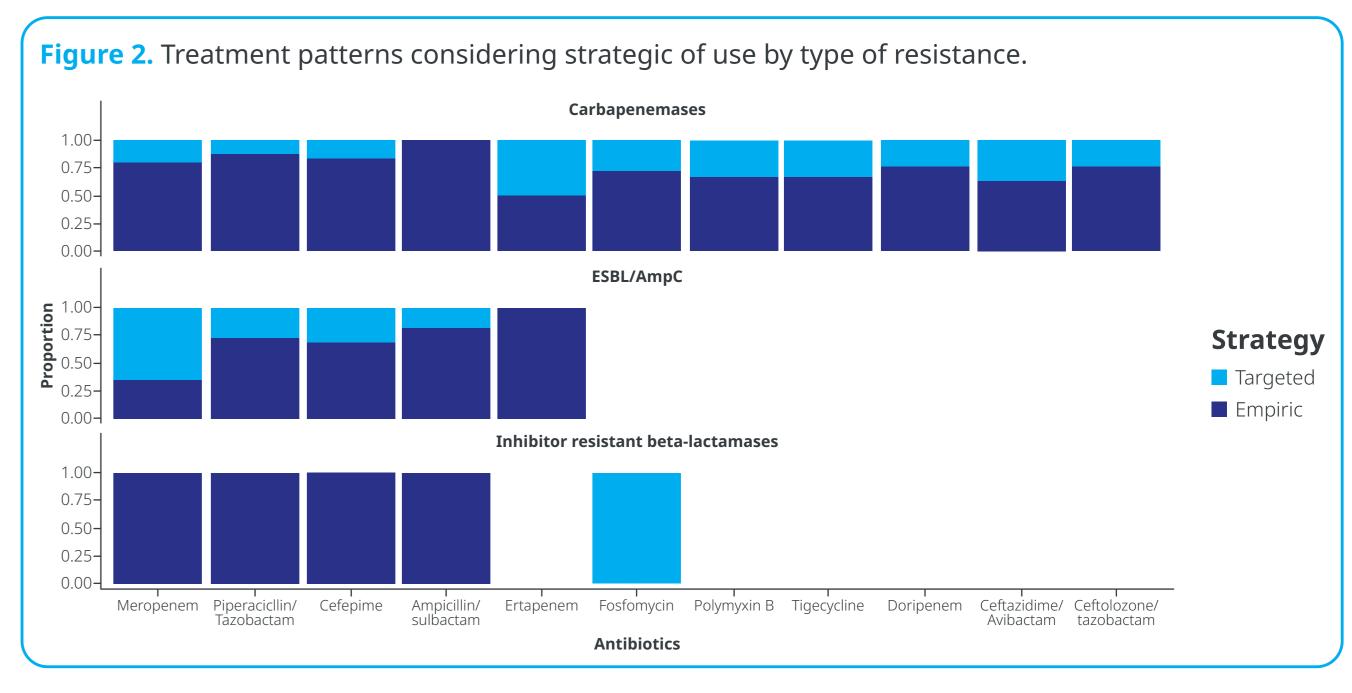
- The most frequent risk factors were central venous catheter (87.6%), use of urinary catheter (54.3%), septic shock (74.1%), previous hospitalization in the last 90 days (41.4%), and previous surgery in the last month (42.6%) (Table 1).
- Meropenem (54.3%), piperaciline tazobactam (22.5%), cefepime (19.9%), and polymyxin B (17.9%) were the most frequent antibiotics. Seventy-nine percent of antibiotics were used empirically.
- For carbapenemases, meropenem was used in 60.2%, followed mainly by polymyxin B (21.1%), cefepime (19.5%), piperacillin/tazobactam (18.8%). Both ESBL/AmpC and inhibidor resistant beta-lactamases, piperacillin/tazobactam and ampicillin/sulbactam were the most frequent antibiotics used (50% and 33.3%; 35.7% and 44.4%, respectively) while meropenem and ceftazidime were used in 21.4% (Figure 1).
- The empiric treatment was used over 66.6% of antibiotics in patients with carbapenemases except ertapenem. In ESBL/AmpC, meropenem was used mainly targeted treatment 66.6% while the other antibiotics were used more frequently empiric. In the case of Inhibitor resistant beta-lactamases, the only antibiotic used targeted was Fosfomycin (Figure 2).

Table 1. Distribution of clinical characteristics of patients with multiresistant infection included in the study by type of resistant.

	ESBL/AmpC n=15	Carbapenemases n=137	Inhibitor resistant beta-lactamases n=10	Total n=162
Central venous catheter, <i>n (%)</i>	13 (86.7)	120 (87.6)	9 (90.0)	142 (87.6)
Septic shock, n (%)	10 (66.7)	105 (76.6)	5 (50.0)	120 (74.1)
Use of urinary catheter, <i>n</i> (%)	5 (33.3)	81 (59.1)	2 (20.0)	88 (54.3)
Previous surgery (within 1 month), <i>n (%)</i>	9 (60.0)	55 (40.1)	5 (50.0)	69 (42.6)
Previous hospitalization in the last 90 days, <i>n (%)</i>	6 (40.0)	59 (43.1)	2 (20.0)	67 (41.4)
Heart attack during hospitalization, <i>n (%)</i>	4 (26.7)	40 (29.2)	0 (0.0)	44 (27.6)
Previous intensive care unit hospitalization in the preceding 90 days, <i>n</i> (%)	2 (13.3)	33 (24.1)	2 (20.0)	37 (22.8)
Immunosuppresive by solid organ transplantation, <i>n</i> (%)	4 (26.7)	17 (12.4)	1 (10.0)	22 (13.6)
Immunosuppresive therapy in the last 30 days, <i>n (%)</i>	2 (13.3)	11 (8.0)	0 (0.0)	13 (8.0)
Chemotherapy in the last 6 months, <i>n (%)</i>	2 (13.3)	10 (7.3)	0 (0.0)	12 (7.4)
Neutropenia, n (%)	1 (6.7)	10 (7.3)	1 (10.0)	12 (7.4)
Human immunodeficiency virus, n (%)	0 (0.0)	3 (2.2)	0 (0.0)	3 (0.2)
Immunosuppresive by cell stem transplantation, <i>n</i> (%)	1 (6.6)	0 (0.0)	0 (0.0)	1 (0.1)
Other condition immunodeficiency, <i>n (%)</i>	13 (86.7)	72 (58.6)	10 (100.0)	95 (58.6)
Charlson score Mean (SD)	4.3 (1.9)	3.8 (2.6)	5.1 (1.7)	3.9 (2.5)
Previous antibiotic exposure (within 3 month), n (%)				
Carbapenem	3 (20.0)	21 (15.3)	1 (10.0)	25 (15.4)
Quinolones	0 (0.0)	1 (0.1)	1 (10.0)	2 (1.2)
Polymyxins	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.2)
Cephalosporins	1 (6.7)	3 (2.1)	0 (0.0)	4 (2.4)
Colonization	1 (6.7)	10 (7.3)	0 (0.0)	11 (6.8)

RESULTS (cont)





CONCLUSION

• Carbapenamases resistance and *K. pneumoniae* were the most frequent bacteria reported in studied population and empiric antibiotics regimens were most used to treat the infections.

REFERENCE

- 1. Bader MS, Hawboldt J, Brooks A. Management of Complicated Urinary Tract Infections in the Era of Antimicrobial Resistance. Postgrad Med. 2010 Nov;122(6):7–15.
- 2. Blot S, De Waele JJ, Vogelaers D. Essentials for Selecting Antimicrobial Therapy for Intra-Abdominal Infections. Drugs. 2012 Apr;72(6):e17–32.
- 3. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia. Am J Respir Crit Care Med. 2005 Feb;171(4):388–416.
- 4. Office of Health Economics. The bacterial challenge: time to react. 2011;5. Sharma P, Towse A. New drugs to tackle antimicrobial resistance: analysis of EU policy options. 2010;
- 6. De Biasi S, Coloretti I, Cossarizza A. Multidrug resistant bacteria in critically ill patients: a step further antibiotic therapy. researchgate.net. 2018;
- De Biasi S, Coloretti I, Cossarizza A. Multidrug resistant bacteria in critically ili patients: a step further antibiotic therapy, researchgate.net. 2018;
- Magira EE, Islam S, Niederman MS. Multi-drug resistant organism infections in a medical ICU: Association to clinical features and impact upon outcome. Med Intensiva. 2018 May;42(4):225–34.
 Ovalle MV, Saavedra S, González M, Hidalgo A. Resultados de la vigilancia nacional de la resistencia antimicrobiana de enterobacterias y bacilos Gram
- negativos no fermentadores en infecciones asociadas a la atención de salud, Colombia, 2012-2014. Biomedica. 2017;37:473–85.

 9. Equipo de Referentes Técnicos de la Subdirección de Vigilancia en Salud Pública. Informe Vigilancia en Salud Pública Bogotá año Epidemiológico 2017. 2018.
- 2. Equipo de Neferentes recincos de la subdirección de vigilancia en salda i abilica. Informe vigilancia en salda i abilica bogota ano Epidemiológico 2017. 2010